

THE STATE OF SOUTH CAROLINA
In The Supreme Court

APPEAL FROM SPARTANBURG COUNTY
Court of Common Pleas

Roger L. Couch, Circuit Court Judge

Case No. 2007-CP-42-1438

State of South Carolina ex. rel. Alan Wilson in his
capacity as Attorney General of the State of South
Carolina, ... Respondent,

v.

Ortho-McNeill-Janssen Pharmaceuticals, Inc., f/k/a
Janssen Pharmaceutica, Inc., and/or Janssen, L.P., and
Johnson & Johnson, Inc., ... Defendants.

Of whom Ortho-McNeill-Janssen Pharmaceuticals, Inc.
is Appellant.

RECORD ON APPEAL – VOLUME XVII

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VII. CERTIFICATE OF COUNSEL

STATE OF SOUTH CAROLINA
COUNTY OF SPARTANBURG

IN THE COURT OF COMMON PLEAS
FOR THE SEVENTH JUDICIAL CIRCUIT

STATE OF SOUTH CAROLINA, ex rel.
Alan Wilson, in his capacity as
Attorney General of the State of South
Carolina,

Civil Action No.: 2007-CP-42-1438

PLAINTIFF,

PLAINTIFF THE STATE OF SOUTH
CAROLINA'S MOTION
TO EXCLUDE THE EXPERT
TESTIMONY OF
DR. WILLIAM E. WECKER

v.

ORTHO-McNEIL-JANSSEN
PHARMACEUTICALS, INC. f/k/a
JANSSEN PHARMACEUTICA, INC.
and/or JANSSEN, LP, and JOHNSON
& JOHNSON, INC.

DEFENDANTS.

TO: STEVEN J. PUGH AND KENNETH A. MURPHY, ATTORNEYS FOR DEFENDANTS

Plaintiff the State of South Carolina, *ex rel.* Alan Wilson¹, in his capacity as Attorney General of the State of South Carolina (the "State"), hereby moves this honorable Court to exclude the testimony of the expert witness, Dr. William E. Wecker, proffered by Defendants Ortho-McNeil-Janssen Pharmaceuticals, Inc., f/k/a Janssen Pharmaceutica, Inc. and/or Janssen, LP, and Johnson & Johnson, Inc., (collectively, "Defendants"), and would respectfully show the Court as follows:

I.
SUMMARY OF MOTION

Defendants offer Dr. William Wecker, a statistician and applied mathematician, to provide various and sundry opinions at the trial of this case—everything from whether the "entire population" of South Carolina doctors views Risperdal as safe and effective, to whether clinical

¹ Pursuant to Rule 25(d)(1) of the South Carolina Rules of Civil Procedure, the Honorable Alan Wilson has been substituted for the Honorable Henry McMaster as Attorney General for the State of South Carolina.

studies and peer-reviewed medical literature lend support to a November 2003 "Dear Doctor" letter that Defendants mailed to South Carolina doctors. But, this Court should not admit such expansive and unreliable testimony from Dr. Wecker.

As a preliminary matter, many of Dr. Wecker's opinions (and underlying "data" gleaned from a purported "survey" conducted by Defense attorneys for this litigation) are irrelevant to the State's narrow South Carolina Unfair Trade Practices Act ("SCUTPA") penalties claim and Defendants' defense thereof. Furthermore, even if those opinions are somehow germane, the "survey" conducted through depositions of 20 South Carolina doctors is so flawed—because of bias created by direct Defense attorney involvement, leading questions, a skewed target population, and other failings—that it cannot be deemed reliable and admissible under South Carolina Rule of Evidence 702. For those same reasons, the "survey" testimony is inadmissible hearsay. The "survey" is also not based on the type of data reasonably relied upon by experts in the fields of medicine or statistics, and therefore its admission would violate Rule 703. Additionally, admission of the "survey" testimony would unfairly prejudice the State's case under Rule 403.

Dr. Wecker's "observational data" testimony fares no better. Dr. Wecker failed to account for the underinclusiveness of diagnosis data that is inherent in the State's Medicaid databases. Therefore, that testimony is also unreliable and should not be admitted.

Moreover, Dr. Wecker is not a medical doctor and has no pharmaceutical or clinical training. Thus, the Court should not admit his testimony regarding the results of clinical trials or peer-reviewed medical literature and whether the same supports medical communications that Defendants sent to South Carolina doctors.

Finally, because Defendants have willfully failed to comply with the Court's deadlines relative to expert discovery in disclosing the opinions of Dr. Wecker near the close of what has been a more-than-three-year-long discovery period, the State has been unable to meaningfully participate in expert discovery or to adequately prepare its case for trial. The State has suffered and will

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continue to suffer significant prejudice should Dr. Wecker's opinions be admitted at trial. His opinions and testimony, therefore, must be excluded.²

II. ARGUMENT & AUTHORITIES

A. Standard

"[T]he trial court in the discharge of its gatekeeping role in determining admissibility must initially answer the always present threshold questions of qualification and reliability." *State v. White*, 676 S.E.2d 684, 688-89 (S.C. 2009).

"While [the South Carolina Supreme Court] does not adopt *Daubert*,³ [it] find[s] the proper analysis for determining admissibility of scientific evidence is . . . under the [South Carolina Rules of Evidence]." *State v. Jones*, 681 S.E.2d 580, 587 n.6 (S.C. 2009) (quoting *State v. Council*, 515 S.E.2d 508, 517-18 (S.C. 1999) and citing *State v. Jones*, 259 S.E.2d 120 (1979)). Therefore, "[i]f scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise." *State v. Jones*, 681 S.E.2d 580, 587 (S.C. 2009). "When admitting scientific evidence under Rule 702, SCRE, the trial judge must find the evidence will assist the trier of fact, the expert witness is qualified, and the underlying science is reliable." *Id.* "The trial judge should apply the *Jones* factors to determine reliability." *Id.* "Further, if the evidence is admissible under Rule 702, SCRE, the trial judge should determine if its probative value is outweighed by its prejudicial effect." *Id.* (citing S.C.R. Evid. 403). "Once the evidence is admitted under these standards, the jury may give it such

² Although the State does not contend that the prejudice caused by Defendants' delay and related failure to comply with discovery deadlines could be cured by the deposition of Dr. Wecker on the eve of trial, the State hereby reserves the right to supplement its Motion to further address Dr. Wecker's deposition testimony if he is deposed.

³ *Daubert v. Merrell-Dow Pharms, Inc.*, 509 U.S. 579 (1993).

weight as it deems appropriate.” *State v. Jones*, 681 S.E.2d at 587 n.6 (quoting *State v. Council*, 515 S.E.2d at 517-18).

In considering the admissibility of scientific evidence under the Jones standard, the Court must consider the following factors. “(1) the publications and peer review of the technique; (2) prior application of the method to the type of evidence involved in the case; (3) the quality control procedures used to ensure reliability; and (4) the consistency of the method with recognized scientific laws and procedures.” *State v. Jones*, 681 S.E.2d at 587 n.5 (quoting *Council*).

B. Dr. Wecker’s Opinions Are Irrelevant.

The State’s case is limited to whether Defendants violated SCUTPA by deceptively communicating Risperdal health risk information in Risperdal labeling and other communications about the drug. Defendants propose to have Dr. Wecker testify, however, that “the great majority of [South Carolina] physicians [deposed by Defendants] affirmed . . . statements” such as the following:

- “Risperdal is generally effective for treating the positive symptoms of schizophrenia” (Wecker Rpt. ¶ 22 (attached as Exhibit A));
- “Risperdal is generally effective for treating the negative symptoms of schizophrenia” (*id.* (Ex. A));
- “Risperdal typically has a more moderate side effect profile than first generation antipsychotics” (*id.* (Ex. A)); and
- “[No] Janssen sales representative ever promoted to them any off-label use of Risperdal” (*id.* ¶ 23 (Ex. A)).

Dr. Wecker’s testimony regarding “time to discontinuation” of Risperdal versus other antipsychotics and “Risperdal use over time” also miss the point of the State’s claim. (*Id.* at 12-16 (Ex. A).) Thus, much if not all of Dr. Wecker’s and the underlying medical physicians’ “survey” opinions are irrelevant to the State’s solitary claim and burden of proof that Defendants’ labeling and communications regarding Risperdal were (objectively) deceptive. The expert testimony should be excluded on that basis alone. *See* S.C.R. Evid. 402.

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C. Dr. Wecker's "Survey" Opinions Are Inadmissible Because They Are Unreliable, Constitute Inadmissible Hearsay and Improper Expert Testimony that Has Been Excluded by Another Court in Similar Litigation, and Their Probative Value Is Outweighed by the Danger of Unfair Prejudice.

1. *The Design and Execution of the Sampling and the Reporting of Results in Defendants' So-Called "Survey" of a Handful of Doctors Render Dr. Wecker's Opinion Unreliable and Inadmissible Under Rule 702.*

In the first part of his report, Dr. Wecker indicates that he intends to testify about other experts' (i.e., South Carolina physicians') opinions regarding Risperdal. Those other experts will not be called to testify at trial by Janssen. Instead, Dr. Wecker claims to have analyzed *deposition testimony* from 20 South Carolina physicians' depositions in this litigation, and that he is prepared to "draw conclusions about the entire population of frequent South Carolina prescribers to [Medicaid fee-for-service ("FFS") and state health plan ("SHP")] patients based on the answers provided in the survey." (Wecker Rpt. ¶ 25 (Ex. A).) But, Defendants' so-called "survey" is so fundamentally flawed, it cannot begin to satisfy the requisites of Rule 702.

As a preliminary matter, there can be no dispute that "[t]he evidentiary value of a survey's results rests upon the underlying *objectivity* of the survey itself. This objectivity, in turn, depends upon many factors, such as whether the survey is properly filtered . . . , whether the questions are directed to the real issues, and whether the questions are leading or suggestive." *Scotts Co. v. United Indus. Corp.*, 315 F.3d 264, 280 (4th Cir. 2002) (citation and internal quotation marks omitted, emphasis added). "The question [for the Court] becomes, 'Was the poll or survey conducted in accordance with generally accepted survey principles, and were the results used in a statistically correct way?'" Federal Judicial Center, *Reference Manual on Scientific Evidence* (Second) at 233-34 (2000) (*Reference Guide on Survey Research* chapter attached as Exhibit B). The answer to those questions as to Defendants' "survey" is unequivocally "no."

(a) The "Survey's" Design Did Not Ensure Objectivity.

One intrinsic flaw in the design and execution of the “survey” is that Defendants’ *own attorneys* conducted the questioning. But, according to the Federal Judicial Center’s *Reference Guide on Survey Research*, “survey interviews [should] be ‘conducted independently of the attorneys in the case.’” *Id.* at 237 (Ex. B). “[T]he attorney should have no part in carrying out the survey.” *Id.* (emphasis added) (Ex. B). Instead, “any potential bias is minimized by having interviewers and respondents blind to the purpose and sponsorship of the survey and by excluding attorneys from any part in conducting interviews” *Id.* at 238 (Ex. B).

Here, each of the “survey” depositions was conducted by an attorney for Defendants, who introduced himself or herself to the deponent as such. Each deponent was also made aware of the litigation between the State and Defendants and, to varying degrees, the nature thereof. Thus, the “survey” design and execution grossly disregarded the rule that the survey “should provide no explicit clues . . . about the sponsorship of the survey or the expected responses.” *Id.* at 266 (Ex. B).⁴ Dr. Wecker’s report is devoid of any evaluation or discussion of the “likely biases introduced by the interviewer or respondent’s awareness of the survey’s sponsorship” in this circumstance, and any means by which they were or might be corrected. *Id.* (Ex. B).

⁴ The Federal Judicial Center’s *Reference Manual on Scientific Evidence* describes this example of sponsor-induced bias:

[I]f a survey concerning attitudes toward gun control is sponsored by the National Rifle Association, it is clear that responses opposing gun control are likely to be preferred. In contrast, if the survey on gun control attitudes is sponsored by the Department of Justice, the identity of the sponsor may not suggest the kind of responses the sponsor expects or would find acceptable. When interviewers are well trained, their awareness of sponsorship may be a less serious threat than respondents’ awareness. The empirical evidence for the effects of interviewers’ prior expectations on respondents’ answers generally reveals modest effects when the interviewers are well trained.

Id. at 266. Of course, there is no indication in Dr. Wecker’s report that the “interviewers” here—Defendants’ own attorneys—were “well trained” in survey techniques and questioning so as to avoid potential bias. More importantly, nothing is mentioned in the report about how Defendants attempted to ameliorate any bias that may have occurred as a result of their awareness of the parties to the litigation, the subject matter of the case, and the inherent bias of the interviewer.

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Also, many of the questions posed to the deponents are leading in that they suggest answers that favor Risperdal and Defendants' position in the litigation. For example, the following sequence of questions (even if relevant, which they are not) leads respondents to the desired answer that Risperdal has a more favorable side-effect profile than certain first generation antipsychotics:

- "In your experience, are patients who take first generation antipsychotics, such as Haldol and Thorazine, more likely to experience extrapyramidal and anticholinergic side effects than patients who take second [generation antipsychotics]?"
- "In your experience, are patients who take first generation antipsychotics, such as Haldol and Thorazine, more likely to experience Tardive Dyskinesia than patients who take second generation antipsychotics?"
- "In your experience, does Risperdal® typically have a more moderate side effect profile than first generation antipsychotics?"

(Wecker Rpt. Exhibit 4 at 2 (Ex. A hereto).) Thus, by first reminding the deponents of supposed negative side effects of first generation antipsychotics in the first two questions above, then asking a favorably worded question about Risperdal—which Defendants have widely marketed for nearly two decades as having a more tolerable side-effect profile than first generation antipsychotics—the "interviewer" effectively leads the deponent to the desired result. *See Reference Manual* at 252 ("[T]he wording of a question . . . can be leading, and the degree of suggestiveness of each question must be considered in evaluating the objectivity of the survey.") (Ex. B); *id.* at 254 ("The order in which questions are asked on a survey and the order in which response alternatives are provided in a closed-ended question can influence the answers.") (Ex. B); *see also R.J. Reynolds Tobacco Co. v. Loews's Theatres, Inc.*, 511 F. Supp. 867, 875 (S.D.N.Y. 1980) (recognizing the biased structure of a survey that disclosed the tar content of the cigarettes being compared before questioning respondents about their cigarette preferences; not surprisingly, respondents expressed a preference for the lower tar product); *accord, Scotts Co.*, 315 F.3d at 280 (admonishing courts to evaluate the objectivity of surveys by evaluating "whether the questions are leading or suggestive"). Other questions employed by the "interviewers" are simply leading in and of themselves. (Wecker Rpt. Exhibit 4 at 3

("Overall, in your experience, is Risperdal® a reasonably safe and effective medication for treating schizophrenia and other psychotic disorders?"; "Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® at all?") (Ex. A hereto).) On the whole, because of flaws in the design of the "survey" questions, as well as Defendants' attorneys' direct involvement in the execution of the "survey," the results should not be deemed objective or trustworthy and should not be admitted.

(b) The "Survey's" Target Population Was Improperly Defined and Yielded a Skewed, Unreliable Result.

A "target population" or "universe" for a survey "consists of *all* elements ([e.g., . . . individuals . . .]) whose characteristics or perceptions the survey is intended to represent."⁵ *Reference Manual* at 239 (Ex. B). "The universe must be defined carefully" so as to not exclude relevant subgroups or overemphasize other subgroups' responses. *Id.* (Ex. B).

Here, instead of the target population selected by Dr. Wecker being the universe of all South Carolina physicians and prescribers, or even all those who have previously prescribed antipsychotics, Dr. Wecker's target population focuses on those prescribers who have demonstrated the greatest propensity to prescribe Risperdal and other antipsychotics. Obviously, that approach entirely and necessarily excludes those doctors who may have prescribed Risperdal or antipsychotics in the past but who—for example—no longer prescribe such medicines because of negative experiences regarding the safety or efficacy of such drugs.

Instead, a better approach—since the "survey" suggests that it represents the "entire population" of South Carolina prescribers to FFS and SHP patients—would be, in fact, to randomly draw from all FFS and SHP prescribers of antipsychotic drugs, without regard to prescription

⁵ Thus, the *Reference Manual on Scientific Evidence* explains, "[i]n a community survey designed to provide evidence for a motion for a change of venue, the relevant population consists of all jury-eligible citizens in the community in which the trial is to take place." *Id.* at 240 (Ex. B). Similarly, "[i]f a survey assessing [a commercial aimed at children for a toy or breakfast cereal's] tendency to mislead were conducted based on the universe of prospective and actual adult purchasers, it would exclude a crucial group of eligible respondents." *Id.* (Ex. B). "Thus, the appropriate population in this instance would include children and parents as well." *Id.* (Ex. B).

"frequency." *That sample would capture the portion of the population that is excluded under Dr. Wecker's model—i.e., those prescribers who less frequently write prescriptions for Risperdal and other antipsychotics, perhaps because of safety concerns. See Reference Manual at 241 ("If [the target population] is underinclusive, the survey's value depends on the extent to which the excluded population is likely to react differently from the included population.") (Ex. B).*⁶ Further, no explanation is offered for the arbitrary cutoff of 101 prescribers as the target population, as opposed to 102 prescribers, or 120, or 200, or 500. Indeed, while prescriber number 101 was included in the "survey's" "universe," Dr. Wecker fails to explain or justify the total exclusion from the possibility of selection of prescriber number 102—who, for sake of argument, may have written one less antipsychotic prescription than prescriber number 101, yet whose opinions the "survey" entirely failed to consider. Nevertheless, Dr. Wecker incorrectly states in his report that his "random selection procedure *guarantees* a statistically representative sample because it rules out *any purposive or inadvertent selection bias that could skew the composition of the sample towards any favored subgroup of doctors.*" (Wecker Rpt. ¶ 17 (Ex. A) (emphasis added).) The inherent law is that the target population was skewed in the first instance before the sample was drawn.

(c) Dr. Wecker Fails to Demonstrate the Limited Sample Size Is Reliable

⁶ The *Reference Manual* provides these examples to illustrate the misperceptions that underinclusiveness fosters:

Thus, a survey of spectators and participants at running events would be sampling a sophisticated subset of those likely to purchase running shoes. Because this subset probably would consist of the consumers most knowledgeable about the trade dress used by companies that sell running shoes, a survey based on this population would be likely to substantially overrepresent the strength of a particular design as a trademark, and the extent of that overrepresentation would be unknown and no susceptible to any reasonable estimation.

Similarly, in a survey designed to project demand for cellular phones, the assumption that businesses would be the primary users of cellular service led surveyors to exclude potential nonbusiness users from the survey. The Federal Communications Commission (FCC) found the assumption unwarranted and concluded that the research was flawed, in part because of this underinclusive universe.

Id. at 241 (Ex. B).

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Indeed, Defendants Have Judicially Admitted that a Minimally Statistically Significant Sample Size Comprises 150 Deponents.

Nothing in Dr. Wecker's report indicates that the "survey" results were drawn from a sufficiently large, reliable sample of South Carolina prescribers. According to the U.S. Department of Health and Human Services, more than 6,900 active patient care physicians practiced in South Carolina as of 2000, together with over 1,200 nurse practitioners.⁷ Dr. Wecker offers no justification for sampling only 20 of the 8,100 arguably eligible prescriber respondents in the State (less than one percent). Instead, he merely offers that he limited the sample to 20 prescribers "[b]ecause the Court limited Janssen to surveying 20 doctors through deposition" (Wecker Rpt. ¶16 (Ex. A).) Even assuming the other flaws inherent in the "survey's" design and execution (discussed above) may be disregarded or corrected, a reliably accurate survey of the 8,100 prescribers in South Carolina would require a sample size of 559 respondents (with a 95% confidence level and +/- 4% margin of error). A sample size of only 20 doctors out of a population of 8,100 at 95% confidence level provides only a +/- 21.89% margin of error, thus yielding a wide range of potentially inaccurate and likely unreliable results—i.e., the actual results may vary by 21.89 percentage points in either direction.

In fact, the wide margin of error in the sample is exemplified in Dr. Wecker's own data: For the question, "Overall, in your experience, is Risperdal® a safer and more effective medication for treating schizophrenia and other psychotic disorders than the first generation medications," only 55% of respondents answered "yes" or "probably yes," but the confidence interval for that question shows that as few as 33.7% of the population may answer "yes" or "probably yes," or as many as 74.3% may give those answers—a range of 40.6 percentage points. With a range so broad, the

⁷ U.S. Dep't of Health & Human Servs., State Health Workforce Profiles, Highlights, South Carolina, available at <http://bhpr.brsa.gov/healthworkforce/reports/statesummaries/southcarolina.htm> (attached as Exhibit C).

⁸ See Creative Research Systems, The Survey System – Sample Size Calculator, available at <http://www.surveysystem.com/sscalc.htm>.

"survey" is not capable of reliably predicting answers for the "entire population" of South Carolina FFS and SHP prescribers, as it purports to do.

Importantly, the Court should also recall that Defendants previously offered testimony of Dr. Wecker from similar litigation against Defendants in Louisiana state court—the trial of which resulted in a jury award against Defendants in excess of \$250 million—in an effort to convince this Court that a minimum of 150 South Carolina physicians' depositions needed to be taken to achieve a statistically valid sample. (Defs.' Mem. for Leave to Depose a Statistically Significant Sample of Prescribing Physicians and Institutions at 3 (attached as Exhibit D).) Of particular note, Dr. Wecker testified in Louisiana attempting to convince that court to also permit 150 doctors' depositions in that case:

I did not feel comfortable. If I would have thought a hundred [doctors' depositions] would do it, I would have picked a hundred. A hundred and fifty in my judgment is going to be what's needed here in order to come up with statistically reliable results.

(*Id.* Exhibit B at 29 (Ex. D hereto).)⁹ Before this Court on May 4, 2009, Defense Counsel Mr. Kenneth Murphy also declared in open court that anything less than a sample size of 150 doctors would be statistically insignificant:

Mr. Trammell responded, or his office responded, in a -- in about ten (10) days with a counter proposal. And where I proposed one hundred and fifty (150) [South Carolina doctors' depositions], [Plaintiff] proposed ten (10). *That, however, just isn't going to work.* In -- in the State of South Carolina, there are not less than seventy-eight hundred (7,800) prescribers of atypicals in the fee-for-service Medicaid program, another twenty-five hundred (2,500) in the -- the State Health Plan. And, so, that is even greater -- that's even a greater pool than what we've seen in Louisiana. But, still our experts says, "I won't need any more than one hundred, fifty (150)."

⁹ As discussed *infra* at 15-16, the Louisiana trial court ultimately *excluded* Dr. Wecker's testimony regarding the opinions gleaned from the 150 doctors' depositions taken in that case.

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(Hr'g Tr. (5/4/2009) at 41 (emphasis added) (attached as Exhibit E).) Defendants simply should not now be permitted to argue that a mere 20 doctors' depositions would produce reliable "survey" results—indeed, Defendants have admitted before this Court that such a number is inadequate.

(d) The Survey Results Were Not Validated In Any Way.

Defendants and Dr. Wecker have offered no evidence ensuring the Court that the "survey" was implemented in an unbiased fashion and according to instructions. Dr. Wecker neither indicates that he attended all the "survey" depositions personally to monitor the "interviews," nor that he reviewed all the deposition transcripts for such purpose. See *Reference Manual* at 267. Thus, there is no indication that the "survey" results were validated through comparison of the work of each individual "interviewer" to identify any response patterns or inconsistencies for further investigation. As the Federal Judicial Center's *Reference Manual* warns:

When a survey is conducted at the request of a party for litigation rather than in the normal course of business, a heightened standard for validation checks may be appropriate. Thus, independent validation of at least 50% of interviews by a third party rather than by the [original interviewers] increases the trustworthiness of the survey results.

Id.; see *Rust Environment & Infrastructure, Inc. v. Teunissen*, 131 F.3d 1210, 1218 (9th Cir. 1997) (criticizing survey in part because it "did not comport with accepted practice for independent validation of the results"). Here, it is without question that none of the validation procedures described above were followed. The "survey" is untrustworthy.

In sum, the survey results are plainly unreliable for all the reasons stated above. Therefore, Defendants cannot satisfy *at least* the third and fourth *Jones* factors for admission of scientific evidence: "(3) the quality control procedures used to ensure reliability; and (4) the consistency of the method with recognized scientific laws and procedures." *Jones*, 681 S.E.2d at 587 n.5. Dr. Wecker's "survey" results and related testimony must be excluded.

2. The "Survey" Results Are Inadmissible Hearsay Under Rule 802.

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Furthermore, the survey results constitute out-of-Court statements offered to prove the truth of the matter asserted—for example, whether South Carolina doctors individually or as a representative sample have the opinion that Risperdal is safer or more effective than first generation antipsychotics—and are, therefore, inadmissible hearsay.¹⁰ Survey evidence is admissible as an exception to the hearsay rule only if the survey is “material, more probative on the issue than other evidence and if it has guarantees of trustworthiness.” *Harold's Stores, Inc. v. Dillard Dept. Stores, Inc.*, 82 F.3d 1533, 1544 (10th Cir. 1996) (citing *Brunswick Corp. v. Spinit Reel Co.*, 832 F.2d 513, 522 (10th Cir. 1987)); accord 5 Jack B. Weinstein & Margaret A. Berger, *Weinstein's Evidence* P 901(b)(9)[03] at 901-140 (1995) (“The admissibility of survey or sampling results depends upon two factors: necessity and trustworthiness.”). “A survey is trustworthy if it is shown to have been conducted according to generally accepted survey principles.” *Brunswick Corp.*, 832 F.2d at 522. “The survey should sample an adequate or proper universe of respondents.” *Harold's Stores*, 82 F.3d at 1544 (citing *Exxon Corp. v. Texas Motor Exchange of Houston, Inc.*, 628 F.2d 500, 507 (5th Cir. 1980)). “That is, the persons interviewed must adequately represent the opinions which are relevant to the litigation.” *Amstar Corp. v. Domino's Pizza, Inc.*, 615 F.2d 252, 264 (5th Cir. 1980). The court should exclude the survey “when the sample is clearly not representative of the universe it is intended to reflect.” *Harold Stores*, 82 F.3d at 1544 (citing *Bank of Utah v. Commercial Sec. Bank*, 369 F.2d 19, 27 (10th Cir. 1966)).

For all the reasons already stated above, Defendants’ “survey” is not a reliable, representative, unbiased sample of the “entire population” of South Carolina FFS and SHP prescribers. Thus, “survey” results, underlying data, and related testimony do not fall under any exception to the hearsay rule and must be excluded.

¹⁰ Again, the State does not concede that any such opinion by South Carolina doctors—even if held, which the survey fails to reliably demonstrate, as shown above—is relevant to the case.

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3. ***Dr. Wecker's Opinion Is Inadmissible Under Rule 703 Because the Facts or Data Underlying It Are Not of the Type Reasonably Relied Upon by Experts in the Particular Field.***

South Carolina Rule of Evidence 703 provides that

The facts or data in the particular case upon which an expert bases an opinion or inference may be those perceived by or made known to the expert at or before the hearing. If of a type reasonably relied upon by experts in the particular field in forming opinions or inferences upon the subject, the facts or data need not be admissible in evidence.

S.C.R. Evid. 703. The State has already demonstrated that the "survey" results, underlying data, and related testimony constitute inadmissible hearsay.

Moreover, "[a]n expert may base his opinion on hearsay evidence *so long as* it is of a type reasonably relied upon by other experts in the field." *State v. Hutto*, 481 S.E.2d 432, 433 (S.C. 1997) (emphasis added). But, the data here is not of a type reasonably relied upon by experts in the particular field—i.e., medical opinions. Here, a *statistician—not a medical doctor*—purports to testify as to the out-of-Court *medical opinions* of 20 licensed South Carolina physicians. There has been no showing whatsoever that Dr. Wecker is qualified to interpret the respondent doctors' medical opinions, or has received any training at all in medicine. *See id.* ("[The] type of information on which experts may rely is that on which they would customarily rely in the day to day decisions of their profession." (citing 31A *Am. Jur. 2d Expert & Opinion Evid.* § 85 (1989))). On an even more fundamental level, neither Defendants nor Dr. Wecker offer any evidence that experts in his field of statistics regularly and reasonably rely upon respondents' collective answers to *deposition questions* posed by a party's attorney in litigation in forming statistical predictions about larger populations of non-respondents, and the State was unable to locate *any South Carolina case* in which a court sanctioned such a methodology.

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Indeed, in the Louisiana litigation, that judge excluded Dr. Wecker from testifying as to "survey" results that mirrored those offered in this Court.¹¹ The exclusion came even *after* the Louisiana court had permitted Defendants to take 150 Louisiana physicians' depositions for the ultimate purpose of offering Dr. Wecker's "survey" testimony. The rationale for the Louisiana judge's decision follows:

[P]rimarily based upon the fact that I find [Dr. Wecker] is not going to be giving us an opinion of the type reasonably relied upon by experts in the particular field in forming opinions entering upon the subject, the facts or data with regard to this case – not his opinion, he is merely acting as a conduit to tell me what others' opinions are. As a result, I'm going to deny his testimony.

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¹¹ Trial Tr., *Caldwell ex rel. the State of Louisiana v. Janssen Pharmaceutica, Inc.*, Nos. 04-C-3967-D, 04-C-3977-D, Trial Day 9 at 33-36 (La. 27th D. Ct. Oct. 12, 2010) (hereinafter, "La. Tr.") attached as Exhibit F).

La. Tr. at 35-36 (Ex. F).¹² Like the Louisiana court, this Court should find that Dr. Wecker's "survey" opinions are not based on facts and data reasonably relied upon by experts in the relevant field, and exclude his testimony on that basis. Compare *Hutto*, 481 S.E.2d at 436 (permitting witness to testify as to other, non-testifying witness's footprint evidence report where the report was not based on any "subjective analysis" but was merely "mechanical"), with *State v. Slocumb*, 521 S.E.2d 507, 516 (S.C. Ct. App. 1999) ("[T]o admit the hearsay opinion of an expert not subject to cross-

¹² Dr. Wecker's expert testimony has reportedly been excluded by numerous other courts across the country, including the following cases cited by the *Buell-Wilson v. Ford Motor Co.* plaintiffs, 141 Cal App. 4th 525 (2006), in their motion to exclude Dr. Wecker:

Significantly, numerous courts across the United States have excluded from trial Dr. Wecker's opinions:

- In January 2002, the San Diego Superior Court excluded from trial Dr. Wecker's opinions in the case *Lajeunesse, et al v. Ford Motor Co., et al*;
- The United States District Court for the Middle District of Georgia, in the case *Howard, et al. v. Ford Motor Co.*, excluded Dr. Wecker's opinions for several reasons, including "the danger of confusion of the issues and misleading the jury....";
- The Bulloch County, Georgia Superior Court, in the case *Stewart, et a. v. Ford Motor Company, et al.* excluded from trial Dr. Wecker's opinions because the collisions underlying his statistical data were not substantially similar;
- In the case *Harsh, at al. v. General Motors Corporation, et a.*, the Pennsylvania Court of Common Pleas precluded Dr. Wecker from testifying at trial;

The Honorable Judge Ronald Gardner, of the Orange County Superior Court provided perhaps the most powerful statement of reasons for excluding Dr. Wecker's opinions at trial. In the case *Wagner, et al. v. General Motors Corp. et al.* (No. 60 06 02), the Honorable Judge Gardner ruled emphatically on plaintiffs counsel's motion to strike Dr. Wecker's testimony:

It is pure garbage plus. Motion granted. I will tell the jury to ignore all of this with pleasure. I consider the last 45 minutes of testimony the biggest waste of time I have listened to in almost 60 years as a trial judge and trial attorney. I refuse to impose this kind of - and I use advisedly - garbage on intelligent jurors. I will advise the jury to ignore everything they have heard.

Reporters Daily Transcript; 1652:14 - 16 and 1653:22 - 1654:1.

Pls.' Mot. in Limine to Exclude Trial Ops. of William Wecker, Ph.D. § III.5, *Buell-Wilson*, 141 Cal. App. 4th 525 (2006) (Nos. D045154, D045579), 2003 WL 25322208 at *8 (attached as Exhibit G). The numerous courts that have excluded Dr. Wecker's opinions have recognized the unfair prejudice and confusion of the issues that his misleading statistics would cause plaintiffs to suffer. This Court too should recognize the unfair prejudice and confusion likely precipitated by his opinions and exclude them from trial. See discussion, § II.C.4, *infra* at 17.

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examination goes against the natural reticence of courts to permit expert opinion unless the expert has been qualified before the jury to render the opinion.”), and *Faulkner v. Markkay of Ind., Inc.*, 663 N.E.2d 798, 800-01 (Ind. Ct. App. 1996) (affirming lower court’s refusal to allow the introduction of non-testifying surgeons through the testimony of a testifying chiropractic doctor because the testifying chiropractor did not have the training or education in medicine to base an opinion on this hearsay, and the chiropractor’s testimony would have been merely a recitation of the opinion of others).

4. Admission of Dr. Wecker’s “Survey” Testimony Violates Rule 403.

The “survey” testimony must additionally be excluded because its “probative value is substantially outweighed by the danger of unfair prejudice, confusion of the issues, or misleading the jury, or by considerations of undue delay, waste of time, or needless presentation of cumulative evidence.” S.C.R. Evid. 403. As shown above, the irrelevant opinions of the 20 deposed doctors have no bearing on the State’s case or Defendants’ defense. Such opinions will undoubtedly confuse and mislead the jury regarding the relatively simple issue before it—i.e., whether Defendants’ Risperdal labeling and other communications regarding Risperdal were objectively deceptive under SCUTPA. Anecdotal experiences of a handful of doctors have no probative value as to that narrowly framed jury issue. Finally, admission of the testimony will lead to the needless and wasteful accumulation of such irrelevant evidence, prejudicing the State’s case and wasting the Court’s and jury’s time.

D. Dr. Wecker’s “Observational Data” Analysis is Also Unreliable and Inadmissible Under Rule 702.

Next, Defendants propose to have Dr. Wecker testify as to so-called “observational data” regarding the incidence rates of “side effects” of Risperdal versus other antipsychotic medications. In his report, Dr. Wecker provides no analysis of how he analyzed or manipulated the State’s claims data to obtain his results. In particular, Dr. Wecker does not describe any limitations as to the data

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itself that would affect the results outcome, nor does he describe any measures he took to deal with such limitations. Dr. Wecker merely states that he culled the database evidence for diagnoses of diabetes, metabolic adverse events (such as diabetes mellitus, secondary diabetes mellitus, abnormal glucose, abnormal weight gain, obesity, and other hyperalimentation), and increased prolactin secretion. (Wecker Rpt. ¶ 30 & n.11 (Ex. A).)

But, the South Carolina claims databases produced by the State have inherent limitations that—at a minimum—must have resulted in the underinclusiveness of the data Dr. Wecker considered. For example, patients treated in a Department of Mental Health facility on an outpatient basis who filled a prescription for Risperdal at a pharmacy outside the DMH facility would have no Medicaid record of the DMH-facility's *treatment* of the patient, but instead the Medicaid records would contain only a pharmacy record of any prescription drugs that were prescribed at the DMH outpatient facility. The medical data record for the patient's treatment (e.g., any diagnoses) would be contained in a separate DMH (non-Medicaid) database, and there is no data "cross-walk" to link DMH database with Medicaid data.¹³ Further, diagnosis codes are not required to be entered into prescription records in the Medicaid database.¹⁴ Therefore, there would be no requirement that the diagnosis of "diabetes" or "obesity" or "prolactin secretion elevation" be entered into the pharmacy database. That record, if it existed at all, would be included in the DMH database treatment records.

To illustrate, suppose a patient is treated on an ongoing outpatient basis for bipolar disorder at a DMH facility. The medical database records for that patient are not included in the Medicaid database, but in the DMH database. If the patient were prescribed Risperdal by a DMH doctor, that prescription may be filled at a commercial pharmacy, which is not required to enter any diagnosis

¹³ See Aug. 31, 2009 Hearing Questions from Judge Couch, filed in *South Carolina v. Eli Lilly & Co., Inc.*, Civil Action No. 2007-CP-42-1855, at 1 (attached as Exhibit H).

¹⁴ Mary Roberts Dep. Tr. at 17:11-18:21 (attached as Exhibit I). Mary Roberts, an employee of First Health Services Corporation, which administers the pharmacy benefits for South Carolina Medicaid, testified as the "clinical manager for the South Carolina Medicaid contract." *Id.* at 7-9 (Ex. I).

code for the prescription drug record. Meanwhile, unless the patient is separately treated and covered by Medicaid (at a non-DMH facility), there would be no medical record for the patient in the Medicaid database—only pharmacy records. But that patient may be diagnosed at the DMH facility with, for example, “obesity” or “abnormal glucose.” The record of such a diagnosis would not appear in the Medicaid database, however, for the reasons stated, and there is no means to cross-reference the DMH and Medicaid database patient records to fill that informational gap. Thus, a patient who took Risperdal and had a diagnosis of “obesity” or “abnormal glucose,” for example, would be excluded from Dr. Wecker’s analysis under those facts.

Further, in the parallel litigation in Louisiana, mentioned *supra*, Dr. Wecker admitted that if Medicaid patient “diagnoses are not routinely and reliably recorded, then the absence of diagnosis [in the Medicaid records] is not proof.”¹⁵ But, here there is no proof offered that diagnoses codes were routinely and reliably recorded in the South Carolina Medicaid claims database. In fact, the evidence is to the contrary.¹⁶

Dr. Wecker himself acknowledges other limitations that are seemingly arbitrary in his report and the fine print of the attached exhibits. For example, he notes in Exhibit 6 that he “excludes patients” from his results “if they are prescribed more than one type of antipsychotic drug” (hereto.) But, such a limitation may exclude a patient who took another antipsychotic for only a short period of time, and then took Risperdal for a significantly longer time period and subsequently developed diabetes. Dr. Wecker imposes unexplained cutoffs of 12 months of pre-antipsychotic use “eligibility” to determine whether patients already suffered from a given side effect, and 36 months to determine whether patients experienced a side effect after treatment with an antipsychotic drug. But he offers no explanation or justification for failing to include patients, for example, who experienced the side effect at 37 months or later. Again, such arbitrary limitations necessarily cause

¹⁵ La. Tr. at 96 (Ex. F).

¹⁶ See n.13 and accompanying discussion, *supra* at 18-19.

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the data surveyed by Dr. Wecker to be underinclusive. Dr. Wecker's "observational data" opinion, therefore, is also unreliable and must be excluded. That evidence, if presented, would also unfairly prejudice the State's case. *See* S.C.R. Evid. 403.

E. Dr. Wecker Is Not Qualified to Testify Regarding His Analysis of Peer-Reviewed Medical Literature and Pharmaceutical Studies.

Finally, Defendants seek to have Dr. Wecker—though not a medical doctor—give his opinion as to whether certain peer-reviewed medical literature and drug studies supported Janssen's November 10, 2003 "Dear Doctor" letter, which the State contends misrepresented Risperdal's safety profile to South Carolina prescribers. Dr. Wecker is simply not qualified to offer such opinions. He has no medical training. He has demonstrated no expertise in reviewing and analyzing peer-reviewed medical literature or pharmaceutical clinical trials. He is not a pharmacologist or toxicologist. He is simply a statistician that Defendants hope to use as a conduit through which to present the cited studies and literature to the jury. Absent a demonstration of Dr. Wecker's qualifications in that regard, he may not testify. *See Jones*, 681 S.E.2d at 587 n.6 (quoting *Council*, 515 S.E.2d at 517-18 and citing *State v. Jones*, 259 S.E.2d 120 (1979)).

F. Dr. Wecker's Opinions Should be Excluded Because They Were Not Timely Disclosed in Advance of Trial and Are, Therefore, Prejudicial.

Despite the Court's long-standing Scheduling Order requiring parties to serve all expert reports by May 14, 2010 and otherwise complete expert-based discovery by December 31, 2010, Defendant disclosed putative expert Dr. Wecker's opinions on December 17, 2010, near the close of what has been a more than three-year long discovery period, *more than seven months after the Court's related deadline*, and, also, more than seven months after producing reports generated by eleven timely designated expert witnesses, without seeking relief from the operative Order or explanation otherwise. As a result, the State has been unable to meaningfully participate in expert discovery and, likewise, prevented from deposing Dr. Wecker. In addition, the State has been unable to adequately prepare its case for trial, as Defendant has withheld certain discoverable liability

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information relative to its expert witness in failing to make requisite disclosures timely. The State has suffered and will continue to suffer significant prejudice should Dr. Wecker's opinions be admitted at the trial. Accordingly, Rule 403 and applicable case law mandate their exclusion. See S.C. R. Evid. 403; *see also Samples v. Mitchell*, 495 S.E.2d 213, 216 (S.C. Ct. App. 1997) (reversing and remanding where defendant failed to timely disclose evidence that was "clearly relevant" to plaintiff's claim during the discovery period, and trial judge admitted such evidence without first weighing the requisite factors for determining what sanction to impose "for failure to disclose evidence during the discovery process"); *Adalman v. Baker*, 807 F.2d 359, 369 (4th Cir. 1986) ("[a]ppellate courts have routinely upheld, as within the discretion of the trial court, the exclusion of witnesses and evidentiary exhibits based on a party's failure to comply with discovery deadlines.").

III. CONCLUSION

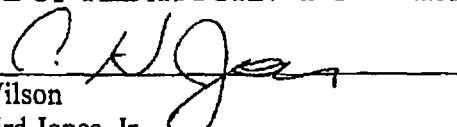
Despite Defendants' desire to utilize Dr. Wecker as a mouthpiece through which to convey the out-of-Court expert opinions of 20 non-testifying South Carolina doctors—putative expert witnesses in their own right—Dr. Wecker may not do so. First, the opinions Dr. Wecker intends to offer are simply inapposite—they are neither relevant to the State's narrow claim or Defendants' defenses. Even if relevant—which the "survey" results are not—the "survey" method contrived by Dr. Wecker and Defendants is irreparably flawed and cannot be presented to a jury as objective, reliable, and trustworthy expert evidence. Because that evidence is not objective, reliable, or trustworthy, it is also inadmissible hearsay that does not satisfy any exception to the hearsay rule. Furthermore, the evidence is not the type reasonably relied upon by experts in either the fields of statistics or medicine. And, admission of the evidence would unfairly prejudice the State's case. Dr. Wecker's "observational data" testimony is also flawed because it does not account for the underinclusiveness of the underlying Medicaid data, and its admission would be prejudicial. Finally,

Dr. Wecker is simply unqualified to opine about whether or not certain clinical studies and peer-reviewed medical literature supported a November 2003 letter that Defendants mailed to South Carolina doctors; there is no indication that he has any medical or other training that would permit him to so testify. Dr. Wecker's opinions, therefore, should not be admitted at trial.

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Respectfully submitted,

**STATE OF SOUTH CAROLINA
OFFICE OF THE ATTORNEY GENERAL**

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Alan Wilson

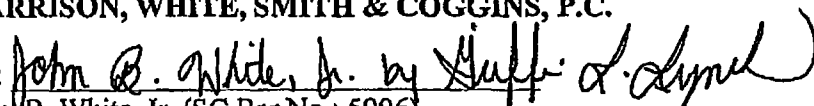
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EXHIBIT A

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STATE OF SOUTH CAROLINA
COUNTY OF SPARTANBURG

STATE OF SOUTH CAROLINA,
ex rel. HENRY McMASTER, in his
capacity as Attorney General of the State
of South Carolina,

PLAINTIFF,

VERSUS

JANSSEN PHARMACEUTICA, INC., et al.

DEFENDANTS.

IN THE COURT OF COMMON PLEAS
FOR THE SEVENTH JUDICIAL CIRCUIT

Case No.: 2007-CP-42-1438

EXPERT REPORT OF WILLIAM E. WECKER, PH.D.

DECEMBER 3, 2010

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Exhibit 5:	Population Estimates from Responses to Deposition Questions
Exhibit 6:	Antipsychotic Drugs and Alleged Side Effects
Exhibit 7:	Antipsychotic Drugs and Alleged Side Effects (Data as of Nov. 10, 2003)
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1. My name is William E. Wecker. I am a statistician and applied mathematician. I received the Bachelor of Science degree (Basic Sciences) from the United States Air Force Academy in 1963. I received both the Master of Science degree (Operations Research, 1970) and Doctor of Philosophy degree (Statistics and Management Science, 1972) from the University of Michigan. I have served on the faculties of the University of Chicago, the University of California, Davis, and Stanford University where I taught statistics and applied mathematics at the graduate level. I have performed research in statistical theory, statistical methods, and applied mathematics since 1972. I am currently President of William E. Wecker Associates, Inc., an applied mathematics consulting firm located in Novato, California. I am a member of the American Statistical Association, the Institute of Mathematical Statistics, and the Society for Risk Analysis. I have served as associate editor of the *Journal of the American Statistical Association* for four years and of the *Journal of Business and Economic Statistics* for eighteen years. These qualifications and a list of my professional publications are shown in my curriculum vitae, which is appended to this report as Exhibit 1.

2. A list of all cases in which I have testified as an expert at trial or by deposition since January 1, 2006, is appended to this report as Exhibit 2. The billing rate for my time working on this matter is \$650 per hour.

3. My report consists of three primary sections that follow this introduction. First, in Section I, I identify and cite some of the primary allegations made by plaintiff of purportedly unlawful conduct by Janssen. Also in Section I, I identify the central questions that plaintiff's allegations raise for my expert analysis in this case and the data sources that are available for statistical analysis and evaluation of plaintiff's allegations. The available data include statistical surveys of South Carolina doctors, patient claims data produced by the

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plaintiff, and peer-reviewed epidemiological and experimental studies. The results of my statistical survey of South Carolina doctors and analysis of patient claims data are presented in Section II. In Section III, I review and analyze the eight peer-reviewed epidemiological studies existing as of November 2003 that compared the risk of diabetes in patients treated with Risperdal to the risk in untreated schizophrenia patients, patients treated with conventional antipsychotics, or patients treated with other second generation antipsychotics. Also in Section III, I discuss the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study.

4. In forming my opinions, I have considered the documents listed on Exhibit 3 and the data and electronic files provided to the plaintiff in conjunction with this report. It is my understanding that plaintiff has thus far provided reports from only two of the three experts it intends to present at trial in this case: Dr. Laura Plunkett and Dr. William Wirshing. I reserve the right to conduct further analysis of plaintiff's allegations and the work of plaintiff's experts, and further reserve the right to review and offer opinions on additional material as it becomes available.

5. I am providing electronic files that document my work and are a part of this report.

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**I. Plaintiff's Allegations and Available Data Sources
for Analysis of Plaintiff's Allegations**

6. In plaintiff's Second Amended Complaint ("2d Am. Compl."), plaintiff alleges that Janssen made misrepresentations about Risperdal's safety and effectiveness and marketed Risperdal for off-label uses. In particular, plaintiff alleges:

a. Defendants made "false and misleading misrepresentations of fact regarding Risperdal's risk profile, including but not limited to misrepresenting the likelihood and severity of the side effects associated with Risperdal, including diabetes, stroke, high blood pressure, weight gain, and other serious and potentially life-threatening conditions." (2d Am. Compl. ¶ 57(a).)

b. Defendants "misrepresent[ed] that Risperdal is safer and more effective than less expensive first generation 'typical' antipsychotics." (2d Am. Compl. ¶ 57(c).)

c. Defendants "heavily marketed Risperdal for multiple non-approved purposes." (2d Am. Compl. ¶ 23.)

d. A November 10, 2003 mailing from defendant Janssen to health care providers misled doctors concerning the risk of diabetes with Risperdal. (2d Am. Compl. ¶ 46.)

e. "[T]he CATIE study proved what Defendants knew since launching Risperdal: (1) that Risperdal is no more effective in treating schizophrenia; (2) that Risperdal is no safer; and (3) that Risperdal has intolerable side effects making it no more desirable than the less expensive atypical antipsychotics." (2d Am. Compl. ¶ 52.)

7. Plaintiff's allegations raise several questions for my analysis. At a broad level, the question for analysis is whether the allegations of wrongful conduct by Janssen are valid. On a more specific level, plaintiff's allegations raise the questions of how Risperdal's safety and efficacy compare to first generation antipsychotics and other second generation antipsychotics, how Janssen marketed Risperdal to doctors in South Carolina, and how South Carolina patients responded when treated with Risperdal, as compared to alternative medications. Plaintiff's allegations concerning Janssen's November 10, 2003 mailing to health

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care providers raise the question of whether data and literature—in the form of South Carolina patient claims data and the eight peer-reviewed epidemiological studies cited by Janssen—support the statements Janssen made in the cover letter that accompanied the revised Risperdal package insert that Janssen sent to South Carolina doctors. Finally, plaintiff's allegations regarding the CATIE study raise the question of whether the conclusions reached by the study or those that plaintiff attempts to draw from it are valid.

8. I have identified three primary, available data sources that provide information related to the fundamental questions raised by plaintiff's allegations:

a. Documented South Carolina physician experience, such as may be found from South Carolina doctors who treat patients with Risperdal, including the doctors' experience with Risperdal's efficacy, experience with the potential side effects of antipsychotic medications, the circumstances in which off-label use is regarded by the physician as appropriate, and Janssen promotional practices.

b. Observational data, such as the claims data produced by plaintiff from the State Fee-for-Service ("FFS") and State Health Plan ("SHP") benefits programs.

c. Published experimental and epidemiological studies.

9. My analysis of physician experience and observational data is explained in Section II, below. I address published experimental and epidemiological studies in Section II. The explanations provided here are supplemented by the presentation of results in the tables and charts at the end of this report and in the electronic files that are being produced with this report and are a part of my expert work in this case.

II. Statistical Analysis of Plaintiff's Allegations

A. Documented Physician Experience

10. Given the size of the relevant prescriber population, it would be prohibitively time-consuming and expensive to interview each prescriber of Risperdal in South

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Carolina concerning his or her experience with Risperdal and other antipsychotic medications. However, a properly representative sample of South Carolina doctors provides an economically feasible, reasonably accurate approximation of the same information. It is generally accepted among professional statisticians as well as scientists and scholars in related fields that statistical sampling is the only generally applicable, scientifically valid method for creating a representative sample from a universe that is too large to process exhaustively. By means of statistical sampling it is possible to produce unbiased, reasonably accurate approximations, having a known degree of potential error, to questions whose exact answers would be impracticably expensive or burdensome to obtain. I therefore obtained information about the experience of South Carolina doctors from legal depositions of randomly identified doctors who treated FFS and SHP beneficiaries in the State.

11. The theory and practice of statistical sampling, including sample surveys of human subjects, has been a fundamental topic within the science of statistics at least since the early twentieth century. During the decades of my education and career as a professional statistician in academia and consulting, I have acquired extensive experience with numerous aspects of sampling theory, sample and survey design, sample and survey implementation, and the analysis of sample and survey data.

12. Richard Johnson and Gouri Bhattacharyya recognized the importance of statistical sampling in their text *Statistics Principles and Methods*: "The subject of statistics provides the methodology to make inferences about the population from the collection and

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analysis of sample data. These methods enable one to derive plausible generalizations and then assess the extent of uncertainty underlying these generalizations."¹

13. Leading statistician William Cochran has also recognized the importance of statistical sampling for decision-makers in his book *Sampling Techniques*.²

14. Johnson and Bhattacharyya emphasize that "[s]tatistical concepts are also essential during the planning stage of an investigation when decisions must be made as to the mode and extent of the sampling process," thus the "design of the sampling process is an important step" and "[a] good design for the process of data collection permits efficient inferences, often with a straightforward analysis."³

15. In this case, the population sampled consists of doctors who prescribed antipsychotic drugs for South Carolina patients in the Fee-for-Service (FFS) or State Health Plan (SHP) claims databases.

16. Generally speaking, physicians who prescribed antipsychotic drugs to greater numbers of patients can be expected to have more experience regarding the efficacy of Risperdal and more experience regarding marketing and promotional activities of Janssen than physicians with fewer such patients. Because the Court limited Janssen to surveying 20 doctors through deposition, my survey sample was randomly identified from the 101 doctors who prescribed antipsychotics most frequently.⁴

¹ Richard Johnson and Gouri Bhattacharyya, *Statistics Principles and Methods*, John Wiley & Sons, 3rd edition, 1996, 14.

² Cochran, William G., *Sampling Techniques*, John Wiley & Sons, New York, 1977.

³ Johnson and Bhattacharyya, *op. cit.*, 14.

⁴ The population to be sampled was the top 100 prescribers. Two doctors tied for 100th place, so the sample was drawn from a population of 101 prescribers.

17. From the 101 most frequent prescribers, I selected, at random, with equal probability of selection, a sample of 20.⁵ I used a random process—a sequence of random numbers generated by a computer—to identify the final sample members from a list of all doctors eligible for selection.⁶ This random selection procedure guarantees a statistically representative sample because it rules out any purposive or inadvertent selection bias that could skew the composition of the sample towards any favored subgroup of doctors. Random sampling of this kind is a standard procedure in scientific survey research.

18. Counsel for Janssen endeavored to contact the selected doctors in the deposition sample to arrange for and conduct their depositions. Certain of the selected doctors were not available for deposition.⁷ In each of those instances, the next member in the random selection sequence was designated as a replacement.

19. The specific questions posed to the 20 doctors who were deposed are set forth in Exhibit 4 together with the doctors' responses. Exhibit 4 also shows the percent of doctor-deponents answering "yes" or "probably yes" to each question.

20. The questions to doctors in deposition asked doctors about their experience with Risperdal and other antipsychotic medications and their specific exposure to Janssen promotional activity and communications. I sought fact-based answers from doctors in response to questions about whether Janssen had marketed Risperdal to them for off-label uses,

⁵ "Equal probability samples" are also called "simple random samples."

⁶ I employed the following standard procedure for selecting the sample. Let N denote the population size, and n the designated sample size. I used the SAS statistical software package to assign independently to each of the N population members a decimal-fraction random number between zero and one, equally likely to fall within either of any given pair of subintervals of equal length within the overall interval from zero to one. I then sorted the list of N population members in order of these assigned random numbers, and selected the first n members of the sorted list as the sample.

⁷ One doctor was unavailable due to terminal illness; one had moved to California; one refused to be deposed; and three could not be located. See Wecker electronic file "sample list.xls".

whether they had received specific correspondence from Janssen, and how their patients fared while taking Risperdal and other antipsychotics.

21. As noted, the methodology I employed is a well-established one that allows statisticians to reach conclusions about a population from the collection and analysis of sample data. Exhibit 5 shows the conclusions that can be derived from the responses of 20 doctor-deponents about the entire population of the 101 most frequent prescribers. In aggregate, those 101 doctors wrote 33 percent of the antipsychotic prescriptions paid for through the FFS and SHP programs.⁸

22. The depositions regarding the actual experience of South Carolina doctors prescribing Risperdal and other antipsychotics yield results that contradict the plaintiff's allegations. For example, the great majority of physicians affirmed the following statements based on their experience: Risperdal is generally effective for treating the positive symptoms of schizophrenia; Risperdal is generally effective for treating the negative symptoms of schizophrenia; Risperdal typically has a more moderate side effect profile than first generation antipsychotics; both efficacy and tolerability increase the likelihood that a patient will take an antipsychotic medication consistently; and patients who consistently take their antipsychotic medications are less likely to require costly follow-up treatment, such as in-patient psychiatric care, than patients who do not consistently take their medications.

23. Plaintiff's allegations are also contradicted by the result that no doctors affirmed that: any Janssen sales representative ever promoted to them any off-label use of Risperdal in children or geriatric patients; or that any Janssen sales representative ever promoted to them any off-label use of Risperdal at all. No Janssen sales representative ever represented

⁸ See Wecker electronic file "ffs_top_101.apd_pct.lst".

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anything inconsistent with the warnings about Risperdal that are provided on the FDA-approved package insert, and no Janssen sales representative ever misrepresented information about the potential side effects associated with Risperdal use to a deposed doctor.

24. Only a small number of physicians recall seeing Janssen's November 10, 2003 mailing to health care professionals. Of those, almost none changed their choice of antipsychotic medication based on the mailing. These responses are consistent with the history of the frequency with which doctors prescribed Risperdal, discussed below, which showed almost no change in Risperdal sales as a percentage of overall antipsychotic prescriptions after the mailing was sent to South Carolina doctors.

25. The commonly-used and accepted statistical tools that allow me to draw conclusions about the entire population of frequent South Carolina prescribers to FFS and SHP patients based on the answers provided in the survey show that the experience of South Carolina doctors contradicts plaintiff's allegations. The sample size of 20 allows me to reach reasonable population estimates for the 101 most frequent prescribers, as shown in Exhibit 5.

B. Observational Data

26. Claims data produced by the plaintiff from South Carolina State databases is also useful for analyzing plaintiff's allegations.⁹ I performed three different analyses. First, I was able to utilize claims data produced by the State to compare the incidence of side effects alleged by plaintiff to be risks from Risperdal use to the incidence of the same side effects in untreated patients suffering from psychotic disorders; patients treated with first generation (conventional) antipsychotics; and patients treated with other second generation (atypical)

⁹ For my analyses of plaintiff's claims data, I combined HMO claims data with the FFS claims data. The two programs use a common patient identification code and some patients had claims records in both data bases.

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antipsychotics. Second, I was able to utilize claims data to compare time to discontinuation—the primary measure of efficacy of the CATIE study—in Risperdal patients to patients using first generation antipsychotics. Third, I was able to determine Risperdal use as a percentage of all antipsychotic use by patients in the FFS or SHP programs over time.

B.1. Incidence of Alleged Side Effects

27. I analyzed the claims data to calculate the incidence of side effects that plaintiff alleges are caused by Risperdal, and to compare the incidence of those side effects in patients receiving Risperdal to the incidence of those side effects in untreated patients suffering from psychotic disorders; patients treated with first generation (conventional) antipsychotics; and patients treated with other second generation (atypical) antipsychotics.

28. In order to perform this analysis, I first identified patients who, based on their FFS or SHP claims, were receiving only Risperdal, only first generation antipsychotics, or only other second generation antipsychotics. I then examined all claims in the 36 months after their first antipsychotic drug prescription for diagnoses indicating an alleged side effect. To attempt to ensure that the first antipsychotic drug prescription recorded in the State claims data was a patient's first use of the drug, I required a minimum of 12 months of uninterrupted eligibility prior to the first antipsychotic drug prescription. To attempt to ensure that I was comparing patients with similar histories with respect to each side effect, I required that there be no diagnosis indicating the side effect prior to the first antipsychotic drug prescription. To analyze untreated patients, I separately identified patients with uninterrupted eligibility for a period of at least 36 months prior to their first antipsychotic drug prescription and no diagnosis indicating the side effect prior to the 36 month period. I then examined all claims in that 36 month period for diagnoses indicating an alleged side effect. I analyzed two time periods: the

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full claims data base, providing data for 1994–2007 and the period limited to claims on or before November 10, 2003.¹⁰

29. The results of a direct comparison of the side effects reported in the claims database, for patients treated with different antipsychotic drugs, is shown in Exhibits 6 and 7. The percents of South Carolina patients with first alleged side effect diagnosis during the 36 months after their first antipsychotic drug prescription (treated patients) or before their first antipsychotic drug prescription reflect elevated side effect rates compared to Risperdal. Statistically significant differences from Risperdal are indicated by asterisks.

30. My analysis shows that:

a. Diabetes. Patients treated with conventional antipsychotics, patients treated with other atypical antipsychotics, and untreated patients had a statistically significantly elevated risk of diabetes compared to patients treated with Risperdal, whether measured based on analysis of all data or data existing as of November 10, 2003.

b. Metabolic adverse events.¹¹ Patients treated with conventional antipsychotics, patients treated with other atypical antipsychotics, and untreated patients had a statistically significantly elevated risk of metabolic adverse events compared to patients treated with Risperdal based on analysis of all data. Patients treated with other atypical antipsychotics had a statistically significantly elevated risk of metabolic adverse events compared to patients treated with Risperdal based on analysis of data existing as of November 10, 2003.

c. Increased prolactin secretion. Patients treated with conventional antipsychotics, patients treated with other atypical antipsychotics, and

¹⁰ I do not believe it is proper to limit analysis to data existing as of November 10, 2003 when seeking to determine whether the South Carolina claims data supports statements made by Janssen about Risperdal in the November 10, 2003 mailing. Instead, statisticians and other scientists should look at all available evidence, regardless of when it became available, to evaluate whether Janssen's statements were true or false. I have nevertheless included analysis of data as of November 10, 2003, in case plaintiff or any of its experts take the position that the truth or falsity of Janssen's communications should be evaluated without reference to anything that occurred after Janssen sent the November 10, 2003 mailing.

¹¹ Includes diabetes mellitus, secondary diabetes mellitus, abnormal glucose, abnormal weight gain, obesity, and other hyperalimentation.

untreated patients had a statistically significantly elevated risk of increased prolactin secretion compared to patients treated with Risperdal based on analysis of all data.¹²

31. The data for South Carolina patients contradicts the opinion of plaintiff's expert Dr. William Wirshing that "risperidone elevates prolactin more than any marketed antipsychotic except the more recently marketed Janssen product paliperidone, a metabolite of risperidone." (Wirshing Report, p. 7). Dr. Wirshing's criticism of Janssen for "believ[ing] that the FDA mandated class labeling change and to a slightly lesser extent the consensus guidelines painted all of the medications with the same toxic brush" (Wirshing Report, p. 8) is similarly contradicted by the experience of South Carolina patients, because patient experience demonstrates differences in risk for Risperdal compared to other antipsychotics.

B.2. Time to Discontinuation

32. Plaintiff alleges in its Petition that the authors of the CATIE study "concluded that Risperdal is no more effective than the first generation, 'typical' antipsychotic, perphenazine, in treating schizophrenia. In addition, the time to discontinuation because of intolerable side effects, including movement disorders, were similar among all groups." (2d Am. Compl., ¶ 52.)

33. The CATIE study used "all-cause discontinuation" as the primary outcome measure of efficacy, meaning that the "failure" of a drug was attributed to the patient's discontinuation of the drug for any reason. The longer a patient took a drug in the CATIE trial, the more effective it was deemed to be by the study authors. I will return to the question of what the CATIE study shows, or does not show, about "all-cause discontinuation" times. But first, I

¹² The November 10, 2003 mailing did not discuss increased prolactin secretion.

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will describe my analysis of all-cause discontinuation times in the South Carolina population of State beneficiaries.

34. I have performed a statistical analysis of claims contained in the FFS and SHP data to determine all-cause discontinuation times in the South Carolina population of State beneficiaries. Using the claims data, I analyzed the comparative time to discontinuation for South Carolina patients treated with different antipsychotics. In order to be confident that I was measuring the first use of a drug, or first use after a substantial period of time in which the patient had not taken the drug for which I was measuring time to discontinuation, I identified those claims that were preceded by a minimum of 12 months of uninterrupted eligibility with no claims for the drug in question.

35. I then measured time to discontinuation following the first prescription by tracking patient claims histories for 18 months, as the CATIE study does. To determine discontinuation, I looked for periods of time without refills that followed the expiration of a patient's last prescription for the drug using three different, alternative time periods without refills to define discontinuation: 15 days, 30 days and 60 days. For example, if a patient received a prescription for a 30-day supply of Risperdal on April 1, but did not obtain another prescription until May 28, the patient would be deemed to have discontinued Risperdal use under the 15 days period, but not the 30 day or 60 day periods, because there was a 28 day period without a Risperdal refill prescription following the expiration of the 30 days supply prescribed on April 1. There is support in the medical literature for each of the time periods I use to define discontinuation: 15 days,¹³ 30 days,¹⁴ and 60 days.¹⁵

¹³ Mullins, C. Daniel, et al., *Risk of discontinuation of atypical antipsychotic agents in the treatment of schizophrenia*, Schizophrenia Research, Vol. 98 (2008), § 2.3.1.1 p. 9; Ren, X. S., et al., *An alternative approach to*

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36. My results show that Risperdal has a longer time to discontinuation compared to first generation antipsychotics in the FFS and SHP population under each of the three definitions of time to discontinuation. The complete results are set out in Exhibit 8. My analysis shows that:

- a. Defining discontinuation as a 60-day period. Average time to discontinuation was 211 days for Risperdal, 133 days for perphenazine, 130 days for Haldol, and 58 days for all other first generation antipsychotics considered as a group.
- b. Defining discontinuation as a 30-day period. Average time to discontinuation was 166 days for Risperdal, 107 days for perphenazine, 99 days for Haldol, and 44 days for all other first generation antipsychotics considered as a group.
- c. Defining discontinuation as a 15-day period. Average time to discontinuation was 126 days for Risperdal, 83 days for perphenazine, 78 days for Haldol, and 35 days for all other first generation antipsychotics considered as a group.

B.3. Risperdal Use Over Time

37. Using the claims data, I was also able to analyze Risperdal prescriptions as a percentage of all antipsychotic prescriptions paid for by the State through the FFS or SHP benefits programs and determine whether the comparative frequency of Risperdal prescriptions changed following events that plaintiff cites in its Complaint: the November 10, 2003 and July 21, 2004 mailings from Janssen to health care providers; the April 2005 FDA advisory and

measuring treatment persistence with antipsychotic agents among patients with schizophrenia in the Veterans Health Administration, Neuropsychiatric Disease and Treatment, Vol. 3, No. 2 (2007), p. 279; Ren, X. S., et al., Treatment persistence: a comparison among patients with schizophrenia who were initiated on atypical antipsychotic agents, J. Clin. Pharm. and Therap., Vol. 31 (2006), p. 59.

¹⁴ Ren, X. S., et al., *An alternative approach to measuring treatment persistence with antipsychotic agents among patients with schizophrenia in the Veterans Health Administration, Neuropsychiatric Disease and Treatment, Vol. 3, No. 2 (2007), p. 279.*

¹⁵ Kilzieh, Nacl, et al., *Time to Discontinuation and Self-Discontinuation of Olanzapine and Risperidone in Patients With Schizophrenia in a Naturalistic Outpatient Setting, J. Clin. Psychopharmacol., Vol 28, No. 1 (Feb. 2008), p. 75; Zhu, Baojin, et al., Time to Discontinuation of Depot and Oral First-Generation Antipsychotics in the Usual Care of Schizophrenia, Psychiatric Services, Vol. 59, No. 3 (Mar. 2008), p. 316.*

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subsequent black box warning for geriatric use; or the publication of the CATIE trial results in September 2005.

38. In order to determine the percentage of all antipsychotic prescriptions that Risperdal accounts for, I first eliminated claims that were reversed and duplicate claims within the database, so that each prescription for an antipsychotic medication would be counted only once. I then counted Risperdal prescriptions for each month from January 2003–December 2005. I separately counted all antipsychotic prescriptions in the same months. It was then straightforward to determine the number of Risperdal prescriptions as a percentage of all antipsychotic prescriptions paid for by the State through the FFS and SHP programs.

39. The results of my analysis are presented numerically and graphically in Exhibit 9. As the graph in Exhibit 9 shows, I was able to specifically analyze whether the events cited in the Complaint were followed by any change in the frequency with which South Carolina doctors prescribed Risperdal to patients in the FFS or SHP programs, as compared to all antipsychotic prescriptions.

40. In particular, I found no change in Risperdal prescribing frequency following Janssen's November 10, 2003 mailing to health care providers. If, as plaintiff contends, Janssen misled doctors about Risperdal's safety compared to other antipsychotics, I would expect to see an increase in the frequency with which doctors prescribed Risperdal compared to other antipsychotics. There was no such increase.

41. There was likewise no change in Risperdal prescribing frequency following July 2004, when Janssen sent its "correction" letter to South Carolina doctors at the request of the DDMAC division of FDA. The data also demonstrates that Risperdal use did not decline after the FDA issued its April 2005 advisory and subsequently required a black box

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warning for risk of death in geriatric patients or in the time period following the publication of the CATIE study results in September 2005. If, as plaintiff contends, these events mark times when doctors were exposed to information previously withheld or when "the public perception of Risperdal created by Defendants was dealt a crushing blow" (2d Am. Compl. ¶ 50), I would expect to see a decline in the frequency with which doctors prescribed Risperdal compared to other antipsychotics. That did not occur.

III. Analysis of Peer-Reviewed Literature

A. The Eight Studies Cited by Janssen in Its November 10, 2003 Mailing

42. Plaintiff alleges that a November 10, 2003 mailing from Janssen to doctors in South Carolina contained misleading information about the risk of diabetes in patients taking Risperdal. As shown in Exhibits 4-7 and addressed above, the experience of South Carolina doctors and South Carolina patients supports the statements that Janssen made in the mailing:

Although confirmatory research is still needed, a body of evidence from published peer-reviewed epidemiological research¹⁴ suggests that RISPERDAL is not associated with an increased risk of diabetes when compared to untreated patients or patients treated with conventional antipsychotics. Evidence also suggests that RISPERDAL is associated with a lower risk of diabetes than some other studied atypical antipsychotics.

Janssen's statements are also supported by the eight then-existing peer-reviewed epidemiological studies addressing the risk of diabetes in patients taking Risperdal compared to untreated patients, patients taking conventional antipsychotics and patients taking other atypical antipsychotics.

43. The eight studies cited by Janssen, which collectively analyze data from 6 million patients,¹⁶ are:

¹⁶ See Wecker electronic file "eight studies patient counts.xls".

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a. Buse JB, Cavazonni P, Hornbuckle K et al. A retrospective cohort study of diabetes mellitus and antipsychotic treatment in the United States. *J Clin Epidemiology* 2003; 56: 164-170.

b. Caro JJ, Ward A, Levinton C and Robinson K. The risk of diabetes during olanzapine use compared with risperidone use: a retrospective database analysis. *J Clin Psychiatry* 2002; 63:1135-1139.

c. Fuller MA, Shermock KM, Scic M and Grogg AL. Comparative study of the development of diabetes mellitus in patients taking risperidone and olanzapine. *Pharmacotherapy* 2003; 23(8): 1037-1043.

d. Gianfrancesco F, White R, Wang RH and Nasrallah HA. Antipsychotic-induced type 2 diabetes: evidence from a large health plan database. *J Clin Psychopharmacol* 2003; 23(4): 328-335 ("Gianfrancesco 1").

e. Gianfrancesco F, Grogg AL, Mahmoud RA et al. Differential effects of antipsychotic agents on the risk of development of type 2 diabetes mellitus in patients with mood disorders. *Clin Therapeutics* 2003; 25(4): 1150-1171 ("Gianfrancesco 2").

f. Gianfrancesco F, Grogg AL, Mahmoud RA et al. Differential effect of risperidone, olanzapine, clozapine and conventional antipsychotics on type II diabetes: Findings from a large health plan database. *J Clin Psychiatry* 2002; 63: 920-930 ("Gianfrancesco 3").

g. Koro CE, Fedder DO, L'Italien GJ et al. Assessment of independent effect of olanzapine and risperidone on risk of diabetes among patients with schizophrenia: population based nested case-control study. *BMJ* 2002; 325: 243-245.

h. Sernyak MJ, Leslie DL, Alarcon RD et al. Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia. *Am J Psychiatry* 2002; 159: 561-566.

44. I have reviewed and analyzed the statistical conclusions presented in the eight studies. Four of the eight studies contain results comparing patients treated with Risperdal to untreated patients: Gianfrancesco 1, Gianfrancesco 2, Gianfrancesco 3 and Koro. All four of these studies find "that RISPERDAL is not associated with an increased risk of diabetes when compared to untreated patients"

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45. Six of the eight studies contain results comparing patients treated with Risperdal to patients treated with conventional antipsychotics: Buse, Gianfrancesco 1, Gianfrancesco 2, Gianfrancesco 3, Koro and Sernyak. All six of these studies find "that RISPERDAL is not associated with an increased risk of diabetes when compared to ... patients treated with conventional antipsychotics."

46. Buse warrants additional attention. Buse found overall that the incidence of diabetes mellitus for patients treated with Risperdal was lower than for patients treated with conventional antipsychotics. The hazard ratio for Risperdal was also lower than the hazard ratio for conventional antipsychotics.¹⁷ Buse separately reported results for a subgroup analysis that compared each of the four atypical antipsychotics, including Risperdal, to the haloperidol cohort.¹⁸ As a part of his subgroup analysis, Buse calculated that Risperdal's hazard ratio compared to haloperidol was 1.23, with a 95% confidence interval of 1.01–1.50 and a p-value of 0.040. A p-value of 0.040 would indicate a statistically significant result for a primary endpoint of a study, but it does not indicate a statistically significant result for a secondary, subgroup analysis. Subgroup p-values need to be interpreted based on the number of comparisons made in subgroups that are analyzed—at least four in this case.¹⁹ Properly interpreted, the p-value of 0.040, which is part of the haloperidol subgroup analysis is not a statistically significant result.

¹⁷ Buse at 168, Table 3.

¹⁸ Buse at 168, Table 4.

¹⁹ Walsh, Bruce. *Multiple Comparisons: Bonferroni Corrections and False Discovery Rates*, Lecture notes for EEB 581, 2004.

²⁰ There are several formulaic ways to assess statistical significance for a subgroup analysis. The most common and easiest method to apply is the method of Bonferroni. (See Walsh, *op. cit.*) In the case of the haloperidol subgroup analysis and the p-value of 0.040, which is a part of that analysis, the Bonferroni p-value is 0.16 ($= 4 \times 0.040$) which is not a statistically significant result.

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47. All eight studies contain results comparing patients treated with Risperdal to patients treated with another atypical antipsychotic, and four of those eight found statistically significant results: Ward, Fuller, Gianfrancesco 2, and Gianfrancesco 3. All four of these studies find "that RISPERDAL is associated with a [statistically significantly] lower risk of diabetes than some other studied atypical antipsychotics."

48. Taken together, the results of the eight studies, like the experience of South Carolina doctors and patients, contradict the contention of plaintiff's expert Laura Plunkett, that "the language of the November 2003 'Dear Health Care Provider' letter was not an accurate reflection of the risks posed by Risperdal." (Plunkett Report, ¶ 50.) Contrary to Dr. Plunkett's opinion, Janssen's statement in the mailing was an accurate reflection of the risks posed by Risperdal, whether judged by the then-existing body of published peer-reviewed epidemiological literature or the data from South Carolina doctors and patients.

B. The CATIE Study

49. As described above, the experience of South Carolina doctors with Risperdal and other antipsychotic medications contradicts plaintiff's interpretation of the CATIE study:

[T]he CATIE study proved what Defendants knew since launching Risperdal: (1) that Risperdal is no more effective in treating schizophrenia; (2) that Risperdal is no safer; and (3) that Risperdal has intolerable side effects making it no more desirable than the less expensive atypical antipsychotics. (2d Am. Compl. ¶ 52.)

In the experience of South Carolina doctors, Risperdal is more effective; has a more moderate side effect profile; and is better tolerated than first generation antipsychotics.

50. The experience of South Carolina patients also contradicts plaintiff's interpretation of the CATIE study. Time to discontinuation of Risperdal, for South Carolina

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patients, is longer than time to discontinuation of perphenazine, Haldol, or other first generation antipsychotics.

51. It takes no deep statistical analysis to show that the CATIE study itself demonstrates that Risperdal is more effective than and safer than perphenazine, the first generation drug included in the CATIE study. The study protocol states that perphenazine is "contraindicated" for patients with a prior history of tardive dyskinesia.²¹ This contraindication alone is sufficient to show that Risperdal is more effective than and safer than perphenazine for at least this large segment of the patient population.

52. Any direct comparisons of results from the perphenazine group to other treatment groups in the CATIE study will produce only ambiguous results, because the perphenazine group excluded patients with tardive dyskinesia while the other groups did not. Thus, the perphenazine group differs from the other groups in two ways: a difference in treatment and a difference in the patients treated. Because the perphenazine group differs from the other groups in more than one way, it is not valid to claim that any difference in outcomes for the perphenazine group versus any of the other treatment groups is due to the difference in treatment alone.

53. In an apparent attempt to cure the problem caused by the difference in patients treated with perphenazine compared to patients who received other treatments, the CATIE study chose to ignore results from patients with a prior history of tardive dyskinesia when making certain comparisons between treatment groups. But ignoring patients with a prior history of tardive dyskinesia is not a cure, because perphenazine, which is contraindicated for such patients, can be expected to have a differential and less satisfactory outcome for such

²¹ Protocol, Comparative Effectiveness of Antipsychotic Medications in Patients with Schizophrenia, 26-27.

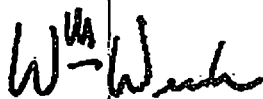
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patients. Ignoring outcomes for patients for whom perphenazine is expected to be ineffective or harmful amounts to ignoring an important difference in treatment results that will occur in the general population, which makes such comparisons inapplicable to the general population.

IV. Conclusion

54. In summary, for the reasons I have explained, statistical analysis of the primary data sources that provide information related to the central questions at issue refutes plaintiff's allegations.

December 3, 2010



William E. Wecker

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EDUCATION

B.S. Basic Science, U.S. Air Force Academy (1963)
M.S. Operations Research, University of Michigan (1970)
Ph.D. Statistics and Management Science, University of Michigan (1972)

EMPLOYMENT

1963-1967 Fighter pilot, U.S. Air Force
1968-1969 Chief of Protocol, U.S. Air Force, Berlin, Germany
1970-1972 Graduate Student, University of Michigan
1973-1976 Assistant Professor, Graduate School of Business, University of Chicago
1977-1983 Associate Professor, Graduate School of Business, University of Chicago
1984-1985 Associate Professor, Graduate School of Management, University of California, Davis
1985-1989 Professor, Graduate School of Management, University of California, Davis
1994-1998 Consulting Professor of Law, School of Law, Stanford University
1990- President, William E. Wecker Associates, Inc.

ACTIVITIES

1977-1981 Associate Editor (Theory and Methods), Journal of the American Statistical Association
1981-1999 Associate Editor, Journal of Business and Economic Statistics
1990-1992 Management Committee, Journal of Business and Economic Statistics
1976-1994 Seminar Leader, NSF/NBER Seminar on Time Series Analysis
1993-1994 National Advisory Council on Environmental Policy and Technology (Lead Subcommittee)
Member of: American Association for the Advancement of Science
American Statistical Association
Institute of Mathematical Statistics
Society for Risk Analysis

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Exhibit 2

William E. Wecker
Deposition and Trial Testimony
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1. Carla P. Cox v. Ford Motor Company and Mullinax Ford South, Inc. Circuit Court, Broward County, Florida, No. 02012391.
2. Cook, et al., v. Rockwell International Corp., et al. USDC, Denver, Colorado, No. 90-K-181.
3. Misty Arias, et al. v. Award Homes, Inc., et al. Superior Court, Monterey County, California, No. M54183.
4. Marjorie Rosenthal, et al. v. Ford Motor Company, et al. USDC, Connecticut, No. 3:05-cv-478(JCH).
5. Karen Jean Hubbard, et al. v. Ford Motor Company, et al. Superior Court, Macon County, Georgia, No. 2003CV-283-P.
6. Ronene J. Bracken, et al. v. Ford Motor Company, et al. USDC, Nevada, No. 03-CV-1543-RLH(RJJ).
7. Thelma Byrd, et al. v. Ford Motor Company, et al. Circuit Court, Copiah County, Mississippi, No. 2002-0446.
8. Yolanda Adams v. Ford Motor Company. District Court of the Virgin Islands, Division of St. Croix.
9. Ford Explorer Cases, Coordination Proceeding (Gray; Tompkins; Katz; Montoya and McLachlan v. Ford Motor Company). Superior Court, Sacramento County, California, JCCP Nos. 4226 and 4270.
10. State of California ex rel. Barakat Consulting Incorporated and Samir F. Barakat v. Los Angeles Department of Water and Power. Superior Court, San Bernardino County, California, No. SCVSS 100293.
11. Hohnbaum, et al. v. Brinker Restaurant Corporation, et al. Superior Court, San Diego County, California, No. GIC834348.
12. Leslie J. Whiteley and Leonard Whiteley v. Raybestos-Manhattan, Inc., et al. Superior Court, San Francisco, California, No. 303184.

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13. Dallas R. Maxwell and Angela J. Maxwell v. U-Haul International, Inc., Ford Motor Company, et al. Circuit Court, Jackson County, Missouri, No. 04CV226516.
14. Lindsay Rae Burnett, et al. v. Pirelli North America, Inc., Ford Motor Company, et al. District Court, Clark County, Nevada, No. A476187.
15. Rodrigo Ibarra, et al. v. Goodyear Tire and Rubber Company, Ford Motor Company, et al. District Court, Clark County, Nevada, No. A485304.
16. National Economic Research Associates, Inc. and Marsh & McLennan Companies, Inc. v. David S. Evans, LECG Corporation and LECG, LLC. Superior Court Department of the Trial Court, Suffolk, Massachusetts, No. 04-2618.
17. Michael Gutzler, et al. vs. General Motors Corporation. Circuit Court, Jackson County, Missouri, No. 03CV208786.
18. Self-Insurers' Security Fund v. Gallagher Bassett Services, Inc. USDC, Northern District of California, San Francisco Division, No. C 06-02828 JSW/JCS.
19. Auntry Petroleum Company and McDonald Oil Company v. BP Products North America, Inc. USDC, Middle District of Georgia, Columbus Division, No. 4:05-CV-113 (CDL).
20. Wyeth v. Impax Laboratories, Inc. USDC, Delaware, No. C.A. 06-222 (JJF).
21. Discover Financial Services, DFS Services LLC, and Discover Bank v. Visa, U.S.A. Inc., Visa International Services Association, Mastercard Incorporated and Mastercard International Incorporated. USDC, Southern District of New York, No. 04-CV-7844 (BSJ).
22. In re: New Motor Vehicles Canadian Export Antitrust Litigation. USDC, Maine MDL No. 03-md-1532.
23. Lyle Verry and Carla Verry v. General Motors Corporation. USDC, Eastern District of California, No. 2:06-CV-01566-LKK-PAN.
24. Equal Employment Opportunity Commission v. University of Phoenix, Inc. and Apollo Group, Inc. USDC, Arizona, No. CV06-2303-PHX-MHM.
25. Charles Foti, Attorney General *ex rel*, State of Louisiana v. Janssen Pharmaceutica, Inc. et al. Judicial District Court, Parish of St. Landry, Louisiana, No. 04-C-3967-D.
26. Sabrina Black Manuel v. Ford Motor Company, et al. Beverly Barber-Crouse v. Ford Motor Company, et al. Eugene Manuel, Jr. v. Ford Motor Company, et al. USDC, North District of Illinois, Eastern District, Nos. 07C5320, 07C5324, 07C5325.

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27. 34i Limited Partnership v. Microsoft Corporation. USDC, Eastern District of Texas, Tyler Division, No. 6:07-CV-113-LED.
28. Wyeth v. Apotex Inc. and Apotex, Corp. USDC, Southern District of Florida, No. 1:2008cv22308.
29. Steven Wirsz v. Nissan North America, Inc., et al. Superior Court, Los Angeles County, California, No. BC 377417.
30. L-3 Communications Integrated Systems, LP v. Lockheed Martin Corporation. USDC, Northern District of Texas, Dallas Division, No. 3-07CV0341-B.
31. Zurn PEX Plumbing Products Liability Litigation. USDC Minnesota, MDL 08-MD-1958.
32. Network-1 Security Solutions, Inc. v. Cisco Systems, Inc. USDC, Eastern Division of Texas, Tyler Division, No. 6:08cv030-LED.
33. In Re Payment Card Interchange Fee and Merchant Discount Antitrust Litigation. USDC, Eastern District of New York, No. 1:05-MD-1720 (JG)(JO).
34. In Re: Tobacco Litigation (Individual Personal Injury Cases). Circuit Court, Ohio County, West Virginia, No. 00-C-5000.
35. City of St. Louis, et al. v. American Tobacco Company, et al. Circuit Court, City of St. Louis, Missouri, No. 982-9652.

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ST. LOUIS COUNTY
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M. ROPE BLACKLEY

Exhibit 3

List of Materials Considered

Datasets and Electronic Files:

South Carolina Fee For Service, State Health Plan, and HMO claims data produced by plaintiff (including eligibility data).

Cover letters, data dictionaries, correspondence between plaintiff and defense counsel regarding data production.

Depositions:

Millard Clinton Trott
Delfin Valite
Eugene F. Smith
Andrew W. Hedgepath
Balbir Coshai
William H. Bragdon
Rosen J. Lawsin
Glenn Hooker
Anil Juneja
James Frank Riddle
Lori W. Barwick
Laurel A. Weston
Sallie Amanda Carter
Kathy Marie Waggett
Kenneth G. Kassebaum
Ricardo J. Fermo
Evan L. Vogel
Michael J. Wood
Paul P. Lowe
James L. Elmore

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Books, Articles and Papers:

Richard Johnson and Gouri Bhattacharyya, *Statistics Principles and Methods*, John Wiley & Sons, 3rd edition, 1996.

Cochran, William G., *Sampling Techniques*, John Wiley & Sons, New York, 1977.

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Ren, X. S., et al., *An alternative approach to measuring treatment persistence with antipsychotic agents among patients with schizophrenia in the Veterans Health Administration*, Neuropsychiatric Disease and Treatment, Vol. 3, No. 2 (2007).

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Kilzieh, Nael, et al., *Time to Discontinuation and Self-Discontinuation of Olanzapine and Risperidone in Patients With Schizophrenia in a Naturalistic Outpatient Setting*, J. Clin. Psychopharmacol., Vol 28, No. 1 (Feb. 2008).

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Buse JB, Cavazonni P, Hornbuckle K, et al., *A retrospective cohort study of diabetes mellitus and antipsychotic treatment in the United States*, J. Clin. Epidemiology 2003, 56:164-170.

Caro JJ, Ward A, Levinton C and Robinson K, *The risk of diabetes during olanzapine use compared with risperidone use: a retrospective database analysis*, J. Clin. Psychiatry 2002, 63:1135-1139.

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Koro CE, Fedder DO, L'Italien GJ et al., *Assessment of independent effect of olanzapine and risperidone on risk of diabetes among patients with schizophrenia: population based nested case-control study*, BMJ 2002, 325:243-245.

Sernyak MJ, Leslie DL, Alarcon RD et al. Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia, Am. J. Psychiatry 2002, 159:561-566.

Lieberman, J., et al., *Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia (CATIE)*, New Eng. J. Med., 353(12) (Sept. 2005).

Rosenheck, R., et al., *Cost Effectiveness of Second-Generation Antipsychotics and Perphenazine in a Randomized Trial of Treatment for Chronic Schizophrenia*, Am. J. of Psych., 163(12) (2006).

Rosenheck RA, et al. (2006), Supplemental table A, Patient characteristics at the time of random assignment by initial treatment, available at <http://ajp.psychiatryonline.org/>.

Walsh, Bruce, *Multiple Comparisons: Bonferroni Corrections and False Discovery Rates*, Lecture notes for EEB 581, 2004.

Pleadings, Court Filings and Discovery:

Second Amended Complaint.

July 1, 2009 Order (a ruling on Janssen's request to take doctor depositions).

Expert Reports of William E. Wirshing, M.D., July 10, 2009.

Expert Report of Laura M. Plunkett, Ph.D., DABT, July 7, 2009.

Declaration of Lon S. Schneider, M.D., July 10, 2009,

Expert Report of John Abramson, M.D., July 10, 2009.

Supplemental Expert Report of Laura M. Plunkett, Ph.D., DABT; August 4, 2010.

Other documents:

Janssen November 10, 2003 mailing to health care providers.

Risperdal package inserts and drug labels.

Protocol, Comparative Effectiveness of Antipsychotic Medications in Patients with Schizophrenia (Rev. Oct. 15, 2001).

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Exhibit 4

Deposition Questions and Responses of 20 Doctors

Question	Yes	Probably Yes	No	Probably No	Refills Only	Don't Recall	Don't Know	It Depends	First Generation Antipsychotic	Second Generation Antipsychotic	More Effective	Safer	Other Answers	Not Asked	Total	Percent Responding "Yes" or "Probably Yes"
Have you ever treated pediatric patients, meaning patients 0 through 12 years old?	19		1												20	95%
Have you ever treated adolescent patients, meaning patients 13 through 17 years old?	20														20	100%
Have you ever treated non-geriatric adult patients, meaning patients 18 through 64 years old?	20														20	100%
Have you ever treated geriatric patients, meaning patients 65 or older?	19		1												20	95%
Have you ever prescribed Risperdal® for any of your patients?	20														20	100%
Have you ever prescribed Risperdal® for a pediatric patient?	14		2		1	3									20	70%
For an adolescent patient?	14		2			4									20	70%
For a non-geriatric adult patient?	20														20	100%
For a geriatric patient?	16	1	2			1									20	85%
For a South Carolina Medicaid patient?	20														20	100%
For a South Carolina State Health Plan patient?	8	3	2			2	5								20	55%
Have you ever prescribed antipsychotic medications other than Risperdal® for any of your patients?	20														20	100%
Have you ever prescribed antipsychotic medications other than Risperdal® for a pediatric patient?	14	2	2		1	1									20	80%
For an adolescent patient?	17	1	1			1									20	90%
For a non-geriatric adult patient?	20														20	100%
For a geriatric patient?	17	2	1												20	95%
Have you ever prescribed first generation antipsychotics for any of your patients?	20														20	100%
Have you ever prescribed second generation antipsychotics other than Risperdal® for any of your patients?	19													1	20	95%
In your experience, is Risperdal® generally effective for treating the positive symptoms of schizophrenia?	20														20	100%
In your experience, is Risperdal® generally effective for treating the negative symptoms of schizophrenia?	13						2						3		20	70%

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Exhibit 4

Deposition Questions and Responses of 20 Doctors

Question	Yes	Probably Yes	No	Probably No	Refills Only	Don't Recall	Don't Know	It Depends	First Generation Antipsychotic	Second Generation Antipsychotic	More Effective	Safer	Other Answers	Not Asked	Total	Percent Responding "Yes" or "Probably Yes"
In your experience, do patients who take Risperdal® have better overall outcomes more frequently than patients who take a first generation antipsychotic?	12	1	3				1	2					1		20	65%
In your practice, for patients requiring antipsychotic medications, do you generally prefer to use first generation antipsychotics, or, second generation antipsychotics? [Percent shown is for "second generation".]								1	1	14			4		20	70%
In your experience, are patients who take first generation antipsychotics, such as Haldol and Thorazine, more likely to experience extrapyramidal and anticholinergic side effects than patients who take second	20														20	100%
generation antipsychotics, such as Haldol and Thorazine, more likely to experience tardive dyskinesia than patients who take second generation antipsychotics?	18						2								20	90%
In your experience, does Risperdal® typically have a more moderate side effect profile than first generation antipsychotics?	14						1	4					1		20	70%
In your experience, is Risperdal® typically better tolerated than first generation antipsychotics?	17							1					2		20	35%
In your experience with antipsychotic medications, are both efficacy and tolerability important considerations in the choice of which antipsychotic to prescribe?	19												1		20	95%
In your experience, do both efficacy and tolerability increase the likelihood that a patient will take an antipsychotic medication consistently?	19													1	20	95%
In your experience, are patients who consistently take their antipsychotic medications less likely to require costly follow-up treatment, such as in-patient psychiatric care, than patients who do not	19						1								20	95%
In your experience, are patients who consistently take their antipsychotic medications less likely, to require costly follow-up treatment, such as emergency room care, than patients who do not	17						1							2	20	85%
In your experience, does increased patient compliance with antipsychotic prescriptions result in overall conservation, as opposed to consumption, of healthcare resources?	17		1				2								20	85%
In your experience, does the use of Risperdal® typically conserve healthcare resources as compared to first generation antipsychotics?	9		1				4	2					4		20	45%
In your experience, does increased patient compliance with antipsychotic prescriptions typically decrease the human consequences of psychiatric illnesses?	20														20	100%
In your experience, does compliance taking antipsychotic medications typically make patients less likely to experience recurrence of	20														20	100%
Less likely to be violent?	17						2								20	90%

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NORTH CAROLINA

Exhibit 4

Deposition Questions and Responses of 20 Doctors

Question	Yes	Probably Yes	No	Probably No	Refills Only	Don't Recall	Don't Know	It Depends	First Generation Antipsychotic	Second Generation Antipsychotic	More Effective	Safer	Other Answers	Not Asked	Total	Percent Responding "Yes" or "Probably Yes"
Less likely to be an extreme burden on family members?	20														20	100%
Less likely to experience worsening of their conditions?	19						1								20	95%
Overall, in your experience, is Risperdal® a reasonably safe and effective medication for treating schizophrenia and other psychotic disorders?	19												1		20	95%
Overall, in your experience, is Risperdal® a safer and more effective medication for treating schizophrenia and other psychotic disorders than the first generation medications?	11		1				3	2			1	2			20	55%
In your experience, are there circumstances when the off-label use of medications is appropriate?	20														20	100%
In your experience, is it fair to say that off-label use of medications is not an uncommon practice?	18												2		20	90%
In your experience, are there circumstances when the off-label use of antipsychotic medications is appropriate?	18			1									1		20	90%
In your experience, is it fair to say that off-label use of antipsychotic medications is not an uncommon practice?	18						1						1		20	90%
Have you ever prescribed a medication for off-label use?	19					1									20	95%
In those circumstances, did you expect your patients to benefit from the off-label use of the medication?	19													1	20	95%
Have you ever prescribed an antipsychotic medication for off-label use?	18		1			1									20	90%
Have you ever prescribed Risperdal® for off-label use?	16	2	1			1									20	90%
Did you expect your patients to benefit from the off-label use of Risperdal®?	18													2	20	90%
Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® in children?			19			1									20	0%
Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® in geriatric patients?			19										1		20	0%
Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® at all?			19										1		20	0%
Have you ever received or seen any communication from Janssen promoting the off-label use of Risperdal®?			20												20	0%
Based on your training and experience, is it common for medications to have both benefits and risks?	20														20	100%

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DISTRICT OF COLUMBIA

Exhibit 4

Deposition Questions and Responses of 20 Doctors

Question	Yes	Probably Yes	No	Probably No	Refills Only	Don't Recall	Don't Know	It Depends	First Generation Antipsychotic	Second Generation Antipsychotic	More Effective	Safer	Other Answers	Not Asked	Total	Percent Responding "Yes" or "Probably Yes"
Based on your training and experience, is it your understanding that all antipsychotic medications -- both first generation and second generation -- have potential side effects?	20														20	100%
Are you aware of an association between antipsychotic medications and weight gain?	20														20	100%
Are you aware of an association between antipsychotic medications and risk of diabetes?	19													1	20	95%
When you prescribe antipsychotic medications, including Risperdal®, do you monitor your patients for weight gain?	20														20	100%
If you see or learn of rapid weight gain in a patient after the patient begins taking antipsychotics, do you typically consider changing the dosage and medication?	12		2					6							20	60%
If you see or learn of a change in blood glucose level in a patient after the patient begins taking antipsychotics, do you typically consider changing the dosage and medication?	12		2					6							20	60%
Would you agree that the 1993 package insert for Risperdal® advised of an association between Risperdal® and weight gain?	20														20	100%
Would you agree that the 1993 package insert for Risperdal® advised of an association between Risperdal® and diabetes?	20														20	100%
Would you agree that the 2004 package insert for Risperdal® incorporated a class warning of hyperglycemia and diabetes?	20														20	100%
Were you aware of an association between second generation antipsychotics, and weight gain or a risk of diabetes, prior to the 2004 revision to the package insert for Risperdal®?	16					2	2								20	80%
Did the change to the package insert for Risperdal® in 2004 cause you to change the circumstances in which you prescribe Risperdal® for patients?	2	1	15				1						1		20	15%
Has any Janssen sales representative ever represented to you anything inconsistent with the warnings about Risperdal® that are provided on the package insert?			19			1									20	0%
Has any Janssen sales representative ever represented to you that there is no association between Risperdal® and increased mortality in the elderly?			20												20	0%
Has any Janssen sales representative ever misrepresented to you information about the potential side effects associated with Risperdal® use?			19											1	20	0%
Have you ever seen this letter before? [November 10, 2003]	1	3	2			10	4								20	20%
Did this letter cause you to change the circumstances in which you prescribe antipsychotics to your patients?	1					1								13	20	5%

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Exhibit 4

Deposition Questions and Responses of 20 Doctors

Question	Yes	Probably Yes	No	Probably No	Refills Only	Dont Recall	Dont Know	It Depends	First Generation Antipsychotic	Second Generation Antipsychotic	More Effective	Safer	Other Answers	Not Asked	Total	Percent Responding "Yes" or "Probably Yes"
Did it cause you to change your choice of which antipsychotic to prescribe?		1	4										1	14	20	5%
Did it cause you to change your methods for monitoring for side effects in your patients on antipsychotic medications?	1		4			1								14	20	5%
Prior to the deposition today, have you had any communications with any of the attorneys for the Plaintiff in this case?	3		15											2	20	15%

See Wecker electronic file summary.dens.xls.

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Exhibit 5

Population Estimates from Responses to Deposition Questions

Question	Estimated Percent Responding "Yes" or "Probably Yes"	95% Confidence Limits
Have you ever treated pediatric patients, meaning patients 0 through 12 years old?	95.0%	(77.2% , 99.0%)
Have you ever treated adolescent patients, meaning patients 13 through 17 years old?	100.0%	(85.1% , 100.0%)
Have you ever treated non-geriatric adult patients, meaning patients 18 through 64 years old.	100.0%	(85.1% , 100.0%)
Have you ever treated geriatric patients, meaning patients 65 or older?	95.0%	(77.2% , 99.0%)
Have you ever prescribed Risperdal® for any of your patients?	100.0%	(85.1% , 100.0%)
Have you ever prescribed Risperdal® for a pediatric patient?	70.0%	(48.5% , 86.1%)
For an adolescent patient?	70.0%	(48.5% , 86.1%)
For a non-geriatric adult patient?	100.0%	(85.1% , 100.0%)
For a geriatric patient?	85.0%	(64.4% , 95.0%)
For a South Carolina Medicaid patient?	100.0%	(85.1% , 100.0%)
For a South Carolina State Health Plan patient?	55.0%	(33.7% , 74.3%)
Have you ever prescribed antipsychotic medications other than Risperdal® for any of your patients?	100.0%	(85.1% , 100.0%)
Have you ever prescribed antipsychotic medications other than Risperdal® for a pediatric patient?	80.0%	(59.4% , 93.1%)
For an adolescent patient?	90.0%	(71.3% , 98.0%)
For a non-geriatric adult patient?	100.0%	(85.1% , 100.0%)
For a geriatric patient?	95.0%	(77.2% , 99.0%)
Have you ever prescribed first generation antipsychotics for any of your patients?	100.0%	(85.1% , 100.0%)
Have you ever prescribed second generation antipsychotics other than Risperdal® for any of your patients?	95.0%	(77.2% , 99.0%)

Exhibit 5

Population Estimates from Responses to Deposition Questions

Question	Estimated Percent Responding "Yes" or "Probably Yes"	95% Confidence Limits
In your experience, is Risperdal® generally effective for treating the positive symptoms of schizophrenia?	100.0%	(85.1% , 100.0%)
In your experience, is Risperdal® generally effective for treating the negative symptoms of schizophrenia?	70.0%	(48.5% , 86.1%)
In your experience, do patients who take Risperdal® have better overall outcomes more frequently than patients who take a first generation antipsychotic?	65.0%	(43.6% , 82.2%)
In your practice, for patients requiring antipsychotic medications, do you generally prefer to use first generation antipsychotics, or, second generation antipsychotics? [Percent shown is for "second generation".]	70.0%	(48.5% , 86.1%)
In your experience, are patients who take first generation antipsychotics, such as Haldol and Thorazine, more likely to experience extrapyramidal and anticholinergic side effects than patients who take second generation antipsychotics?	100.0%	(85.1% , 100.0%)
In your experience, are patients who take first generation antipsychotics, such as Haldol and Thorazine, more likely to experience Tardive Dyskinesia than patients who take second generation antipsychotics?	90.0%	(71.3% , 98.0%)
In your experience, does Risperdal® typically have a more moderate side effect profile than first generation antipsychotics?	70.0%	(48.5% , 86.1%)
In your experience, is Risperdal® typically better tolerated than first generation antipsychotics?	85.0%	(64.4% , 95.0%)
In your experience with antipsychotic medications, are both efficacy and tolerability important considerations in the choice of which antipsychotic to prescribe?	95.0%	(77.2% , 99.0%)
In your experience, do both efficacy and tolerability increase the likelihood that a patient will take an antipsychotic medication consistently?	95.0%	(77.2% , 99.0%)
In your experience, are patients who consistently take their antipsychotic medications less likely to require costly follow-up treatment, such as in-patient psychiatric care, than patients who do not consistently take their medications?	95.0%	(77.2% , 99.0%)
In your experience, are patients who consistently take their antipsychotic medications less likely, to require costly follow-up treatment, such as emergency room care, than patients who do not consistently take their medications?	85.0%	(64.4% , 95.0%)
In your experience, does increased patient compliance with antipsychotic prescriptions result in overall conservation, as opposed to consumption, of healthcare resources?	85.0%	(64.4% , 95.0%)
In your experience, does the use of Risperdal® typically conserve healthcare resources as compared to first generation antipsychotics?	45.0%	(25.7% , 66.3%)

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Exhibit 5

Population Estimates from Responses to Deposition Questions

Question	Estimated Percent Responding "Yes" or "Probably Yes"	95% Confidence Limits
In your experience, does increased patient compliance with antipsychotic prescriptions typically decrease the human consequences of psychiatric illnesses?	100.0%	(85.1% , 100.0%)
In your experience, does compliance taking antipsychotic medications typically make patients less likely to experience recurrence of psychosis?	100.0%	(85.1% , 100.0%)
Less likely to be violent?	90.0%	(71.3% , 98.0%)
Less likely to be an extreme burden on family members?	100.0%	(85.1% , 100.0%)
Less likely to experience worsening of their conditions?	95.0%	(77.2% , 99.0%)
Overall, in your experience, is Risperdal® a reasonably safe and effective medication for treating schizophrenia and other psychotic disorders?	95.0%	(77.2% , 99.0%)
Overall, in your experience, is Risperdal® a safer and more effective medication for treating schizophrenia and other psychotic disorders than the first generation medications?	55.0%	(33.7% , 74.3%)
In your experience, are there circumstances when the off-label use of medications is appropriate?	100.0%	(85.1% , 100.0%)
In your experience, is it fair to say that off-label use of medications is not an uncommon practice?	90.0%	(71.3% , 98.0%)
In your experience, are there circumstances when the off-label use of antipsychotic medications is appropriate?	90.0%	(71.3% , 98.0%)
In your experience, is it fair to say that off-label use of antipsychotic medications is not an uncommon practice?	90.0%	(71.3% , 98.0%)
Have you ever prescribed a medication for off-label use?	95.0%	(77.2% , 99.0%)
In those circumstances, did you expect your patients to benefit from the off-label use of the medication?	95.0%	(77.2% , 99.0%)
Have you ever prescribed an antipsychotic medication for off-label use?	90.0%	(71.3% , 98.0%)
Have you ever prescribed Risperdal® for off-label use?	90.0%	(71.3% , 98.0%)
Did you expect your patients to benefit from the off-label use of Risperdal®?	90.0%	(71.3% , 98.0%)

R. 7902

Exhibit 5

Population Estimates from Responses to Deposition Questions

Question	Estimated Percent Responding "Yes" or "Probably Yes"	95% Confidence Limits
Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® in children?	0.0%	(0.0% , 11.9%)
Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® in geriatric patients?	0.0%	(0.0% , 11.9%)
Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® at all?	0.0%	(0.0% , 11.9%)
Have you ever received or seen any communication from Janssen promoting the off-label use of Risperdal®?	0.0%	(0.0% , 11.9%)
Based on your training and experience, is it common for medications to have both benefits and risks?	100.0%	(85.1% , 100.0%)
Based on your training and experience, is it your understanding that all antipsychotic medications -- both first generation and second generation -- have potential side effects?	100.0%	(85.1% , 100.0%)
Are you aware of an association between antipsychotic medications and weight gain?	100.0%	(85.1% , 100.0%)
Are you aware of an association between antipsychotic medications and risk of diabetes?	95.0%	(77.2% , 99.0%)
When you prescribe antipsychotic medications, including Risperdal®, do you monitor your patients for weight gain?	100.0%	(85.1% , 100.0%)
If you see or learn of rapid weight gain in a patient after the patient begins taking antipsychotics, do you typically consider changing the dosage and medication?	60.0%	(38.6% , 78.2%)
If you see or learn of a change in blood glucose level in a patient after the patient begins taking antipsychotics, do you typically consider changing the dosage and medication?	60.0%	(38.6% , 78.2%)
Would you agree that the 1993 package insert for Risperdal® advised of an association between Risperdal® and weight gain?	100.0%	(85.1% , 100.0%)
Would you agree that the 1993 package insert for Risperdal® advised of an association between Risperdal® and diabetes?	100.0%	(85.1% , 100.0%)
Would you agree that the 2004 package insert for Risperdal® incorporated a class warning of hyperglycemia and diabetes?	100.0%	(85.1% , 100.0%)
Were you aware of an association between second generation antipsychotics, and weight gain or a risk of diabetes, prior to the 2004 revision to the package insert for Risperdal®?	80.0%	(59.4% , 93.1%)
Did the change to the package insert for Risperdal® in 2004 cause you to change the circumstances in which you prescribe Risperdal® for patients?	15.0%	(5.0% , 35.6%)

R. 7903

Exhibit 5

Population Estimates from Responses to Deposition Questions

Question	Estimated Percent Responding "Yes" or "Probably Yes"	95% Confidence Limits
Has any Janssen sales representative ever represented to you anything inconsistent with the warnings about Risperdal® that are provided on the package insert?	0.0%	(0.0% , 11.9%)
Has any Janssen sales representative ever represented to you that there is no association between Risperdal® and increased mortality in the elderly?	0.0%	(0.0% , 11.9%)
Has any Janssen sales representative ever misrepresented to you information about the potential side effects associated with Risperdal® use?	0.0%	(0.0% , 11.9%)
Have you ever seen this letter before? [November 10, 2003]	20.0%	(6.9% , 40.6%)
Did this letter cause you to change the circumstances in which you prescribe antipsychotics to your patients?	5.0%	(1.0% , 22.8%)
Did it cause you to change your choice of which antipsychotic to prescribe?	5.0%	(1.0% , 22.8%)
Did it cause you to change your methods for monitoring for side effects in your patients on antipsychotic medications?	5.0%	(1.0% , 22.8%)
Prior to the deposition today, have you had any communications with any of the attorneys for the Plaintiff in this case?	15.0%	(5.0% , 35.6%)

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M. HOPE BLACKLEY

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R. 7904

Exhibit 6

Analysis of South Carolina Fee for Service, State Health Plan, and HMO Claims
Antipsychotic Drugs and Alleged Side Effects

Excess Side Effect Risk
Relative to Risperdal

		Alleged Side Effect		
		Diabetes	Metabolic Adverse Events	Increased Prolactin Secretion
Antipsychotic Drug Prescribed:	1st Generation	1.62% (*)	1.46% (*)	3.64% (*)
	Other 2nd Generation	2.33% (*)	4.47% (*)	1.82% (*)
	Untreated	1.29% (*)	0.99% (*)	2.22% (*)

Notes: 1. Percent of Patients with First Alleged Side Effect Diagnosis within 36 Months from First Antipsychotic Drug Prescription.

2. Treated patients excluded if prescribed more than one type of antipsychotic drug; if less than 12 months of uninterrupted eligibility prior to their first antipsychotic drug prescription; if diagnosis of alleged side effect occurs prior to their first antipsychotic drug prescription; or if less than 36 months of uninterrupted eligibility following their first antipsychotic drug prescription.

3. Untreated patients excluded if less than 48 months of uninterrupted eligibility prior to their first antipsychotic drug prescription; or if diagnosis of alleged side effect occurs prior to 36 months before their first antipsychotic drug prescription.

4. Asterisk (*) indicates value is statistically significantly different from Risperdal value at 95% confidence level.

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See Wecker electronic files side.effect.diag.lst, side.effect.mac.lst, and side.effect.pric.lst.

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Exhibit 7

Analysis of South Carolina Fee for Service, State Health Plan, and HMO Claims
Antipsychotic Drugs and Alleged Side Effects
Data as of November 10, 2003

Excess Side Effect Risk
Relative to Risperdal

		Alleged Side Effect	
		Diabetes	Metabolic Adverse Events
Antipsychotic Drug Prescribed:	1st Generation	1.17% (*)	0.65%
	Other 2nd Generation	1.84% (*)	3.02% (*)
	Untreated	1.32% (*)	0.78%

Notes: 1. Percent of Patients with First Alleged Side Effect Diagnosis within 36 Months from First Antipsychotic Drug Prescription.

2. Treated patients excluded if prescribed more than one type of antipsychotic drug; if less than 12 months of uninterrupted eligibility prior to their first antipsychotic drug prescription; if diagnosis of alleged side effect occurs prior to their first antipsychotic drug prescription; or if less than 36 months of uninterrupted eligibility following their first antipsychotic drug prescription.

3. Untreated patients excluded if less than 48 months of uninterrupted eligibility prior to their first antipsychotic drug prescription; or if diagnosis of alleged side effect occurs prior to 36 months before their first antipsychotic drug prescription.

4. Asterisk (*) indicates value is statistically significantly different from Risperdal value at 95% confidence level.

5. The November 10, 2003 mailing did not list increased prolactin secretion.

See Wecker electronic files side.effect.diag.lst, side.effect.diag.lst, side.effect.pric.lst.

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Exhibit 8

Analysis of South Carolina Fee for Service, State Health Plan, and HMO Claims
Antipsychotic Drugs and Time to Discontinuation

Average Days to Discontinuation

		Patient Count	"Treatment Discontinuation" Defined as X or More Days without Drug Supply		
			X=15 Days	X=30 Days	X=60 Days
Antipsychotic Drug Prescribed:	Risperdal	27,197	125.59	166.00	211.23
	Perphenazine	976	82.70 (*)	106.50 (*)	132.84 (*)
	Haldol	7,071	77.86 (*)	98.96 (*)	130.43 (*)
	Other 1st Generation	18,531	34.81 (*)	44.40 (*)	58.14 (*)

(*) Value is statistically significantly different from Risperdal value at 95% confidence level.

Notes: Patients are followed up for 18 months.

Patients excluded if less than 12 months of uninterrupted eligibility prior to start of treatment, or
less than 18 months of uninterrupted eligibility after start of treatment.

See Wecker electronic file time_to_discontinuation.lst.

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Exhibit 9

South Carolina Fee for Service, State Health Plan, and HMO Claims Data
Antipsychotic Prescriptions by Month

Month and Year	Risperdal	First Generation Antipsychotics	Other Second Generation Antipsychotics	Total	Percent Risperdal
Jan 2003	6,945	3,798	13,034	23,777	29.21%
Feb 2003	6,518	3,503	12,415	22,436	29.05%
Mar 2003	7,068	3,606	13,569	24,243	29.15%
Apr 2003	7,254	3,696	13,742	24,692	29.38%
May 2003	7,199	3,601	14,082	24,882	28.93%
Jun 2003	6,906	3,464	13,916	24,286	28.44%
Jul 2003	7,179	3,669	14,593	25,441	28.22%
Aug 2003	7,111	3,564	14,341	25,016	28.43%
Sep 2003	7,131	3,490	14,820	25,441	28.03%
Oct 2003	7,603	3,558	15,278	26,439	28.76%
Nov 2003	6,809	3,230	14,067	24,106	28.25%
Dec 2003	7,648	3,644	15,918	27,210	28.11%
Jan 2004	7,073	3,272	14,546	24,891	28.42%
Feb 2004	6,954	3,107	14,254	24,315	28.60%
Mar 2004	7,811	3,505	16,540	27,856	28.04%
Apr 2004	7,653	3,336	15,607	26,596	28.78%
May 2004	7,429	3,177	15,276	25,882	28.70%
Jun 2004	7,884	3,345	16,177	27,406	28.77%
Jul 2004	7,721	3,266	15,901	26,888	28.72%
Aug 2004	7,886	3,273	16,447	27,606	28.57%
Sep 2004	7,764	3,234	16,312	27,310	28.43%
Oct 2004	7,809	3,233	16,184	27,226	28.68%
Nov 2004	8,047	3,314	16,852	28,213	28.52%
Dec 2004	8,090	3,373	17,011	28,474	28.41%
Jan 2005	7,460	3,094	16,041	26,595	28.05%
Feb 2005	7,199	2,947	15,516	25,662	28.05%
Mar 2005	7,975	3,266	17,410	28,651	27.83%
Apr 2005	7,748	3,152	16,995	27,895	27.78%
May 2005	7,970	3,175	17,483	28,628	27.84%
Jun 2005	7,918	3,300	17,641	28,859	27.44%
Jul 2005	7,549	2,970	16,632	27,151	27.80%
Aug 2005	8,625	3,296	18,350	30,271	28.49%
Sep 2005	8,204	3,294	17,616	29,114	28.18%
Oct 2005	8,336	3,246	17,614	29,196	28.55%
Nov 2005	8,471	3,221	18,037	29,729	28.49%
Dec 2005	8,227	3,108	17,102	28,437	28.93%

Notes: 1. Percent=Risperdal/Total x 100
2. Claims counts are net of reversals.

See Wecker electronic file risp.percent.lst.

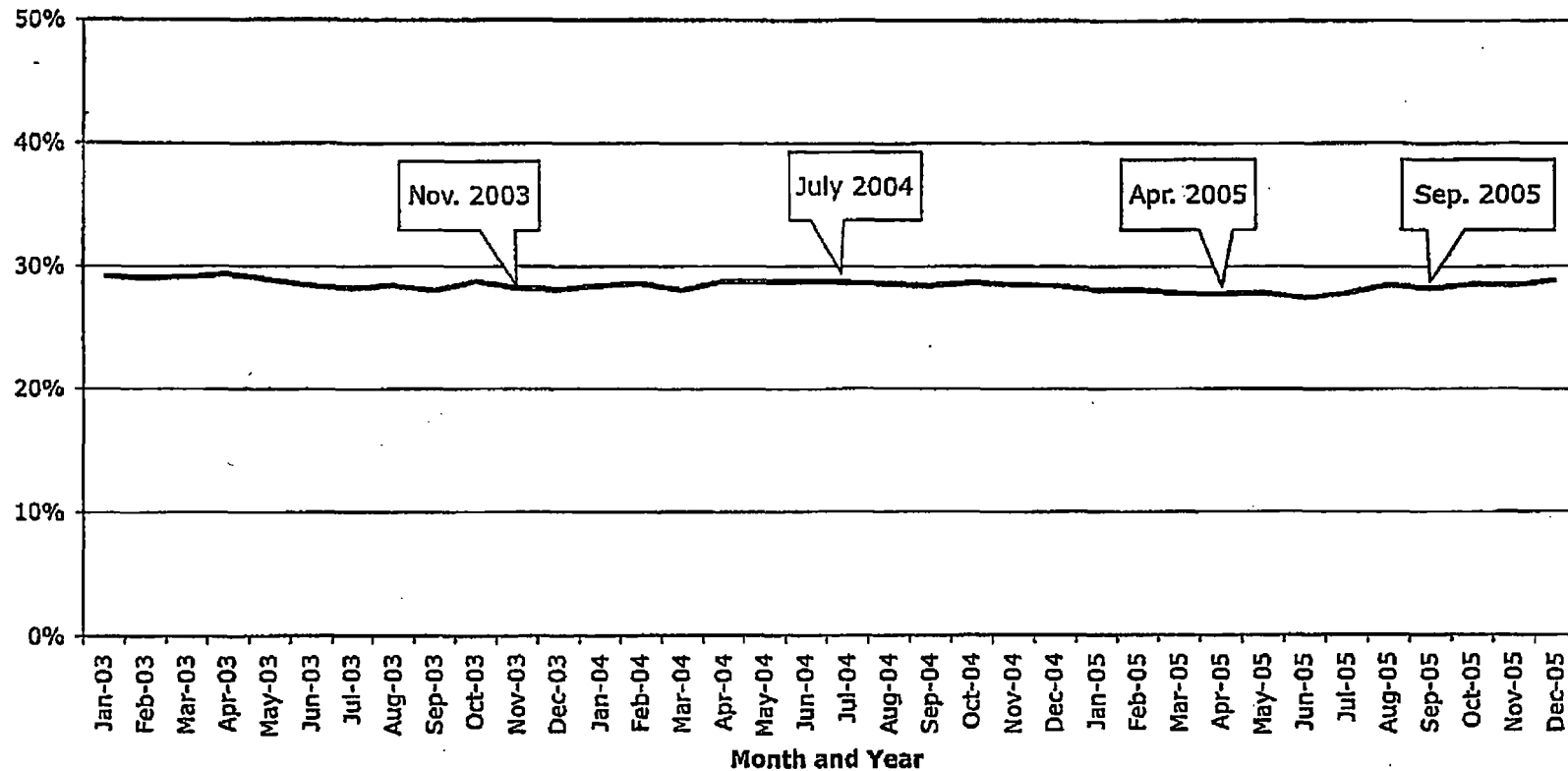
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Exhibit 9 (cont.)

South Carolina Fee for Service, State Health Plan, and HMO Claims Data
Percent Risperdal Prescriptions by Month



Notes: Percent=Risperdal/(Antipsychotic Prescriptions Total) x 100

November 2003: Janssen's November 10, 2003 mailing to health care providers.

July 2004: Janssen's "correction" letter.

April 2005: FDA advisory.

September 2005: publication of the CATIE trial results in *Engl J Med*.

See Wecker electronic file *risp.percent.lst*.

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EXHIBIT B

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Reference Manual on Scientific Evidence

Second Edition

Federal Judicial Center 2000

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Reference Guide on Survey Research

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I. Introduction

Surveys are used to describe or enumerate objects or the beliefs, attitudes, or behavior of persons or other social units.¹ Surveys typically are offered in legal proceedings to establish or refute claims about the characteristics of those objects, individuals, or social units. Although surveys may count or measure every member of the relevant population (e.g., all plaintiffs eligible to join in a suit, all employees currently working for a corporation, all trees in a forest), sample surveys count or measure only a portion of the objects, individuals, or social units that the survey is intended to describe.²

Some statistical and sampling experts apply the phrase "sample survey" only to a survey in which probability sampling techniques are used to select the sample.³ Although probability sampling offers important advantages over nonprobability sampling,⁴ experts in some fields (e.g., marketing) regularly rely on various forms of nonprobability sampling when conducting surveys. Consistent with Federal Rule of Evidence 703, courts generally have accepted such evidence.⁵ Thus, in this reference guide, both the probability sample and the nonprobability sample are discussed. The strengths of probability sampling and the weaknesses of various types of nonprobability sampling are described so that the trier of fact can consider these features in deciding what weight to give to a particular sample survey.

As a method of data collection, surveys have several crucial potential advantages over less systematic approaches.⁶ When properly designed, executed, and

1. Social scientists describe surveys as "conducted for the purpose of collecting data from individuals about themselves, about their households, or about other larger social units." Peter H. Rossi et al., *Sample Surveys: History, Current Practice, and Future Prospects*, in *Handbook of Survey Research* 1, 2 (Peter H. Rossi et al. eds., 1983). Used in its broader sense, however, the term *survey* applies to any description or enumeration, whether or not a person is the source of this information. Thus, a report on the number of trees destroyed in a forest fire might require a survey of the trees and stumps in the damaged area.

2. In *J.H. Miles & Co. v. Brown*, 910 F. Supp. 1138 (E.D. Va. 1995), clam processors and fishing vessel owners sued the Secretary of Commerce for failing to use the unexpectedly high results from 1994 survey data on the size of the clam population to determine clam fishing quotas for 1995. The estimate of clam abundance is obtained from surveys of the amount of fishing time the research survey vessels require to collect a specified yield of clams in major fishing areas over a period of several weeks. *Id.* at 1144-45.

3. E.g., Leslie Kish, *Survey Sampling* 26 (1965).

4. See *infra* § III.C.

5. Fed. R. Evid. 703 recognizes facts or data "of a type reasonably relied upon by experts in the particular field"

6. This does not mean that surveys can be relied on to address all types of questions. For example, some respondents may not be able to predict accurately whether they would volunteer for military service if Washington, D.C., were to be bombed. Their inaccuracy may arise not because they are unwilling to answer the question or to say they don't know, but because they believe they can predict accurately, and they are simply wrong. Thus, the availability of a "don't know" option cannot cure the inaccuracy. Although such a survey is suitable for assessing their predictions, it may not provide a very accurate estimate of what their actual responses would be.

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described, surveys (1) economically present the characteristics of a large group of objects or respondents and (2) permit an assessment of the extent to which the measured objects or respondents are likely to adequately represent a relevant group of objects, individuals, or social units.⁷ All questions asked of respondents and all other measuring devices used can be examined by the court and the opposing party for objectivity, clarity, and relevance, and all answers or other measures obtained can be analyzed for completeness and consistency. To make it possible for the court and the opposing party to closely scrutinize the survey so that its relevance, objectivity, and representativeness can be evaluated, the party proposing to offer the survey as evidence should describe in detail the design and execution of the survey.

The questions listed in this reference guide are intended to assist judges in identifying, narrowing, and addressing issues bearing on the adequacy of surveys either offered as evidence or proposed as a method for developing information.⁸ These questions can be (1) raised from the bench during a pretrial proceeding to determine the admissibility of the survey evidence; (2) presented to the contending experts before trial for their joint identification of disputed and undisputed issues; (3) presented to counsel with the expectation that the issues will be addressed during the examination of the experts at trial; or (4) raised in bench trials when a motion for a preliminary injunction is made to help the judge evaluate what weight, if any, the survey should be given.⁹ These questions are intended to improve the utility of cross-examination by counsel, where appropriate, not to replace it.

All sample surveys, whether they measure objects, individuals, or other social units, should address the issues concerning purpose and design (section II), population definition and sampling (section III), accuracy of data entry (section VI), and disclosure and reporting (section VII). Questionnaire and interview surveys raise methodological issues involving survey questions and structure (section IV) and confidentiality (section VII.C), and interview surveys introduce additional issues (e.g., interviewer training and qualifications) (section V). The sections of this reference guide are labeled to direct the reader to those topics that are relevant to the type of survey being considered. The scope of this reference guide is necessarily limited, and additional issues might arise in particular cases.

7. The ability to quantitatively assess the limits of the likely margin of error is unique to probability sample surveys.

8. See *infra* text accompanying note 27.

9. Lanham Act cases involving trademark infringement or deceptive advertising frequently require expedited hearings that request injunctive relief, so judges may need to be more familiar with survey methodology when considering the weight to accord a survey in these cases than when presiding over cases being submitted to a jury. Even in a case being decided by a jury, however, the court must be prepared to evaluate the methodology of the survey evidence in order to rule on admissibility. See *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 589 (1993).

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A. Use of Surveys in Court

Forty years ago the question whether surveys constituted acceptable evidence still was unsettled.¹⁰ Early doubts about the admissibility of surveys centered on their use of sampling techniques¹¹ and their status as hearsay evidence.¹² Federal Rule of Evidence 703 settled both matters for surveys by redirecting attention to the "validity of the techniques employed."¹³ The inquiry under Rule 703 focuses on whether facts or data are "of a type reasonably relied upon by experts in the particular field in forming opinions or inferences upon the subject."¹⁴ For a survey, the question becomes, "Was the poll or survey conducted in accordance with generally accepted survey principles, and were the results used in a

10. Hans Zeisel, *The Uniqueness of Survey Evidence*, 45 Cornell L.Q. 322, 345 (1960).

11. In an early use of sampling, *Sears, Roebuck & Co.* claimed a tax refund based on sales made to individuals living outside city limits. Sears randomly sampled 33 of the 826 working days in the relevant working period, computed the proportion of sales to out-of-city individuals during those days, and projected the sample result to the entire period. The court refused to accept the estimate based on the sample. When a complete audit was made, the result was almost identical to that obtained from the sample. *Sears, Roebuck & Co. v. City of Inglewood*, tried in Los Angeles Superior Court in 1955, is described in R. Clay Sprowls, *The Admissibility of Sample Data into a Court of Law: A Case History*, 4 UCLA L. Rev. 222, 226-29 (1956-1957).

12. Judge Wilfred Feinberg's thoughtful analysis in *Zippo Manufacturing Co. v. Rogers Imports, Inc.*, 216 F. Supp. 670, 682-83 (S.D.N.Y. 1963), provides two alternative grounds for admitting opinion surveys: (1) surveys are not hearsay because they are not offered in evidence to prove the truth of the matter asserted; and (2) even if they are hearsay, they fall under one of the exceptions as a "present sense impression." In *Schering Corp. v. Pfizer Inc.*, 189 F.3d 218 (2d Cir. 1999), the Second Circuit distinguished between perception surveys designed to reflect the present sense impressions of respondents and "memory" surveys designed to collect information about a past occurrence based on the recollections of the survey respondents. The court in *Schering* suggested that if a survey is offered to prove the existence of a specific idea in the public mind, then the survey does constitute hearsay evidence. As the court observed, Federal Rule of Evidence 803(3), creating "an exception to the hearsay rule for such statements [i.e., state of mind expressions] rather than excluding the statements from the definition of hearsay, makes sense only in this light." *Id.* at 230 n.3.

Two additional exceptions to the hearsay exclusion can be applied to surveys. First, surveys may constitute a hearsay exception if the survey data were collected in the normal course of a regularly conducted business activity, unless "the source of information or the method or circumstances of preparation indicate lack of trustworthiness." Fed. R. Evid. 803(6); see also *Ortho Pharm. Corp. v. Cosprophar, Inc.*, 828 F. Supp. 1114, 1119-20 (S.D.N.Y. 1993) (marketing surveys prepared in the course of business were properly excluded due to lack of foundation from a person who saw the original data or knew what steps were taken in preparing the report), *aff'd*, 32 F.3d 690 (2d Cir. 1994). In addition, if a survey shows guarantees of trustworthiness equivalent to those in other hearsay exceptions, it can be admitted if the court determines that the statement is offered as evidence of a material fact, it is more probative on the point for which it is offered than any other evidence which the proponent can procure through reasonable efforts, and admissibility serves the interests of justice. Fed. R. Evid. 807; e.g., *Keith v. Volpe*, 618 F. Supp. 1132 (C.D. Cal. 1985); *Schering*, 189 F.3d at 232. Admissibility as an exception to the hearsay exclusion thus depends on the trustworthiness of the survey.

13. Fed. R. Evid. 703 advisory committee's note.

14. Fed. R. Evid. 703.

statistically correct way?"¹⁵ This focus on the adequacy of the methodology used in conducting and analyzing results from a survey is also consistent with the Supreme Court's discussion of admissible scientific evidence in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*¹⁶

Because the survey method provides an economical and systematic way to gather information about a large number of individuals or social units, surveys are used widely in business, government, and, increasingly, administrative settings and judicial proceedings. Both federal and state courts have accepted survey evidence on a variety of issues. In a case involving allegations of discrimination in jury panel composition, the defense team surveyed prospective jurors to obtain age, race, education, ethnicity, and income distribution.¹⁷ Surveys of employees or prospective employees are used to support or refute claims of employment discrimination.¹⁸ In ruling on the admissibility of scientific claims, courts have examined surveys of scientific experts to assess the extent to which the theory or technique has received widespread acceptance.¹⁹ Some courts have admitted surveys in obscenity cases to provide evidence about community standards.²⁰ Requests for a change of venue on grounds of jury pool bias often are backed by evidence from a survey of jury-eligible respondents in the area of the original venue.²¹ The plaintiff in an antitrust suit conducted a survey to assess what characteristics, including price, affected consumers' preferences. The sur-

15. Manual for Complex Litigation § 2.712 (1982). Survey research also is addressed in the Manual for Complex Litigation, Second § 21.484 (1985) [hereinafter MCL 2d] and the Manual for Complex Litigation, Third § 21.493 (1995) [hereinafter MCL 3d]. Note, however, that experts who collect survey data, along with the professions that rely on those surveys, may differ in some of their methodological standards and principles. An assessment of the precision of sample estimates and an evaluation of the sources and magnitude of likely bias are required to distinguish methods that are acceptable from methods that are not.

16. 509 U.S. 579 (1993). See also *General Elec. Co. v. Joiner*, 522 U.S. 136, 147 (1997).

17. *People v. Harris*, 679 P.2d 433 (Cal.), cert. denied, 469 U.S. 965 (1984).

18. *BEOC v. Sears, Roebuck & Co.*, 628 F. Supp. 1264, 1308 (N.D. Ill. 1986), *aff'd*, 839 F.2d 302 (7th Cir. 1988); *Stender v. Lucky Stores, Inc.*, 803 F. Supp. 259, 326 (N.D. Cal. 1992); *Richardson v. Quik Trip Corp.*, 591 F. Supp. 1151, 1153 (S.D. Iowa 1984).

19. *United States v. Scheffer*, 523 U.S. 303, 309 (1998); *Meyers v. Arcudi*, 947 F. Supp. 581, 588 (D. Conn. 1996); *United States v. Varoudakis*, No. 97-10158, 1998 WL 151238 (D. Mass. Mar. 27, 1998); *United States v. Bishop*, 64 F. Supp. 2d 1149 (D. Utah 1999); *United States v. Orians*, 9 F. Supp. 2d 1168, 1174 (D. Ariz. 1998) (all cases in which courts determined, based on the inconsistent reactions revealed in several surveys, that the polygraph test has failed to achieve general acceptance in the scientific community).

20. *E.g.*, *People v. Page Books, Inc.*, 601 N.E.2d 273, 279-80 (Ill. App. Ct. 1992); *People v. Nelson*, 410 N.E.2d 476, 477-79 (Ill. App. Ct. 1980); *State v. Williams*, 598 N.E.2d 1250, 1256-58 (Ohio Ct. App. 1991).

21. *E.g.*, *United States v. Eagle*, 586 F.2d 1193, 1195 (8th Cir. 1978); *United States v. Tokars*, 839 F. Supp. 1578, 1583 (D. Ga. 1993), *aff'd*, 95 F.3d 1520 (11th Cir. 1996); *Powell v. Superior Court*, 283 Cal. Rptr. 777, 783 (Ct. App. 1991).

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vey was offered as one way to estimate damages.²² A routine use of surveys in federal courts occurs in Lanham Act²³ cases, where the plaintiff alleges trademark infringement²⁴ or claims that false advertising²⁵ has confused or deceived consumers. The pivotal legal question in such cases virtually demands survey research because it centers on consumer perception and memory (i.e., is the consumer likely to be confused about the source of a product, or does the advertisement imply an inaccurate message?).²⁶ In addition, survey methodology has been used creatively to assist federal courts in managing mass torts litigation. Faced with the prospect of conducting discovery concerning 10,000 plaintiffs, the plaintiffs and defendants in *Wilhoite v. Olin Corp.*²⁷ jointly drafted a discovery survey that was administered in person by neutral third parties, thus replacing interrogatories and depositions. It resulted in substantial savings in both time and cost.

B. A Comparison of Survey Evidence and Individual Testimony

To illustrate the value of a survey, it is useful to compare the information that can be obtained from a competently done survey with the information obtained

22. *Dolphin Tours, Inc. v. Pacifico Creative Servs., Inc.*, 773 F.2d 1506, 1508 (9th Cir. 1985). See also *SMS Sys. Maintenance Servs., Inc. v. Digital Equip. Corp.*, 188 F.3d 11 (1st Cir. 1999); Benjamin F. King, *Statistics in Antitrust Litigation*, in *Statistics and the Law* 49 (Morris H. DeGroot et al. eds. 1986). Surveys also are used in litigation to help define relevant markets. In *United States v. E.I. DuPont de Nemours & Co.*, 118 F. Supp. 41, 60 (D. Del. 1953), *aff'd*, 351 U.S. 377 (1956), a survey was used to develop the "market setting" for the sale of cellophane. In *Mukand, Ltd. v. United States*, 937 F. Supp. 910 (Ct. Int'l Trade 1996), a survey of purchasers of stainless steel wire rods was conducted to support a determination of competition and fungibility between domestic and Indian wire rod.

23. Lanham Act § 43(a), 15 U.S.C. § 1125(a) (1946) (amended 1992).

24. *E.g.*, *Union Carbide Corp. v. Ever-Ready, Inc.*, 531 F.2d 366 (7th Cir.), *cert. denied*, 429 U.S. 830 (1976); *Qualitex Co. v. Jacobson Prods. Co.*, No. CIV-90-1183HLH, 1991 U.S. Dist. LEXIS 21172 (C.D. Cal. Sept. 3, 1991), *aff'd in part & rev'd on other grounds*, 13 F.3d 1297 (9th Cir. 1994), *rev'd on other grounds*, 514 U.S. 159 (1995). According to Neal Miller, *Facts, Expert Facts, and Statistics: Descriptive and Experimental Research Methods in Litigation*, 40 Rutgers L. Rev. 101, 137 (1987), trademark law has relied on the institutionalized use of statistical evidence more than any other area of the law.

25. *E.g.*, *Southland Sod Farms v. Stover Seed Co.*, 108 F.3d 1134, 1142-43 (9th Cir. 1997); *American Home Prods. Corp. v. Johnson & Johnson*, 577 F.2d 160 (2d Cir. 1978).

26. Courts have observed that "the court's reaction is at best not determinative and at worst irrelevant. The question in such cases is, what does the person to whom the advertisement is addressed find to be the message?" *American Brands, Inc. v. R.J. Reynolds Tobacco Co.*, 413 F. Supp. 1352, 1357 (S.D.N.Y. 1976). The wide use of surveys in recent years was foreshadowed in *Triangle Publications, Inc. v. Rohrlid*, 167 F.2d 969, 974 (2d Cir. 1948) (Frank, J., dissenting). Called on to determine whether a manufacturer of girdles labeled "Miss Seventeen" infringed the trademark of the magazine *Seventeen*, Judge Frank suggested that, in the absence of a test of the reactions of "numerous girls and women," the trial court judge's finding as to what was likely to confuse was "nothing but a surmise, a conjecture, a guess," noting that "neither the trial judge nor any member of this court is (or resembles) a teen-age girl or the mother or sister of such a girl." *Id.* at 976-77.

27. No. CV-83-C-5021-NE (N.D. Ala. filed Jan. 11, 1983). The case ultimately settled before trial. See Francis E. McGovern & E. Allan Lind, *The Discovery Survey*, *Law & Contemp. Probs.*, Autumn 1988, at 41.

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by other means. A survey is presented by a survey expert who testifies about the responses of a substantial number of individuals who have been selected according to an explicit sampling plan and asked the same set of questions by interviewers who were not told who sponsored the survey or what answers were predicted or preferred. Although parties presumably are not obliged to present a survey conducted in anticipation of litigation by a nontestifying expert if it produced unfavorable results,²⁸ the court can and should scrutinize the method of respondent selection for any survey that is presented.

A party using a nonsurvey method generally identifies several witnesses who testify about their own characteristics, experiences, or impressions. While the party has no obligation to select these witnesses in any particular way or to report on how they were chosen, the party is not likely to select witnesses whose attributes conflict with the party's interests. The witnesses who testify are aware of the parties involved in the case and have discussed the case before testifying.

Although surveys are not the only means of demonstrating particular facts, presenting the results of a well-done survey through the testimony of an expert is an efficient way to inform the trier of fact about a large and representative group of potential witnesses. In some cases, courts have described surveys as the most direct form of evidence that can be offered.²⁹ Indeed, several courts have drawn negative inferences from the absence of a survey, taking the position that failure to undertake a survey may strongly suggest that a properly done survey would not support the plaintiff's position.³⁰

II. Purpose and Design of the Survey

A. Was the Survey Designed to Address Relevant Questions?

The report describing the results of a survey should include a statement describing the purpose or purposes of the survey. One indication that a survey offers probative evidence is that it was designed to collect information relevant to the legal controversy (e.g., to estimate damages in an antitrust suit or to assess con-

28. *Loctite Corp. v. National Starch & Chem. Corp.*, 516 F. Supp. 190, 205 (S.D.N.Y. 1981) (distinguishing between surveys conducted in anticipation of litigation and surveys conducted for nonlitigation purposes which cannot be reproduced because of the passage of time, concluding that parties should not be compelled to introduce the former at trial, but may be required to provide the latter).

29. *E.g.*, *Charles Jacquin et Cie, Inc. v. Destileria Serralles, Inc.*, 921 F.2d 467, 475 (3d Cir. 1990). See also *Brunswick Corp. v. Spinit Reel Co.*, 832 F.2d 513, 522 (10th Cir. 1987).

30. *B.S. Originals, Inc. v. Stride Rite Corp.*, 656 F. Supp. 484, 490 (S.D.N.Y. 1987); see also *Ortho Pharm. Corp. v. Cosprophar, Inc.*, 32 F.3d 690, 695 (2d Cir. 1994); *Henri's Food Prods. Co. v. Kraft, Inc.*, 717 F.2d 352, 357 (7th Cir. 1983); *Information Clearing House, Inc. v. Find Magazine*, 492 F. Supp. 147, 160 (S.D.N.Y. 1980).

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sumer confusion in a trademark case). Surveys not conducted specifically in preparation for, or in response to, litigation may provide important information,³¹ but they frequently ask irrelevant questions³² or select inappropriate samples of respondents for study.³³ Nonetheless, surveys do not always achieve their stated goals. Thus, the content and execution of a survey must be scrutinized even if the survey was designed to provide relevant data on the issue before the court. Moreover, if a survey was not designed for purposes of litigation, one source of bias is less likely: The party presenting the survey is less likely to have designed and constructed the survey to prove its side of the issue in controversy.

B. Was Participation in the Design, Administration, and Interpretation of the Survey Appropriately Controlled to Ensure the Objectivity of the Survey?

An early handbook for judges recommended that survey interviews be "conducted independently of the attorneys in the case."³⁴ Some courts have interpreted this to mean that any evidence of attorney participation is objectionable.³⁵ A better interpretation is that the attorney should have no part in carrying out the survey.³⁶ However, some attorney involvement in the survey design is

31. See, e.g., *Wright v. Jeep Corp.*, 547 F. Supp. 871, 874 (E.D. Mich. 1982). Indeed, as courts increasingly have been faced with scientific issues, parties have requested in a number of recent cases that the courts compel production of research data and testimony by unretained experts. The circumstances under which an unretained expert can be compelled to testify or to disclose research data and opinions, as well as the extent of disclosure that can be required when the research conducted by the expert has a bearing on the issues in the case, are the subject of considerable current debate. See, e.g., Richard L. Marcus, *Discovery Along the Litigation/Science Interface*, 57 Brook. L. Rev. 381, 393-428 (1991); Joe S. Cecil, *Judicially Compelled Disclosure of Research Data*, 1 Cts. Health Sci. & L. 434 (1998); see also Symposium, *Court-Ordered Disclosure of Academic Research: A Clash of Values of Science and Law*, Law & Contemp. Probs., Summer 1996, at 1.

32. *Loctite Corp. v. National Starch & Chem. Corp.*, 516 F. Supp. 190, 206 (S.D.N.Y. 1981) (marketing surveys conducted before litigation were designed to test for brand awareness, whereas the "single issue at hand . . . [was] whether consumers understood the term 'Super Glue' to designate glue from a single source").

33. In *Craig v. Boren*, 429 U.S. 190 (1976), the state unsuccessfully attempted to use its annual roadside survey of the blood alcohol level, drinking habits, and preferences of drivers to justify prohibiting the sale of 3.2% beer to males under the age of 21 and to females under the age of 18. The data were biased because it was likely that the male would be driving if both the male and female occupants of the car had been drinking. As pointed out in 2 Joseph L. Gastwirth, *Statistical Reasoning in Law and Public Policy: Tort Law, Evidence, and Health* 527 (1988), the roadside survey would have provided more relevant data if all occupants of the cars had been included in the survey (and if the type and amount of alcohol most recently consumed had been requested so that the consumption of 3.2% beer could have been isolated).

34. Judicial Conference of the U.S., *Handbook of Recommended Procedures for the Trial of Protracted Cases* 75 (1960).

35. E.g., *Boehringer Ingelheim G.m.b.H. v. Pharmadyne Lab.*, 532 F. Supp. 1040, 1058 (D.N.J. 1980).

36. *Upjohn Co. v. American Home Prods. Corp.*, No. 1-95-CV-237, 1996 U.S. Dist. LEXIS 8049, at *42 (W.D. Mich. Apr. 5, 1996) (objection that "counsel reviewed the design of the survey

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necessary to ensure that relevant questions are directed to a relevant population.³⁷ The trier of fact evaluates the objectivity and relevance of the questions on the survey and the appropriateness of the definition of the population used to guide sample selection. These aspects of the survey are visible to the trier of fact and can be judged on their quality, irrespective of who suggested them. In contrast, the interviews themselves are not directly visible, and any potential bias is minimized by having interviewers and respondents blind to the purpose and sponsorship of the survey and by excluding attorneys from any part in conducting interviews and tabulating results.

C. Are the Experts Who Designed, Conducted, or Analyzed the Survey Appropriately Skilled and Experienced?

Experts prepared to design, conduct, and analyze a survey generally should have graduate training in psychology (especially social, cognitive, or consumer psychology), sociology, marketing, communication sciences, statistics, or a related discipline; that training should include courses in survey research methods, sampling, measurement, interviewing, and statistics. In some cases, professional experience in conducting and publishing survey research may provide the requisite background. In all cases, the expert must demonstrate an understanding of survey methodology, including sampling,³⁸ instrument design (questionnaire and interview construction), and statistical analysis.³⁹ Publication in peer-reviewed journals, authored books, membership in professional organizations, faculty appointments, consulting experience, research grants, and membership on scientific advisory panels for government agencies or private foundations are indications of a professional's area and level of expertise. In addition, if the survey involves highly technical subject matter (e.g., the particular preferences of electrical engineers for various pieces of electrical equipment and the bases for those preferences) or involves a special population (e.g., developmentally disabled adults with limited cognitive skills), the survey expert also should be able to demonstrate sufficient familiarity with the topic or population (or assistance from an individual on the research team with suitable expertise) to design a survey instrument that will communicate clearly with relevant respondents.

carries little force with this Court because [opposing party] has not identified any flaw in the survey that might be attributed to counsel's assistance").

37. 3 J. Thomas McCarthy, *McCarthy on Trademarks and Unfair Competition* § 32:166 (4th ed. 1996).

38. The one exception is that sampling expertise is unnecessary if the survey is administered to all members of the relevant population. See, e.g., *McGovern & Lind*, *supra* note 27.

39. If survey expertise is being provided by several experts, a single expert may have general familiarity but not special expertise in all these areas.

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D. Are the Experts Who Will Testify About Surveys Conducted by Others Appropriately Skilled and Experienced?

Parties often call on an expert to testify about a survey conducted by someone else. The secondary expert's role is to offer support for a survey commissioned by the party who calls the expert, to critique a survey presented by the opposing party, or to introduce findings or conclusions from a survey not conducted in preparation for litigation or by any of the parties to the litigation. The trial court should take into account the exact issue that the expert seeks to testify about and the nature of the expert's field of expertise.⁴⁰ The secondary expert who gives an opinion about the adequacy and interpretation of a survey not only should have general skills and experience with surveys and be familiar with all of the issues addressed in this reference guide, but also should demonstrate familiarity with the following properties of the survey being discussed:

1. the purpose of the survey;
2. the survey methodology, including
 - a. the target population,
 - b. the sampling design used in conducting the survey,
 - c. the survey instrument (questionnaire or interview schedule), and
 - d. (for interview surveys) interviewer training and instruction;
3. the results, including rates and patterns of missing data; and
4. the statistical analyses used to interpret the results.

III. Population Definition and Sampling

A. Was an Appropriate Universe or Population Identified?

One of the first steps in designing a survey or in deciding whether an existing survey is relevant is to identify the target population (or universe).⁴¹ The target population consists of all elements (i.e., objects, individuals, or other social units) whose characteristics or perceptions the survey is intended to represent. Thus, in trademark litigation, the relevant population in some disputes may include all prospective and actual purchasers of the plaintiff's goods or services and all prospective and actual purchasers of the defendant's goods or services. Similarly, the population for a discovery survey may include all potential plaintiffs or all em-

40. Margaret A. Berger, The Supreme Court's Trilogy on the Admissibility of Expert Testimony § IV.C, in this manual.

41. Identification of the proper universe is recognized uniformly as a key element in the development of a survey. See, e.g., Judicial Conference of the U.S., *supra* note 34; MCL 3d, *supra* note 15, § 21.493. See also 3 McCarthy, *supra* note 37, § 32:166; Council of Am. Survey Res. Orgs., Code of Standards and Ethics for Survey Research § III.B.4 (1997).

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employees who worked for Company A between two specific dates. In a community survey designed to provide evidence for a motion for a change of venue, the relevant population consists of all jury-eligible citizens in the community in which the trial is to take place.⁴² The definition of the relevant population is crucial because there may be systematic differences in the responses of members of the population and nonmembers. (For example, consumers who are prospective purchasers may know more about the product category than consumers who are not considering making a purchase.)

The universe must be defined carefully. For example, a commercial for a toy or breakfast cereal may be aimed at children, who in turn influence their parents' purchases. If a survey assessing the commercial's tendency to mislead were conducted based on the universe of prospective and actual adult purchasers, it would exclude a crucial group of eligible respondents. Thus, the appropriate population in this instance would include children as well as parents.⁴³

B. Did the Sampling Frame Approximate the Population?

The target population consists of all the individuals or units that the researcher would like to study. The sampling frame is the source (or sources) from which the sample actually is drawn. The surveyor's job generally is easier if a complete list of every eligible member of the population is available (e.g., all plaintiffs in a discovery survey), so that the sampling frame lists the identity of all members of the target population. Frequently, however, the target population includes members who are inaccessible or who cannot be identified in advance. As a result, compromises are sometimes required in developing the sampling frame. The survey report should contain a description of the target population, a description of the survey population actually sampled, a discussion of the difference between the two populations, and an evaluation of the likely consequences of that difference.

42. A second relevant population may consist of jury-eligible citizens in the community where the party would like to see the trial moved. By questioning citizens in both communities, the survey can test whether moving the trial is likely to reduce the level of animosity toward the party requesting the change of venue. See *United States v. Haldeman*, 559 F.2d 31, 140, 151, app. A at 176-79 (D.C. Cir. 1976) (court denied change of venue over the strong objection of Judge MacKinnon, who cited survey evidence that Washington, D.C., residents were substantially more likely to conclude, before trial, that the defendants were guilty), *cert. denied*, 431 U.S. 933 (1977); see also *People v. Venegas*, 31 Cal. Rptr. 2d 114, 117 (Ct. App. 1994) (change of venue denied because defendant failed to show that the defendant would face a less hostile jury in a different court).

43. Children and some other populations create special challenges for researchers. For example, very young children should not be asked about sponsorship or licensing, concepts that are foreign to them. Concepts, as well as wording, should be age-appropriate.

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A survey that provides information about a wholly irrelevant universe of respondents is itself irrelevant.⁴⁴ Courts are likely to exclude the survey or accord it little weight. Thus, when the plaintiff submitted the results of a survey to prove that the green color of its fishing rod had acquired a secondary meaning, the court gave the survey little weight in part because the survey solicited the views of fishing rod dealers rather than consumers.⁴⁵ More commonly, however, the sampling frame is either underinclusive or overinclusive relative to the target population. If it is underinclusive, the survey's value depends on the extent to which the excluded population is likely to react differently from the included population. Thus, a survey of spectators and participants at running events would be sampling a sophisticated subset of those likely to purchase running shoes. Because this subset probably would consist of the consumers most knowledgeable about the trade dress used by companies that sell running shoes, a survey based on this population would be likely to substantially overrepresent the strength of a particular design as a trademark, and the extent of that overrepresentation would be unknown and not susceptible to any reasonable estimation.⁴⁶

Similarly, in a survey designed to project demand for cellular phones, the assumption that businesses would be the primary users of cellular service led surveyors to exclude potential nonbusiness users from the survey. The Federal Communications Commission (FCC) found the assumption unwarranted and concluded that the research was flawed, in part because of this underinclusive universe.⁴⁷

44. A survey aimed at assessing how persons in the trade respond to an advertisement should be conducted on a sample of persons in the trade and not on a sample of consumers. *Home Box Office v. Showtime/The Movie Channel*, 665 F. Supp. 1079, 1083 (S.D.N.Y.), *aff'd in part & vacated in part*, 832 F.2d 1311 (2d Cir. 1987). *But see* *Lon Tai Shing Co. v. Koch + Lowy*, No. 90-C4464, 1990 U.S. Dist. LEXIS 19123, at *50 (S.D.N.Y. Dec. 14, 1990), in which the judge was willing to find likelihood of consumer confusion from a survey of lighting store salespersons questioned by a survey researcher posing as a customer. The court was persuaded that the salespersons who were misstating the source of the lamp, whether consciously or not, must have believed reasonably that the consuming public would be misled by the salespersons' inaccurate statements about the name of the company that manufactured the lamp they were selling.

45. *R.L. Winston Rod Co. v. Sage Mfg. Co.*, 838 F. Supp. 1396, 1401-02 (D. Mont. 1993).

46. *Brooks Shoe Mfg. Co. v. Suave Shoe Corp.*, 533 F. Supp. 75, 80 (S.D. Fla. 1981), *aff'd*, 716 F.2d 854 (11th Cir. 1983). *See also* *Winning Ways, Inc. v. Holloway Sportswear, Inc.*, 913 F. Supp. 1454, 1467 (D. Kan. 1996) (survey flawed in failing to include sporting goods customers who constituted a major portion of customers). *But see* *Thontas & Betts Corp. v. Panduit Corp.*, 138 F.3d 277, 294-95 (7th Cir. 1998) (survey of store personnel admissible because relevant market included both distributors and ultimate purchasers).

47. *Gencom, Inc.*, 56 Rad. Reg. 2d (P&F) 1597, 1604 (1984). This position was affirmed on appeal. *See Gencom, Inc. v. FCC*, 832 F.2d 171, 186 (D.C. Cir. 1987).

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In some cases, it is difficult to determine whether an underinclusive universe distorts the results of the survey and, if so, the extent and likely direction of the bias. For example, a trademark survey was designed to test the likelihood of confusing an analgesic currently on the market with a new product that was similar in appearance.⁴⁸ The plaintiff's survey included only respondents who had used the plaintiff's analgesic, and the court found that the universe should have included users of other analgesics, "so that the full range of potential customers for whom plaintiff and defendants would compete could be studied."⁴⁹ In this instance, it is unclear whether users of the plaintiff's product would be more or less likely to be confused than users of the defendant's product or users of a third analgesic.⁵⁰

An overinclusive universe generally presents less of a problem in interpretation than does an underinclusive universe. If the survey expert can demonstrate that a sufficiently large (and representative) subset of respondents in the survey was drawn from the appropriate universe, the responses obtained from that subset can be examined, and inferences about the relevant universe can be drawn based on that subset.⁵¹ If the relevant subset cannot be identified, however, an overbroad universe will reduce the value of the survey.⁵² If the sample is drawn from an underinclusive universe, there is generally no way to know how the unrepresented members would have responded.⁵³

C. How Was the Sample Selected to Approximate the Relevant Characteristics of the Population?

Identification of a survey population must be followed by selection of a sample that accurately represents that population.⁵⁴ The use of probability sampling techniques maximizes both the representativeness of the survey results and the ability to assess the accuracy of estimates obtained from the survey.

Probability samples range from simple random samples to complex multi-stage sampling designs that use stratification, clustering of population elements into various groupings, or both. In simple random sampling, the most basic type

48. *American Home Prods. Corp. v. Barr Lab., Inc.*, 656 F. Supp. 1058 (D.N.J.), *aff'd*, 834 F.2d 368 (3d Cir. 1987).

49. *Id.* at 1070.

50. *See also* *Craig v. Boren*, 429 U.S. 190 (1976).

51. This occurred in *National Football League Properties, Inc. v. Wichita Falls Sportswear, Inc.*, 532 F. Supp. 651, 657-58 (W.D. Wash. 1982).

52. *Schieffelin & Co. v. Jack Co. of Boca*, 850 F. Supp. 232, 246 (S.D.N.Y. 1994).

53. *See, e.g., Amstar Corp. v. Domino's Pizza, Inc.*, 615 F.2d 252, 263-64 (5th Cir.) (court found both plaintiff's and defendant's surveys substantially defective for a systematic failure to include parts of the relevant population), *cert. denied*, 449 U.S. 899 (1980).

54. MCL 3d, *supra* note 15, § 21.493. *See also* David H. Kaye & David A. Freedman, *Reference Guide on Statistics* § II.B, in this manual.

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of probability sampling, every element in the population has a known, equal probability of being included in the sample, and all possible samples of a given size are equally likely to be selected.⁵⁵ In all forms of probability sampling, each element in the relevant population has a known, nonzero probability of being included in the sample.⁵⁶

Probability sampling offers two important advantages over other types of sampling. First, the sample can provide an unbiased estimate of the responses of all persons in the population from which the sample was drawn; that is, the expected value of the sample estimate is the population value being estimated. Second, the researcher can calculate a confidence interval that describes explicitly how reliable the sample estimate of the population is likely to be. Thus, suppose a survey tested a sample of 400 dentists randomly selected from the population of all dentists licensed to practice in the United States and found that 80, or 20%, of them mistakenly believed that a new toothpaste, Goldgate, was manufactured by the makers of Colgate. A survey expert could properly compute a confidence interval around the 20% estimate obtained from this sample. If the survey was repeated a large number of times, and a 95% confidence interval was computed each time, 95% of the confidence intervals would include the actual percentage of dentists in the entire population who would believe that Goldgate was manufactured by the makers of Colgate.⁵⁷ In this example, the confidence interval, or margin of error, is the estimate (20%) plus or minus 4%, or the distance between 16% and 24%.

All sample surveys produce estimates of population values, not exact measures of those values. Strictly speaking, the margin of sampling error associated with the sample estimate assumes probability sampling. Assuming a probability sample, a confidence interval describes how stable the mean response in the sample is likely to be. The width of the confidence interval depends on three characteristics:

55. Systematic sampling, in which every *n*th unit in the population is sampled and the starting point is selected randomly, fulfills the first of these conditions. It does not fulfill the second, because no systematic sample can include elements adjacent to one another on the list of population members from which the sample is drawn. Except in very unusual situations when periodicities occur, systematic samples and simple random samples generally produce the same results. Seymour Sudman, *Applied Sampling*, in *Handbook of Survey Research*, *supra* note 1, at 145, 169.

56. Other probability sampling techniques include (1) stratified random sampling, in which the researcher subdivides the population into mutually exclusive and exhaustive subpopulations, or strata, and then randomly selects samples from within these strata; and (2) cluster sampling, in which elements are sampled in groups or clusters, rather than on an individual basis. Martin Frankel, *Sampling Theory*, in *Handbook of Survey Research*, *supra* note 1, at 21, 37, 47.

57. Actually, since survey interviewers would be unable to locate some dentists and some dentists would be unwilling to participate in the survey, technically the population to which this sample would be projectable would be all dentists with current addresses who would be willing to participate in the survey if they were asked.

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1. the size of the sample (the larger the sample, the narrower the interval);
2. the variability of the response being measured; and
3. the confidence level the researcher wants to have.

Traditionally, scientists adopt the 95% level of confidence, which means that if 100 samples of the same size were drawn, the confidence interval expected for at least 95 of the samples would be expected to include the true population value.⁵⁸

Although probability sample surveys often are conducted in organizational settings and are the recommended sampling approach in academic and government publications on surveys, probability sample surveys can be expensive when in-person interviews are required, the target population is dispersed widely, or qualified respondents are scarce. A majority of the consumer surveys conducted for Lanham Act litigation present results from nonprobability convenience samples.⁵⁹ They are admitted into evidence based on the argument that nonprobability sampling is used widely in marketing research and that "results of these studies are used by major American companies in making decisions of considerable consequence."⁶⁰ Nonetheless, when respondents are not selected randomly from the relevant population, the expert should be prepared to justify the method used to select respondents. Special precautions are required to reduce the likelihood of biased samples.⁶¹ In addition, quantitative values computed from such samples (e.g., percentage of respondents indicating confusion) should be viewed as rough indicators rather than as precise quantitative estimates. Confidence intervals should not be computed.

58. To increase the likelihood that the confidence interval contains the actual population value (e.g., from 95% to 99%), the width of the confidence interval can be expanded. An increase in the confidence interval brings an increase in the confidence level. For further discussion of confidence intervals, see David H. Kaye & David A. Freedman, Reference Guide on Statistics § IV.A, in this manual.

59. Jacob Jacoby & Amy H. Handlin, *Non-Probability Sampling Designs for Litigation Surveys*, 81 Trademark Rep. 169, 173 (1991). For probability surveys conducted in trademark cases, see *National Football League Properties, Inc. v. Wichita Falls Sportswear, Inc.*, 532 F. Supp. 651 (W.D. Wash. 1982); *James Burrough, Ltd. v. Sign of Beefeater, Inc.*, 540 F.2d 266 (7th Cir. 1976).

60. *National Football League Properties, Inc. v. New Jersey Giants, Inc.*, 637 F. Supp. 507, 515 (D.N.J. 1986). A survey of members of the Council of American Survey Research Organizations, the national trade association for commercial survey research firms in the United States, revealed that 95% of the in-person independent contacts in studies done in 1985 took place in malls or shopping centers. Jacoby & Handlin, *supra* note 59, at 172-73, 176.

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D. Was the Level of Nonresponse Sufficient to Raise Questions About the Representativeness of the Sample? If So, What Is the Evidence That Nonresponse Did Not Bias the Results of the Survey?

Even when a sample is drawn randomly from a complete list of elements in the target population, responses or measures may be obtained on only part of the selected sample. If this lack of response were distributed randomly, valid inferences about the population could be drawn from the characteristics of the available elements in the sample. The difficulty is that nonresponse often is not random, so that, for example, persons who are single typically have three times the "not at home" rate in U.S. Census Bureau surveys as do family members.⁶² Efforts to increase response rates include making several attempts to contact potential respondents and providing financial incentives for participating in the survey.

One suggested formula for quantifying a tolerable level of nonresponse in a probability sample is based on the guidelines for statistical surveys issued by the former U.S. Office of Statistical Standards.⁶³ According to these guidelines, response rates of 90% or more are reliable and generally can be treated as random samples of the overall population. Response rates between 75% and 90% usually yield reliable results, but the researcher should conduct some check on the representativeness of the sample. Potential bias should receive greater scrutiny when the response rate drops below 75%. If the response rate drops below 50%, the survey should be regarded with significant caution as a basis for precise quantitative statements about the population from which the sample was drawn.⁶⁴

Determining whether the level of nonresponse in a survey is critical generally requires an analysis of the determinants of nonresponse. For example, even a survey with a high response rate may seriously underrepresent some portions of the population, such as the unemployed or the poor. If a general population sample was used to chart changes in the proportion of the population that knows someone with HIV, the survey would underestimate the population value if some groups more likely to know someone with HIV (e.g., intravenous drug users) were underrepresented in the sample. The survey expert should be prepared to provide evidence on the potential impact of nonresponse on the survey results.

61. See *infra* § III.B.

62. 2 Gastwirth, *supra* note 33, at 501. This volume contains a useful discussion of sampling, along with a set of examples. *Id.* at 467.

63. This standard is cited with approval by Gastwirth. *Id.* at 502.

64. For thoughtful examples of judges closely scrutinizing potential sample bias when response rates were below 75%, see *Vuyanich v. Republic National Bank*, 505 F. Supp. 224 (N.D. Tex. 1980); *Rosado v. Wyman*, 322 F. Supp. 1173 (E.D.N.Y.), *aff'd*, 437 F.2d 619 (2d Cir. 1970), *aff'd*, 402 U.S. 991 (1971).

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In surveys that include sensitive or difficult questions, particularly surveys that are self-administered, some respondents may refuse to provide answers or may provide incomplete answers. To assess the impact of nonresponse to a particular question, the survey expert should analyze the differences between those who answered and those who did not answer. Procedures to address the problem of missing data include recontacting respondents to obtain the missing answers and using the respondent's other answers to predict the missing response.⁶⁵

E. What Procedures Were Used to Reduce the Likelihood of a Biased Sample?

If it is impractical for a survey researcher to sample randomly from the entire target population, the researcher still can apply probability sampling to some aspects of respondent selection to reduce the likelihood of biased selection. For example, in many studies the target population consists of all consumers or purchasers of a product. Because it is impractical to randomly sample from that population, research is conducted in shopping malls where some members of the target population may not shop. Mall locations, however, can be sampled randomly from a list of possible mall sites. By administering the survey at several different malls, the expert can test for and report on any differences observed across sites. To the extent that similar results are obtained in different locations using different on-site interview operations, it is less likely that idiosyncrasies of sample selection or administration can account for the results.⁶⁶ Similarly, since the characteristics of persons visiting a shopping center vary by day of the week and time of day, bias in sampling can be reduced if the survey design calls for sampling time segments as well as mall locations.⁶⁷

In mall intercept surveys, the organization that manages the on-site interview facility generally employs recruiters who approach potential survey respondents in the mall and ascertain if they are qualified and willing to participate in the survey. If a potential respondent agrees to answer the questions and meets the specified criteria, he or she is escorted to the facility where the survey interview takes place. If recruiters are free to approach potential respondents without controls on how an individual is to be selected for screening, shoppers who spend more time in the mall are more likely to be approached than shoppers who visit the mall only briefly. Moreover, recruiters naturally prefer to approach friendly-

65. Andy B. Anderson et al., *Missing Data: A Review of the Literature*, in *Handbook of Survey Research*, *supra* note 1, at 415.

66. Note, however, that differences in results across sites may be due to genuine differences in respondents across geographic locations or to a failure to administer the survey consistently across sites.

67. Seymour Sudman, *Improving the Quality of Shopping Center Sampling*, 17 J. Marketing Res. 423 (1980).

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looking potential respondents, so that it is more likely that certain types of individuals will be selected. These potential biases in selection can be reduced by providing appropriate selection instructions and training recruiters effectively. Training that reduces the interviewer's discretion in selecting a potential respondent is likely to reduce bias in selection, as are instructions to approach every n th person entering the facility through a particular door.⁶⁸

F. What Precautions Were Taken to Ensure That Only Qualified Respondents Were Included in the Survey?

In a carefully executed survey, each potential respondent is questioned or measured on the attributes that determine his or her eligibility to participate in the survey. Thus, the initial questions screen potential respondents to determine if they are within the target population of the survey (e.g., Is she at least fourteen years old? Does she own a dog? Does she live within ten miles?). The screening questions must be drafted so that they do not convey information that will influence the respondent's answers on the main survey. For example, if respondents must be prospective and recent purchasers of Sunshine orange juice in a trademark survey designed to assess consumer confusion with Sun Time orange juice, potential respondents might be asked to name the brands of orange juice they have purchased recently or expect to purchase in the next six months. They should not be asked specifically if they recently have purchased, or expect to purchase, Sunshine orange juice, because this may affect their responses on the survey either by implying who is conducting the survey or by supplying them with a brand name that otherwise would not occur to them.

The content of a screening questionnaire (or screener) can also set the context for the questions that follow. In *Pfizer, Inc. v. Astra Pharmaceutical Products, Inc.*,⁶⁹ physicians were asked a screening question to determine whether they prescribed particular drugs. The court found that the screener conditioned the physicians to respond with the name of a drug rather than a condition.⁷⁰

The criteria for determining whether to include a potential respondent in the survey should be objective and clearly conveyed, preferably using written instructions addressed to those who administer the screening questions. These instructions and the completed screening questionnaire should be made avail-

68. In the end, even if malls are randomly sampled and shoppers are randomly selected within malls, results from mall surveys technically can be used to generalize only to the population of mall shoppers. The ability of the mall sample to describe the likely response pattern of the broader relevant population will depend on the extent to which a substantial segment of the relevant population (1) is not found in malls and (2) would respond differently to the interview.

69. 858 F. Supp. 1305, 1321 & n.13 (S.D.N.Y. 1994).

70. *Id.* at 1321.

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able to the court and the opposing party along with the interview form for each respondent.

IV. Survey Questions and Structure

A. Were Questions on the Survey Framed to Be Clear, Precise, and Unbiased?

Although it seems obvious that questions on a survey should be clear and precise, phrasing questions to reach that goal is often difficult. Even questions that appear clear can convey unexpected meanings and ambiguities to potential respondents. For example, the question "What is the average number of days each week you have butter?" appears to be straightforward. Yet some respondents wondered whether margarine counted as butter, and when the question was revised to include the introductory phrase "not including margarine," the reported frequency of butter use dropped dramatically.⁷¹

When unclear questions are included in a survey, they may threaten the validity of the survey by systematically distorting responses if respondents are misled in a particular direction, or by inflating random error if respondents guess because they do not understand the question.⁷² If the crucial question is sufficiently ambiguous or unclear, it may be the basis for rejecting the survey. For example, a survey was designed to assess community sentiment that would warrant a change of venue in trying a case for damages sustained when a hotel skywalk collapsed.⁷³ The court found that the question "Based on what you have heard, read or seen, do you believe that in the current compensatory damage trials, the defendants, such as the contractors, designers, owners, and operators of the Hyatt Hotel, should be punished?" could neither be correctly understood nor easily answered.⁷⁴ The court noted that the phrase "compensatory damages," although well-defined for attorneys, was unlikely to be meaningful for laypersons.⁷⁵

Texts on survey research generally recommend pretests as a way to increase the likelihood that questions are clear and unambiguous,⁷⁶ and some courts have

71. Floyd J. Fowler, Jr., *How Unclear Terms Affect Survey Data*, 56 Pub. Opinion Q. 218, 225-26 (1992).

72. *Id.* at 219.

73. *Firestone v. Crown Ctr. Redevelopment Corp.*, 693 S.W.2d 99 (Mo. 1985) (en banc).

74. *Id.* at 102, 103.

75. *Id.* at 103. When there is any question about whether some respondent will understand a particular term or phrase, the term or phrase should be defined explicitly.

76. For a thorough treatment of pretesting methods, see Jean M. Converse & Stanley Presser, *Survey Questions: Handcrafting the Standardized Questionnaire* 51 (1986). See also Fred W. Morgan, *Judicial Standards for Survey Research: An Update and Guidelines*, 54 J. Marketing 59, 64 (1990).

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recognized the value of pretests.⁷⁷ In a pretest or pilot test,⁷⁸ the proposed survey is administered to a small sample (usually between twenty-five and seventy-five)⁷⁹ of the same type of respondents who would be eligible to participate in the full-scale survey. The interviewers observe the respondents for any difficulties they may have with the questions and probe for the source of any such difficulties so that the questions can be rephrased if confusion or other difficulties arise. Attorneys who commission surveys for litigation sometimes are reluctant to approve pilot work or to reveal that pilot work has taken place because they are concerned that if a pretest leads to revised wording of the questions, the trier of fact may believe that the survey has been manipulated and is biased or unfair. A more appropriate reaction is to recognize that pilot work can improve the quality of a survey and to anticipate that it often results in word changes that increase clarity and correct misunderstandings. Thus, changes may indicate informed survey construction rather than flawed survey design.⁸⁰

B. Were Filter Questions Provided to Reduce Guessing?

Some survey respondents may have no opinion on an issue under investigation, either because they have never thought about it before or because the question mistakenly assumes a familiarity with the issue. For example, survey respondents may not have noticed that the commercial they are being questioned about guaranteed the quality of the product being advertised and thus they may have no opinion on the kind of guarantee it indicated. Likewise, in an employee survey, respondents may not be familiar with the parental leave policy at their company and thus may have no opinion on whether they would consider taking advantage of the parental leave policy if they became parents. The following three alternative question structures will affect how those respondents answer and how their responses are counted.

First, the survey can ask all respondents to answer the question (e.g., "Do you understand the guarantee offered by Clover to be a one-year guarantee, a sixty-day guarantee, or a thirty-day guarantee?"). Faced with a direct question, particularly one that provides response alternatives, the respondent obligingly may supply an answer even if (in this example) the respondent did not notice the guarantee (or is unfamiliar with the parental leave policy). Such answers will

77. *E.g.*, *Zippo Mfg. Co. v. Rogers Imports, Inc.*, 216 F. Supp. 670 (S.D.N.Y. 1963).

78. The terms *pretest* and *pilot test* are sometimes used interchangeably to describe pilot work done in the planning stages of research. When they are distinguished, the difference is that a pretest tests the questionnaire, whereas a pilot test generally tests proposed collection procedures as well.

79. Converse & Presser, *supra* note 76, at 69. Converse and Presser suggest that a pretest with twenty-five respondents is appropriate when the survey uses professional interviewers.

80. See *infra* § VII.B for a discussion of obligations to disclose pilot work.

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reflect only what the respondent can glean from the question, or they may reflect pure guessing. The imprecision introduced by this approach will increase with the proportion of respondents who are unfamiliar with the topic at issue.

Second, the survey can use a quasi-filter question to reduce guessing by providing "don't know" or "no opinion" options as part of the question (e.g., "Did you understand the guarantee offered by Clover to be for more than a year, a year, or less than a year, or don't you have an opinion?").⁸¹ By signaling to the respondent that it is appropriate not to have an opinion, the question reduces the demand for an answer and, as a result, the inclination to hazard a guess just to comply. Respondents are more likely to choose a "no opinion" option if it is mentioned explicitly by the interviewer than if it is merely accepted when the respondent spontaneously offers it as a response. The consequence of this change in format is substantial. Studies indicate that, although the relative distribution of the respondents selecting the *listed* choices is unlikely to change dramatically, presentation of an explicit "don't know" or "no opinion" alternative commonly leads to a 20%-25% increase in the proportion of respondents selecting that response.⁸²

Finally, the survey can include full-filter questions, that is, questions that lay the groundwork for the substantive question by first asking the respondent if he or she has an opinion about the issue or happened to notice the feature that the interviewer is preparing to ask about (e.g., "Based on the commercial you just saw, do you have an opinion about how long Clover stated or implied that its guarantee lasts?"). The interviewer then asks the substantive question only of those respondents who have indicated that they have an opinion on the issue.

Which of these three approaches is used and the way it is used can affect the rate of "no opinion" responses that the substantive question will evoke.⁸³ Respondents are more likely to say they do not have an opinion on an issue if a full filter is used than if a quasi-filter is used.⁸⁴ However, in maximizing respondent expressions of "no opinion," full filters may produce an underreporting of opinions. There is some evidence that full-filter questions discourage respondents who actually have opinions from offering them by conveying the implicit suggestion that respondents can avoid difficult follow-up questions by saying that they have no opinion.⁸⁵

81. Norbert Schwarz & Hans-Jürgen Hippler, *Response Alternatives: The Impact of Their Choice and Presentation Order*, in *Measurement Errors in Surveys* 41, 45-46 (Paul P. Biemer et al. eds., 1991).

82. Howard Schuman & Stanley Presser, *Questions and Answers in Attitude Surveys: Experiments on Question Form, Wording and Context* 113-46 (1981).

83. Considerable research has been conducted on the effects of filters. For a review, see George F. Bishop et al., *Effects of Filter Questions in Public Opinion Surveys*, 47 *Pub. Opinion Q.* 528 (1983).

84. Schwarz & Hippler, *supra* note 81, at 45-46.

85. *Id.* at 46.

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In general, then, a survey that uses full filters tends to provide a conservative estimate of the number of respondents holding an opinion, whereas a survey that uses neither full filters nor quasi-filters tends to overestimate the number of respondents with opinions, because some respondents offering opinions are guessing. The strategy of including a "no opinion" or "don't know" response as a quasi-filter avoids both of these extremes. Thus, rather than asking, "Based on the commercial, do you believe that the two products are made in the same way, or are they made differently?"⁸⁶ or prefacing the question with a preliminary, "Do you have an opinion, based on the commercial, concerning the way that the two products are made?" the question could be phrased, "Based on the commercial, do you believe that the two products are made in the same way, or that they are made differently, or don't you have an opinion about the way they are made?"

*C. Did the Survey Use Open-Ended or Closed-Ended Questions?
How Was the Choice in Each Instance Justified?*

The questions that make up a survey instrument may be open-ended, closed-ended, or a combination of both. Open-ended questions require the respondent to formulate and express an answer in his or her own words (e.g., "What was the main point of the commercial?" "Where did you catch the fish you caught in these waters?"⁸⁷). Closed-ended questions provide the respondent with an explicit set of responses from which to choose; the choices may be as simple as yes or no (e.g., "Is Colby College coeducational?"⁸⁸) or as complex as a range of alternatives (e.g., "The two pain relievers have (1) the same likelihood of causing gastric ulcers; (2) about the same likelihood of causing gastric ulcers; (3) somewhat different likelihood of causing gastric ulcers; (4) a very different likelihood of causing gastric ulcers; or (5) none of the above."⁸⁹).

Open-ended and closed-ended questions may elicit very different responses.

86. The question in the example without the "no opinion" alternative was based on a question rejected by the court in *Coors Brewing Co. v. Anheuser-Busch Cos.*, 802 F. Supp. 965, 972-73 (S.D.N.Y. 1992).

87. A relevant example from *Wilhoite v. Olin Corp.* is described in McGovern & Lind, *supra* note 27, at 76.

88. *Presidents & Trustees of Colby College v. Colby College-N.H.*, 508 F.2d 804, 809 (1st Cir. 1975).

89. This question is based on one asked in *American Home Products Corp. v. Johnson & Johnson*, 654 F. Supp. 568, 581 (S.D.N.Y. 1987), that was found to be a leading question by the court, primarily because the choices suggested that the respondent had learned about aspirin's and ibuprofen's relative likelihood of causing gastric ulcers. In contrast, in *McNeilab, Inc. v. American Home Products Corp.*, 501 F. Supp. 517, 525 (S.D.N.Y. 1980), the court accepted as nonleading the question, "Based only on what the commercial said, would Maximum Strength Anacin contain more pain reliever, the same amount of pain reliever, or less pain reliever than the brand you, yourself, currently use most often?"

90. Howard Schuman & Stanley Presser, *Question Wording as an Independent Variable in Survey Analysis*,

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Most responses are less likely to be volunteered by respondents who are asked an open-ended question than they are to be chosen by respondents who are presented with a closed-ended question. The response alternatives in a closed-ended question may remind respondents of options that they would not otherwise consider or which simply do not come to mind as easily.⁹¹

The advantage of open-ended questions is that they give the respondent fewer hints about the answer that is expected or preferred. Precoded responses on a closed-ended question, in addition to reminding respondents of options that they might not otherwise consider,⁹² may direct the respondent away from or toward a particular response. For example, a commercial reported that in shampoo tests with more than 900 women, the sponsor's product received higher ratings than other brands.⁹³ According to a competitor, the commercial deceptively implied that each woman in the test rated more than one shampoo, when in fact each woman rated only one. To test consumer impressions, a survey might have shown the commercial and asked an open-ended question: "How many different brands mentioned in the commercial did each of the 900 women try?"⁹⁴ Instead, the survey asked a closed-ended question; respondents were given the choice of "one," "two," "three," "four," or "five or more." The fact that four of the five choices in the closed-ended question provided a response that was greater than one implied that the correct answer was probably more than one.⁹⁵ Note, however, that the open-ended question also may suggest that the answer is more than one. By asking "how many different brands," the question suggests (1) that the viewer should have received some message from the commercial about the number of brands each woman tried and (2) that different brands were tried. Thus, the wording of a question, open-ended or closed-ended, can be leading, and the degree of suggestiveness of each question must be considered in evaluating the objectivity of a survey.

6 Soc. Methods & Res. 151 (1977); Schuman & Presser, *supra* note 82, at 79-112; Converse & Presser, *supra* note 76, at 33.

91. For example, when respondents in one survey were asked, "What is the most important thing for children to learn to prepare them for life?", 62% picked "to think for themselves" from a list of five options, but only 5% spontaneously offered that answer when the question was open-ended. Schuman & Presser, *supra* note 82, at 104-07. An open-ended question presents the respondent with a free-recall task, whereas a closed-ended question is a recognition task. Recognition tasks in general reveal higher performance levels than recall tasks. Mary M. Smyth et al., *Cognition in Action* 25 (1987). In addition, there is evidence that respondents answering open-ended questions may be less likely to report some information that they would reveal in response to a closed-ended question when that information seems self-evident or irrelevant.

92. Schwarz & Hippler, *supra* note 81, at 43.

93. See *Vidal Sassoon, Inc. v. Bristol-Myers Co.*, 661 F.2d 272, 273 (2d Cir. 1981).

94. This was the wording of the stem of the closed-ended question in the survey discussed in *Vidal Sassoon*, 661 F.2d at 275-76.

95. Ninety-five percent of the respondents who answered the closed-ended question in the plaintiff's survey said that each woman had tried two or more brands. The open-ended question was never asked.

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Closed-ended questions have some additional potential weaknesses that arise if the choices are not constructed properly. If the respondent is asked to choose one response from among several choices, the response chosen will be meaningful only if the list of choices is exhaustive, that is, if the choices cover all possible answers a respondent might give to the question. If the list of possible choices is incomplete, a respondent may be forced to choose one that does not express his or her opinion.⁹⁶ Moreover, if respondents are told explicitly that they are not limited to the choices presented, most respondents nevertheless will select an answer from among the listed ones.⁹⁷

Although many courts prefer open-ended questions on the grounds that they tend to be less leading, the value of any open-ended or closed-ended question depends on the information it is intended to elicit. Open-ended questions are more appropriate when the survey is attempting to gauge what comes first to a respondent's mind, but closed-ended questions are more suitable for assessing choices between well-identified options or obtaining ratings on a clear set of alternatives.

D. If Probes Were Used to Clarify Ambiguous or Incomplete Answers, What Steps Were Taken to Ensure That the Probes Were Not Leading and Were Administered in a Consistent Fashion?

When questions allow respondents to express their opinions in their own words, some of the respondents may give ambiguous or incomplete answers. In such instances, interviewers may be instructed to record any answer that the respondent gives and move on to the next question, or they may be instructed to probe to obtain a more complete response or clarify the meaning of the ambiguous response. In either situation, interviewers should record verbatim both what the respondent says and what the interviewer says in the attempt to get clarification. Failure to record every part of the exchange in the order in which it occurs raises questions about the reliability of the survey, because neither the court nor the opposing party can evaluate whether the probe affected the views expressed by the respondent.

Vidal Sassoon, 661 F.2d at 276. Norbert Schwarz, *Assessing Frequency Reports of Mundane Behaviors: Contributions of Cognitive Psychology to Questionnaire Construction*, in *Research Methods in Personality and Social Psychology* 98 (Clyde Hendrick & Margaret S. Clark eds., 1990), suggests that respondents often rely on the range of response alternatives as a frame of reference when they are asked for frequency judgments. See, e.g., Roger Tourangeau & Tom W. Smith, *Asking Sensitive Questions: The Impact of Data Collection Mode, Question Format, and Question Context*, 60 Pub. Opinion Q. 275, 292 (1996).

96. See, e.g., *American Home Prods. Corp. v. Johnson & Johnson*, 654 F. Supp. 568, 581 (S.D.N.Y. 1987).

97. See Howard Schuman, *Ordinary Questions, Survey Questions, and Policy Questions*, 50 Pub. Opinion Q. 432, 435-36 (1986).

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If the survey is designed to allow for probes, interviewers must be given explicit instructions on when they should probe and what they should say in probing. Standard probes used to draw out all that the respondent has to say (e.g., "Any further thoughts?" "Anything else?" "Can you explain that a little more?") are relatively innocuous and noncontroversial in content, but persistent continued requests for further responses to the same or nearly identical questions may convey the idea to the respondent that he or she has not yet produced the "right" answer.⁹⁸ Interviewers should be trained in delivering probes to maintain a professional and neutral relationship with the respondent (as they should during the rest of the interview), which minimizes any sense of passing judgment on the content of the answers offered. Moreover, interviewers should be given explicit instructions on when to probe, so that probes are administered consistently.

A more difficult type of probe to construct and deliver reliably is one that requires a substantive question tailored to the answer given by the respondent. The survey designer must provide sufficient instruction to interviewers so that they avoid giving directive probes that suggest one answer over another. Those instructions, along with all other aspects of interviewer training, should be made available for evaluation by the court and the opposing party.

E. What Approach Was Used to Avoid or Measure Potential Order or Context Effects?

The order in which questions are asked on a survey and the order in which response alternatives are provided in a closed-ended question can influence the answers.⁹⁹ Thus, although asking a general question before a more specific question on the same topic is unlikely to affect the response to the specific question, reversing the order of the questions may influence responses to the general question. As a rule, then, surveys are less likely to be subject to order effects if

98. See, e.g., *Johnson & Johnson-Merck Consumer Pharms. Co. v. Rhone-Poulenc Rorer Pharms., Inc.*, 19 F.3d 125, 135 (3d Cir. 1994); *American Home Prods. Corp. v. Procter & Gamble Co.*, 871 F. Supp. 739, 748 (D.N.J. 1994).

99. See Schuman & Presser, *supra* note 82, at 23, 56-74; Norman M. Bradburn, *Response Effects*, in *Handbook of Survey Research*, *supra* note 1, at 289, 302. In *R.J. Reynolds Tobacco Co. v. Loew's Theatres, Inc.*, 511 F. Supp. 867, 875 (S.D.N.Y. 1980), the court recognized the biased structure of a survey which disclosed the tar content of the cigarettes being compared before questioning respondents about their cigarette preferences. Not surprisingly, respondents expressed a preference for the lower tar product. See also *B. & J. Gallo Winery v. Pasatiempos Gallo, S.A.*, 905 F. Supp. 1403, 1409-10 (B.D. Cal. 1994) (court recognized that earlier questions referring to playing cards, board or table games, or party supplies, such as confetti, increased the likelihood that respondents would include these items in answers to the questions that followed).

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the questions go from the general (e.g., "What do you recall being discussed in the advertisement?") to the specific (e.g., "Based on your reading of the advertisement, what companies do you think the ad is referring to when it talks about rental trucks that average five miles per gallon?").¹⁰⁰

The mode of questioning can influence the form that an order effect takes. In mail surveys, respondents are more likely to select the first choice offered (a primacy effect); in telephone surveys, respondents are more likely to choose the last choice offered (a recency effect). Although these effects are typically small, no general formula is available that can adjust values to correct for order effects, because the size and even the direction of the order effects may depend on the nature of the question being asked and the choices being offered. Moreover, it may be unclear which order is most appropriate. For example, if the respondent is asked to choose between two different products, and there is a tendency for respondents to choose the first product mentioned,¹⁰¹ which order of presentation will produce the more accurate response?¹⁰²

To control for order effects, the order of the questions and the order of the response choices in a survey should be rotated,¹⁰³ so that, for example, one-third of the respondents have Product A listed first, one-third of the respondents have Product B listed first, and one-third of the respondents have Product C listed first. If the three different orders¹⁰⁴ are distributed randomly among respondents, no response alternative will have an inflated chance of being selected because of its position, and the average of the three will provide a reasonable estimate of response level.¹⁰⁵

100. This question was accepted by the court in *U-Haul International, Inc. v. Jartran, Inc.*, 522 F. Supp. 1238, 1249 (D. Ariz. 1981), *aff'd*, 681 F.2d 1159 (9th Cir. 1982).

101. Similarly, candidates in the first position on the ballot tend to attract extra votes when the candidates are not well known. Henry M. Bain & Donald S. Hecock, *Ballot Position and Voter's Choice: The Arrangement of Names on the Ballot and Its Effect on the Voter* (1973).

102. See *Rust Env't & Infrastructure, Inc. v. Teunissen*, 131 F.3d 1210, 1218 (7th Cir. 1997) (survey did not pass muster in part because of failure to incorporate random rotation of corporate names that were the subject of a trademark dispute).

103. See, e.g., *Stouffer Foods Corp.*, 118 F.T.C. 746, No. 9250, 1994 FTC LEXIS 196, at *24-25 (Sept. 26, 1994); cf. *Winning Ways, Inc. v. Holloway Sportswear, Inc.*, 913 F. Supp. 1454, 1465-67 (D. Kan. 1996) (failure to rotate the order in which the jackets were shown to the consumers led to reduced weight for the survey).

104. Actually, there are six possible orders of the three alternatives: ABC, ACB, BAC, BCA, CAB, and CBA. Thus, the optimal survey design would allocate equal numbers of respondents to each of the six possible orders.

105. Although rotation is desirable, many surveys are conducted with no attention to this potential bias. Since it is impossible to know in the abstract whether a particular question suffers much, little, or not at all from an order bias, lack of rotation should not preclude reliance on the answer to the question, but it should reduce the weight given to that answer.

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F. If the Survey Was Designed to Test a Causal Proposition, Did the Survey Include an Appropriate Control Group or Question?

Most surveys that are designed to provide evidence of trademark infringement or deceptive advertising are not conducted to describe consumer beliefs. Instead, they are intended to show how a trademark or the content of a commercial influences respondents' perceptions or understanding of a product or commercial. Thus, the question is whether the commercial misleads the consumer into thinking that Product A is a superior pain reliever, not whether consumers hold inaccurate beliefs about the product. Yet if consumers already believe, before viewing the commercial, that Product A is a superior pain reliever, a survey that records consumers' impressions after they view the commercial may reflect those preexisting beliefs rather than impressions produced by the commercial.

Surveys that record consumer impressions have a limited ability to answer questions about the origins of those impressions. The difficulty is that the consumer's response to any question on the survey may be the result of information or misinformation from sources other than the trademark the respondent is being shown or the commercial he or she has just watched. In a trademark survey attempting to show secondary meaning, for example, respondents were shown a picture of the stripes used on Mennen stick deodorant and asked, "[W]hich [brand] would you say uses these stripes on their package?"¹⁰⁶ The court recognized that the high percentage of respondents selecting "Mennen" from an array of brand names may have represented "merely a playback of brand share"¹⁰⁷; that is, respondents asked to give a brand name may guess the one that is most familiar, generally the brand with the largest market share.¹⁰⁸

Some surveys attempt to reduce the impact of preexisting impressions on respondents' answers by instructing respondents to focus solely on the stimulus as a basis for their answers. Thus, the survey includes a preface (e.g., "based on the commercial you just saw") or directs the respondent's attention to the mark at issue (e.g., "these stripes on the package"). Such efforts are likely to be only partially successful. It is often difficult for respondents to identify accurately the source of their impressions.¹⁰⁹ The more routine the idea being examined in the survey (e.g., that the advertised pain reliever is more effective than others on the

106. *Mennen Co. v. Gillette Co.*, 565 F. Supp. 648, 652 (S.D.N.Y. 1983), *aff'd*, 742 F.2d 1437 (2d Cir. 1984). To demonstrate secondary meaning, "the [c]ourt must determine whether the mark has been so associated in the mind of consumers with the entity that it identifies that the goods sold by that entity are distinguished by the mark or symbol from goods sold by others." *Id.*

107. *Id.*

108. See also *Upjohn Co. v. American Home Prods. Corp.*, No. 1-95-CV-237, 1996 U.S. Dist. LEXIS 8049, at *42-44 (W.D. Mich. Apr. 5, 1996).

109. See Richard E. Nisbett & Timothy D. Wilson, *Telling More Than We Can Know: Verbal Reports on Mental Processes*, 84 Psychol. Rev. 231 (1977).

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market; that the mark belongs to the brand with the largest market share), the more likely it is that the respondent's answer is influenced by preexisting impressions, by expectations about what commercials generally say (e.g., the product being advertised is better than its competitors), or by guessing, rather than by the actual content of the commercial message or trademark being evaluated.

It is possible to adjust many survey designs so that causal inferences about the effect of a trademark or an allegedly deceptive commercial become clear and unambiguous. By adding an appropriate control group, the survey expert can test directly the influence of the stimulus.¹¹⁰ In the simplest version of a survey experiment, respondents are assigned randomly to one of two conditions.¹¹¹ For example, respondents assigned to the experimental condition view an allegedly deceptive commercial, and respondents assigned to the control condition either view a commercial that does not contain the allegedly deceptive material or do not view any commercial.¹¹² Respondents in both the experimental and control groups answer the same set of questions. The effect of the allegedly deceptive message is evaluated by comparing the responses made by the experimental group members with those of the control group members. If 40% of the respondents in the experimental group responded with the deceptive message (e.g., the advertised product has fewer calories than its competitor), whereas only 8% of the respondents in the control group gave that response, the difference between 40% and 8% (within the limits of sampling error¹¹³) can be attributed only to the allegedly deceptive commercial. Without the control group, it is not possible to determine how much of the 40% is due to respondents' preexisting beliefs or other background noise (e.g., respondents who misunderstand the question or misstate their responses). Both preexisting beliefs and other background noise should have produced similar response levels in the experimental

110. See Shari S. Diamond, *Using Psychology to Control Law: From Deceptive Advertising to Criminal Sentencing*, 13 *Law & Hum. Behav.* 239, 244-46 (1989); Shari S. Diamond & Linda Dimitropoulos, *Deception and Puffery in Advertising: Behavioral Science Implications for Regulation* (American Bar Found. Working Paper Series No. 9105, 1994); Jacob Jacoby & Constance Small, *Applied Marketing: The FDA Approach to Defining Misleading Advertising*, 39 *J. Marketing* 65, 68 (1975). For a more general discussion of the role of control groups, see David H. Kaye & David A. Freedman, *Reference Guide on Statistics*, § II.A, in this manual.

111. Random assignment should not be confused with random selection. When respondents are assigned randomly to different treatment groups (e.g., respondents in each group watch a different commercial), the procedure ensures that within the limits of sampling error the two groups of respondents will be equivalent except for the different treatments they receive. Respondents selected for a mail intercept study, and not from a probability sample, may be assigned randomly to different treatment groups. Random selection, in contrast, describes the method of selecting a sample of respondents in a probability sample. See *supra* § III.C.

112. This alternative commercial could be a "tombstone" advertisement that includes only the name of the product or a more elaborate commercial that does not include the claim at issue.

113. For a discussion of sampling error, see David H. Kaye & David A. Freedman, *Reference Guide on Statistics*, § IV, in this manual.

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and control groups. In addition, if respondents who viewed the allegedly deceptive commercial respond differently than respondents who viewed the control commercial, the difference cannot be the result of a leading question, because both groups answered the same question. The ability to evaluate the effect of the wording of a particular question makes the control group design particularly useful in assessing responses to closed-ended questions,¹¹⁴ which may encourage guessing or particular responses. Thus, the focus on the response level in a control group design is not on the absolute response level, but on the difference between the response level of the experimental group and that of the control group.

In designing a control group study, the expert should select a stimulus for the control group that shares as many characteristics with the experimental stimulus as possible, with the key exception of the characteristic whose influence is being assessed. A survey with an imperfect control group generally provides better information than a survey with no control group at all, but the choice of the specific control group requires some care and should influence the weight that the survey receives. For example, a control stimulus should not be less attractive than the experimental stimulus if the survey is designed to measure how familiar the experimental stimulus is to respondents, since attractiveness may affect perceived familiarity.¹¹⁵ Nor should the control stimulus share with the experimental stimulus the feature whose impact is being assessed. If, for example, the control stimulus in a case of alleged trademark infringement is itself a likely source of consumer confusion, reactions to the experimental and control stimuli may not differ because both cause respondents to express the same level of confusion.¹¹⁶

Explicit attention to the value of control groups in trademark and deceptive advertising litigation is a recent phenomenon, but it is becoming more common.¹¹⁷ A LEXIS search using *Lanham Act* and *control group* revealed four

114. The Federal Trade Commission has long recognized the need for some kind of control for closed-ended questions, although it has not specified the type of control that is necessary. *Stouffer Foods Corp.*, 118 F.T.C. 746, No. 9250, 1994 FTC LEXIS 196, at *31 (Sept. 26, 1994).

115. See, e.g., *Indianapolis Colts, Inc. v. Metropolitan Baltimore Football Club Ltd. Partnership*, 34 F.3d 410, 415-16 (7th Cir. 1994) (The court recognized that the name "Baltimore Horses" was less attractive for a sports team than the name "Baltimore Colts."). See also *Reed-Union Corp. v. Turtle Wax, Inc.*, 77 F.3d 909, 912 (7th Cir. 1996) (court noted that one expert's choice of a control brand with a well-known corporate source was less appropriate than the opposing expert's choice of a control brand whose name did not indicate a specific corporate source).

116. See, e.g., *Western Publ'g Co. v. Publications Int'l, Ltd.*, No. 94-C-6803, 1995 U.S. Dist. LEXIS 5917, at *45 (N.D. Ill. May 2, 1995) (court noted that the control product was "arguably more infringing than" the defendant's product) (emphasis omitted).

117. See, e.g., *American Home Prods. Corp. v. Procter & Gamble Co.*, 871 F. Supp. 739, 749 (D.N.J. 1994) (discounting survey results based on failure to control for participants' preconceived notions); *ConAgra, Inc. v. Geo. A. Hormel & Co.*, 784 F. Supp. 700, 728 (D. Neb. 1992) ("Since no control was used, the . . . study, standing alone, must be significantly discounted."), *aff'd*, 990 F.2d 368 (8th Cir. 1993).

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district court cases in the six years since the first edition of this manual in 1994,¹¹⁸ five district court cases in the seven years from 1987 to 1993,¹¹⁹ and only one case before 1987¹²⁰ in which surveys with control groups were discussed. Other cases, however, have described or considered surveys using control group designs without labeling the comparison group a control group.¹²¹ Indeed, one reason why cases involving surveys with control groups may be underrepresented in reported cases is that a survey with a control group produces less ambiguous findings, which may lead to a resolution before a preliminary injunction hearing or trial occurs.¹²²

Another more common use of control methodology is a control question. Rather than administering a control stimulus to a separate group of respondents,

118. *National Football League Properties, Inc. v. Prostyle, Inc.*, 57 F. Supp. 2d 665 (E.D. Wis. 1999); *Nabisco, Inc. v. PF Brands, Inc.*, 50 F. Supp. 2d 188 (S.D.N.Y. 1999); *Proctor & Gamble Co. v. Colgate-Palmolive Co.*, No. 96 Civ. 9123, 1998 U.S. Dist. LEXIS 17773 (S.D.N.Y. Nov. 5, 1998); *Mattel, Inc. v. MCA Records, Inc.*, 28 F. Supp. 2d 1120 (C.D. Cal. 1998); *Westchester Media Co. v. PRL USA Holdings*, No. H-97-3278, 1998 U.S. Dist. LEXIS 11737 (S.D. Tex. July 2, 1998); *Time Inc. v. Petersen Publ'g Co.*, 976 F. Supp. 263 (S.D.N.Y. 1997), *aff'd*, 173 F.3d 113 (2d Cir. 1999); *Adjusters Int'l, Inc. v. Public Adjusters Int'l, Inc.*, No. 92-CV-1426, 1996 U.S. Dist. LEXIS 12604 (N.D.N.Y. Aug. 27, 1996); *Upjohn Co. v. American Home Prods. Corp.*, No. 1-95-CV-237, 1996 U.S. Dist. LEXIS 8049 (W.D. Mich. Apr. 5, 1996); *Copy Cop, Inc. v. Task Printing, Inc.*, 908 F. Supp. 37 (D. Mass. 1995); *Volkswagen Aktiengesellschaft v. Uptown Motors*, No. 91-CIV-3447, 1995 U.S. Dist. LEXIS 13869 (S.D.N.Y. July 13, 1995); *Western Publ'g Co. v. Publications Int'l, Ltd.*, No. 94-C-6803, 1995 U.S. Dist. LEXIS 5917 (N.D. Ill. May 2, 1995); *Dogloo, Inc. v. Doskocil Mfg. Co.*, 893 F. Supp. 911 (C.D. Cal. 1995); *Reed-Union Corp. v. Turtle Wax, Inc.*, 869 F. Supp. 1304 (N.D. Ill. 1994), *aff'd*, 77 F.3d 909 (7th Cir. 1996); *Pfizer, Inc. v. Miles, Inc.*, 868 F. Supp. 437 (D. Conn. 1994).

119. *ConAgra, Inc. v. Geo. A. Hormel & Co.*, 784 F. Supp. 700 (D. Neb. 1992), *aff'd*, 990 F.2d 368 (8th Cir. 1993); *Johnson & Johnson-Merck Consumer Pharms. Co. v. Smithkline Beecham Corp.*, No. 91 Civ. 0960, 1991 U.S. Dist. LEXIS 13689 (S.D.N.Y. Sept. 30, 1991), *aff'd*, 960 F.2d 294 (2d Cir. 1992); *Goya Foods, Inc. v. Condal Distribs., Inc.*, 732 F. Supp. 453 (S.D.N.Y. 1990); *Stunneb Ruger & Co. v. Arcadia Mach. & Tool, Inc.*, No. 85-8459, 1988 U.S. Dist. LEXIS 16451 (C.D. Cal. Nov. 7, 1988); *Frisch's Restaurant, Inc. v. Elby's Big Boy, Inc.*, 661 F. Supp. 971 (S.D. Ohio 1988), *aff'd*, 849 F.2d 1012 (6th Cir. 1988).

120. *American Basketball Ass'n v. AMF Voit, Inc.*, 358 F. Supp. 981 (S.D.N.Y.), *aff'd*, 487 F.2d 1393 (2d Cir. 1973).

121. *Indianapolis Colts, Inc. v. Metropolitan Baltimore Football Club Ltd. Partnership*, No. 94-727-C, 1994 U.S. Dist. LEXIS 19277, at *10-11 (S.D. Ind. June 27, 1994), *aff'd*, 34 F.3d 410 (7th Cir. 1994). In *Indianapolis Colts*, the district court described a survey conducted by the plaintiff's expert in which half of the interviewees were shown a shirt with the name "Baltimore CFL Colts" on it and half were shown a shirt on which the word "Horses" had been substituted for the word "Colts." *Id.* The court noted that the comparison of reactions to the horse and colt versions of the shirt made it possible "to determine the impact from the use of the word 'Colts.'" *Id.* at *11. See also *Quality Inns Int'l, Inc. v. McDonald's Corp.*, 695 F. Supp. 198, 218 (D. Md. 1988) (survey revealed confusion between McDonald's and McSleep, but control survey revealed no confusion between McDonald's and McTavish).

122. The relatively infrequent mention of control groups in surveys discussed in federal cases is not confined to Lanham Act litigation. A LEXIS search using *survey* and *control group* revealed thirty district court cases in the six years from 1994 in which *control group* was used to refer to a methodological feature: the fourteen Lanham Act cases cited *supra* note 118; nine that referred to medical, physiological, or pharmacological experiments; and seven others.

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the survey asks all respondents one or more control questions along with the question about the product or service. In a trademark dispute, for example, a survey indicated that 7.2% of respondents believed that "The Mart" and "K-Mart" were owned by the same individuals. The court found no likelihood of confusion based on survey evidence that 5.7% of the respondents also thought that "The Mart" and "King's Department Store" were owned by the same source.¹²³

Similarly, a standard technique used to evaluate whether a brand name is generic is to present survey respondents with a series of product or service names and ask them to indicate in each instance whether they believe the name is a brand name or a common name. By showing that 68% of respondents considered Teflon a brand name (a proportion similar to the 75% of respondents who recognized the acknowledged trademark Jell-O as a brand name, and markedly different from the 13% who thought aspirin was a brand name), the makers of Teflon retained their trademark.¹²⁴

Every measure of opinion or belief in a survey reflects some degree of error. Control groups and control questions are the most reliable means for assessing response levels against the baseline level of error associated with a particular question.

G. What Limitations Are Associated with the Mode of Data Collection Used in the Survey?

Three primary methods are used to collect survey data: (1) in-person interviews (2) telephone surveys, and (3) mail surveys.¹²⁵ The choice of a data collection method for a survey should be justified by its strengths and weaknesses.

1. In-person interviews

Although costly, in-person interviews generally are the preferred method of data collection, especially when visual materials must be shown to the respondent under controlled conditions.¹²⁶ When the questions are complex and the interviewers are skilled, in-person interviewing provides the maximum oppor-

123. *S.S. Kresge Co. v. United Factory Outlet, Inc.*, 598 F.2d 694, 697 (1st Cir. 1979). Note that the aggregate percentages reported here do not reveal how many of the same respondents were confused by both names, an issue that may be relevant in some situations. See Joseph L. Gastwirth, *Reference Guide on Survey Research*, 36 *Jurimetrics J.* 181, 187-88 (1996) (review essay).

124. *B.I. DuPont de Nemours & Co. v. Yoshida Int'l, Inc.*, 393 F. Supp. 502, 526-27 & n.54 (E.D.N.Y. 1975).

125. Methods also may be combined, as when the telephone is used to "screen" for eligible respondents, who then are invited to participate in an in-person interview.

126. A mail survey also can include limited visual materials but cannot exercise control over when and how the respondent views them.

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tunity to clarify or probe. Unlike a mail survey, both in-person and telephone interviews have the capability to implement complex skip sequences (in which the respondent's answer determines which question will be asked next) and the power to control the order in which the respondent answers the questions. As described in section V.A, appropriate interviewer training is necessary if these potential benefits are to be realized. Objections to the use of in-person interviews arise primarily from their high cost or, on occasion, from evidence of inept or biased interviewers.

2. Telephone surveys

Telephone surveys offer a comparatively fast and low-cost alternative to in-person surveys and are particularly useful when the population is large and geographically dispersed. Telephone interviews (unless supplemented with mailed materials) can be used only when it is unnecessary to show the respondent any visual materials. Thus, an attorney may present the results of a telephone survey of jury-eligible citizens in a motion for a change of venue in order to provide evidence that community prejudice raises a reasonable suspicion of potential jury bias.¹²⁷ Similarly, potential confusion between a restaurant called McBagel's and the McDonald's fast-food chain was established in a telephone survey. Over objections from defendant McBagel's that the survey did not show respondents the defendant's print advertisements, the court found likelihood of confusion based on the survey, noting that "by soliciting audio responses [the telephone survey] was closely related to the radio advertising involved in the case."¹²⁸ In contrast, when words are not sufficient because, for example, the survey is assessing reactions to the trade dress or packaging of a product that is alleged to promote confusion, a telephone survey alone does not offer a suitable vehicle for questioning respondents.¹²⁹

In evaluating the sampling used in a telephone survey, the trier of fact should consider

- (when prospective respondents are not business personnel) whether some form of random-digit dialing¹³⁰ was used instead of or to supplement tele-

127. *United States v. Partin*, 320 F. Supp. 275, 279-80 (E.D. La. 1970). For a discussion of surveys used in motions for change of venue, see Neal Miller, *Facts, Expert Facts, and Statistics: Descriptive and Experimental Research Methods in Litigation, Part II*, 40 Rutgers L. Rev. 467, 470-74 (1988); National Jury Project, *Jurywork: Systematic Techniques* (Elissa Krauss & Beth Bonora eds., 2d ed. 1983).

128. *McDonald's Corp. v. McBagel's, Inc.*, 649 F. Supp. 1268, 1278 (S.D.N.Y. 1986).

129. *Thompson Med. Co. v. Pfizer Inc.*, 753 F.2d 208 (2d Cir. 1985); *Incorporated Publ'g Corp. v. Manhattan Magazine, Inc.*, 616 F. Supp. 370 (S.D.N.Y. 1985), *aff'd without op.*, 788 F.2d 3 (2d Cir. 1986).

130. Random digit dialing provides coverage of households with both listed and unlisted telephone numbers by generating numbers at random from the frame of all possible telephone numbers. James M. Lepkowski, *Telephone Sampling Methods in the United States*, in *Telephone Survey Methodology* 81-91 (Robert M. Groves et al. eds., 1988).

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phone numbers obtained from telephone directories, because up to 65% of all residential telephone numbers in some areas may be unlisted;¹³¹

- whether the sampling procedures required the interviewer to sample within the household or business, instead of allowing the interviewer to administer the survey to any qualified individual who answered the telephone;¹³² and
- whether interviewers were required to call back at several different times of the day and on different days to increase the likelihood of contacting individuals or businesses with different schedules.

Telephone surveys that do not include these procedures may, like other nonprobability sampling approaches, be adequate for providing rough approximations. The vulnerability of the survey depends on the information being gathered. More elaborate procedures for achieving a representative sample of respondents are advisable if the survey instrument requests information that is likely to differ for individuals with listed telephone numbers and individuals with unlisted telephone numbers, or individuals rarely at home and those usually at home.

The report submitted by a survey expert who conducts a telephone survey should specify

1. the procedures that were used to identify potential respondents;
2. the number of telephone numbers for which no contact was made; and
3. the number of contacted potential respondents who refused to participate in the survey.

Computer-assisted telephone interviewing, or CATI, is increasingly used in the administration and data entry of large-scale surveys.¹³³ A computer protocol may be used to generate telephone numbers and dial them as well as to guide the interviewer. The interviewer conducting a computer-assisted interview (CAI), whether by telephone or in a face-to-face setting, follows the script for the interview generated by the computer program and types in the respondent's answers as the interview proceeds. A primary advantage of CATI and other CAI procedures is that skip patterns can be built into the program so that, for example, if the respondent is asked whether she has ever been the victim of a burglary and she says yes, the computer will generate further questions about

131. In 1992, the percentage of households with unlisted numbers reached 65% in Las Vegas and 62% in Los Angeles. Survey Sampling, Inc., *The Frame 2* (March 1993). Studies comparing listed and unlisted household characteristics show some important differences. Lepkowski, *supra* note 130, at 76.

132. This is a consideration only if the survey is sampling individuals. If the survey is seeking information on the household, more than one individual may be able to answer questions on behalf of the household.

133. William L. Nicholls II & R.M. Groves, *The Status of Computer-Assisted Telephone Interviewing*, 2J. Official Stat. 93 (1986); Mary A. Spaeth, *CATI Facilities at Academic Research Organizations*, 21 Surv. Res. 11 (1990); William B. Saris, *Computer-Assisted Interviewing* (1991).

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the burglary, but if she says no, the program will automatically skip the follow-up burglary questions. Interviewer errors in following the skip patterns are therefore avoided, making CAI procedures particularly valuable when the survey involves complex branching and skip patterns.¹³⁴ CAI procedures can also be used to control for order effects by having the program rotate the order in which questions or choices are presented.¹³⁵ CAI procedures, however, require additional planning to take advantage of the potential for improvements in data quality. When a CAI protocol is used in a survey presented in litigation, the party offering the survey should supply for inspection the computer program that was used to generate the interviews. Moreover, CAI procedures do not eliminate the need for close monitoring of interviews to ensure that interviewers are accurately reading the questions in the interview protocol and accurately entering the answers that the respondent is giving to those questions.

3. Mail surveys

In general, mail surveys tend to be substantially less costly than both in-person and telephone surveys.¹³⁶ Although response rates for mail surveys are often low, researchers have obtained 70% response rates in some general public surveys and response rates of over 90% with certain specialized populations.¹³⁷ Procedures that encourage high response rates include multiple mailings, highly personalized communications, prepaid return envelopes and incentives or gratuities, assurances of confidentiality, and first-class outgoing postage.¹³⁸

A mail survey will not produce a high rate of return unless it begins with an accurate and up-to-date list of names and addresses for the target population. Even if the sampling frame is adequate, the sample may be unrepresentative if some individuals are more likely to respond than others. For example, if a survey targets a population that includes individuals with literacy problems, these individuals will tend to be underrepresented. Open-ended questions are generally of limited value on a mail survey because they depend entirely on the respondent to answer fully and do not provide the opportunity to probe or clarify

134. Saxi, *supra* note 133, at 20, 27.

135. See, e.g., *Intel Corp. v. Advanced Micro Devices, Inc.*, 756 F. Supp. 1292, 1296-97 (N.D. Cal. 1991) (survey designed to test whether the term 386 as applied to a microprocessor was generic used a CATI protocol that tested reactions to five terms presented in rotated order).

136. Don A. Dillman, *Mail and Other Self-Administered Questionnaires*, in *Handbook of Survey Research*, *supra* note 1, at 359, 373.

137. *Id.* at 360.

138. See, e.g., Richard J. Fox et al., *Mail Survey Response Rate: A Meta-Analysis of Selected Techniques for Inducing Response*, 52 Pub. Opinion Q. 467, 482 (1988); Eleanor Singer et al., *Confidentiality Assurances and Response: A Quantitative Review of the Experimental Literature*, 59 Pub. Opinion Q. 66, 71 (1995); Kenneth D. Hopkins & Arlen R. Gullickson, *Response Rates in Survey Research: A Meta-Analysis of the Effects of Monetary Gratuities*, 61 J. Experimental Educ. 52, 54-57, 59 (1992).

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unclear answers. Similarly, if eligibility to answer some questions depends on the respondent's answers to previous questions, such skip sequences may be difficult for some respondents to follow. Finally, because respondents complete mail surveys without supervision, survey personnel are unable to prevent respondents from discussing the questions and answers with others before completing the survey and to control the order in which respondents answer the questions. If it is crucial to have respondents answer questions in a particular order, a mail survey cannot be depended on to provide adequate data.¹³⁹

4. Internet surveys

A more recent innovation in survey technology is the Internet survey in which potential respondents are contacted and their responses are collected over the Internet. Internet surveys can substantially reduce the cost of reaching potential respondents and offer some of the advantages of in-person interviews by allowing the computer to show the respondent pictures or lists of response choices in the course of asking the respondent questions. The key limitation is that the respondents accessible over the Internet must fairly represent the relevant population whose responses the survey was designed to measure. Thus, a litigant presenting the results of a web-based survey should be prepared to provide evidence on the potential bias in sampling that the web-based survey is likely to introduce. If the target population consists of computer users, the bias may be minimal. If the target population consists of owners of television sets, significant bias is likely.

V. Surveys Involving Interviewers

A. Were the Interviewers Appropriately Selected and Trained?

A properly defined population or universe, a representative sample, and clear and precise questions can be depended on to produce trustworthy survey results only if "sound interview procedures were followed by competent interviewers."¹⁴⁰ Properly trained interviewers receive detailed written instructions on everything they are to say to respondents, any stimulus materials they are to use in the survey, and how they are to complete the interview form. These instructions should be made available to the opposing party and to the trier of fact. Thus, interviewers should be told, and the interview form on which answers are recorded should indicate, which responses, if any, are to be read to the respondent. Interviewers also should be instructed to record verbatim the respondent's

139. Dillman, *supra* note 136, at 368-70.

140. Toys "R" Us, Inc. v. Canarsie Kiddie Shop, Inc., 559 F. Supp. 1189, 1205 (E.D.N.Y. 1983).

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answers, to indicate explicitly whenever they repeat a question to the respondent, and to record any statements they make to or supplementary questions they ask the respondent.

Interviewers require training to ensure that they are able to follow directions in administering the survey questions. Some training in general interviewing techniques is required for most interviews (e.g., practice in pausing to give the respondent enough time to answer and practice in resisting invitations to express the interviewer's beliefs or opinions). Although procedures vary, one treatise recommends at least five hours of training in general interviewing skills and techniques for new interviewers.¹⁴¹

The more complicated the survey instrument is, the more training and experience the interviewers require. Thus, if the interview includes a skip pattern (where, e.g., Questions 4-6 are asked only if the respondent says yes to Question 3, and Questions 8-10 are asked only if the respondent says no to Question 3), interviewers must be trained to follow the pattern. Similarly, if the questions require specific probes to clarify ambiguous responses, interviewers must receive instruction on when to use the probes and what to say. In some surveys, the interviewer is responsible for last-stage sampling (i.e., selecting the particular respondents to be interviewed), and training is especially crucial to avoid interviewer bias in selecting respondents who are easiest to approach or easiest to find.

Training and instruction of interviewers should include directions on the circumstances under which interviews are to take place (e.g., question only one respondent at a time out of the hearing of any other respondent). The trustworthiness of a survey is questionable if there is evidence that some interviews were conducted in a setting in which respondents were likely to have been distracted or in which others were present and could overhear. Such evidence of careless administration of the survey was one ground used by a court to reject as inadmissible a survey that purported to demonstrate consumer confusion.¹⁴²

Some compromises may be accepted when surveys must be conducted swiftly. In trademark and deceptive advertising cases, the plaintiff's usual request is for a preliminary injunction, because a delay means irreparable harm. Nonetheless, careful instruction and training of interviewers who administer the survey and complete disclosure of the methods used for instruction and training are crucial elements that, if compromised, seriously undermine the trustworthiness of any survey.

141. Eve Weinberg, *Data Collection: Planning and Management*, in *Handbook of Survey Research*, *supra* note 1, at 329, 332.

142. *Toys "R" Us*, 559 F. Supp. at 1204 (some interviews apparently were conducted in a bowling alley; some interviewees waiting to be interviewed overheard the substance of the interview while they were waiting).

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B. What Did the Interviewers Know About the Survey and Its Sponsorship?

One way to protect the objectivity of survey administration is to avoid telling interviewers who is sponsoring the survey. Interviewers who know the identity of the survey's sponsor may affect results inadvertently by communicating to respondents their expectations or what they believe are the preferred responses of the survey's sponsor. To ensure objectivity in the administration of the survey, it is standard interview practice to conduct double-blind research whenever possible: both the interviewer and the respondent are blind to the sponsor of the survey and its purpose. Thus, the survey instrument should provide no explicit clues (e.g., a sponsor's letterhead appearing on the survey) and no implicit clues (e.g., reversing the usual order of the yes and no response boxes on the interviewer's form next to a crucial question, thereby potentially increasing the likelihood that *no* will be checked¹⁴³) about the sponsorship of the survey or the expected responses.

Nonetheless, in some surveys (e.g., some government surveys), disclosure of the survey's sponsor to respondents (and thus to interviewers) is required. Such surveys call for an evaluation of the likely biases introduced by interviewer or respondent awareness of the survey's sponsorship. In evaluating the consequences of sponsorship awareness, it is important to consider (1) whether the sponsor has views and expectations that are apparent and (2) whether awareness is confined to the interviewers or involves the respondents. For example, if a survey concerning attitudes toward gun control is sponsored by the National Rifle Association, it is clear that responses opposing gun control are likely to be preferred. In contrast, if the survey on gun control attitudes is sponsored by the Department of Justice, the identity of the sponsor may not suggest the kind of responses the sponsor expects or would find acceptable.¹⁴⁴ When interviewers are well trained, their awareness of sponsorship may be a less serious threat than respondents' awareness. The empirical evidence for the effects of interviewers' prior expectations on respondents' answers generally reveals modest effects when the interviewers are well trained.¹⁴⁵

143. *Centaur Communications, Ltd. v. A/S/M Communications, Inc.*, 652 F. Supp. 1105, 1111 n.3 (S.D.N.Y.) (pointing out that reversing the usual order of response choices, yes or no, to no or yes may confuse interviewers as well as introduce bias), *aff'd*, 830 F.2d 1217 (2d Cir. 1987).

144. See, e.g., Stanley Presser et al., *Survey Sponsorship, Response Rates, and Response Effects*, 73 Soc. Sci. Q. 699, 701 (1992) (different responses to a university-sponsored telephone survey and a newspaper-sponsored survey for questions concerning attitudes toward the mayoral primary, an issue on which the newspaper had taken a position).

145. See, e.g., Seymour Sudman et al., *Modest Expectations: The Effects of Interviewers' Prior Expectations on Responses*, 6 Soc. Methods & Res. 171, 181 (1977).

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C. What Procedures Were Used to Ensure and Determine That the Survey Was Administered to Minimize Error and Bias?

Three methods are used to ensure that the survey instrument was implemented in an unbiased fashion and according to instructions. The first, monitoring the interviews as they occur, is done most easily when telephone surveys are used. A supervisor listens to a sample of interviews for each interviewer. Field settings make monitoring more difficult, but evidence that monitoring has occurred provides an additional indication that the survey has been reliably implemented.

Second, validation of interviews occurs when respondents in a sample are recontacted to ask whether the initial interviews took place and to determine whether the respondents were qualified to participate in the survey. The standard procedure for validation of in-person interviews is to telephone a random sample of about 10% to 15% of the respondents.¹⁴⁶ Some attempts to reach the respondent will be unsuccessful, and occasionally a respondent will deny that the interview took place even though it did. Because the information checked is limited to whether the interview took place and whether the respondent was qualified, this validation procedure does not determine whether the initial interview as a whole was conducted properly. Nonetheless, this standard validation technique warns interviewers that their work is being checked and can detect gross failures in the administration of the survey.

A third way to verify that the interviews were conducted properly is to compare the work done by each individual interviewer. By reviewing the interviews and individual responses recorded by each interviewer, researchers can identify any response patterns or inconsistencies for further investigation.

When a survey is conducted at the request of a party for litigation rather than in the normal course of business, a heightened standard for validation checks may be appropriate. Thus, independent validation of at least 50% of interviews by a third party rather than by the field service that conducted the interviews increases the trustworthiness of the survey results.¹⁴⁷

146. See, e.g., *National Football League Properties, Inc. v. New Jersey Giants, Inc.*, 637 F. Supp. 507, 515 (D.N.J. 1986); *Davis v. Southern Bell Tel. & Tel. Co.*, No. 89-2839, 1994 U.S. Dist. LEXIS 13257, at *16 (S.D. Fla. Feb. 1, 1994).

147. In *Rust Environment & Infrastructure, Inc. v. Teunissen*, 131 F.3d 1210, 1218 (7th Cir. 1997), the court criticized a survey in part because it "did not comport with accepted practice for independent validation of the results."

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VI. Data Entry and Grouping of Responses

A. What Was Done to Ensure That the Data Were Recorded Accurately?

Analyzing the results of a survey requires that the data obtained on each sampled element be recorded, edited, and often coded before the results can be tabulated and processed. Procedures for data entry should include checks for completeness, checks for reliability and accuracy, and rules for resolving inconsistencies. Accurate data entry is maximized when responses are verified by duplicate entry and comparison, and when data entry personnel are unaware of the purposes of the survey.

B. What Was Done to Ensure That the Grouped Data Were Classified Consistently and Accurately?

Coding of answers to open-ended questions requires a detailed set of instructions so that decision standards are clear and responses can be scored consistently and accurately. Two trained coders should independently score the same responses to check for the level of consistency in classifying responses. When the criteria used to categorize verbatim responses are controversial or allegedly inappropriate, those criteria should be sufficiently clear to reveal the source of disagreements. In all cases, the verbatim responses should be available so that they can be recoded using alternative criteria.¹⁴⁸

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148. See, e.g., *Coca-Cola Co. v. Tropicana Prods., Inc.*, 538 F. Supp. 1091, 1094-96 (S.D.N.Y.) (plaintiff's expert stated that respondents' answers to the several open-ended questions revealed that 43% of respondents thought Tropicana was portrayed as fresh squeezed; the court's own tabulation found no more than 15% believed this was true), *rev'd on other grounds*, 690 F.2d 312 (2d Cir. 1982). See also *McNeilab, Inc. v. American Home Prods. Corp.*, 501 F. Supp. 517 (S.D.N.Y. 1980); *Rock v. Zimmerman*, 959 F.2d 1237, 1253 n.9 (3d Cir. 1992) (court found that responses on a change of venue survey incorrectly categorized respondents who believed the defendant was insane as believing he was guilty); *Revlon Consumer Prods. Corp. v. Jennifer Leather Broadway, Inc.*, 858 F. Supp. 1268, 1276 (S.D.N.Y. 1994) (inconsistent scoring and subjective coding led court to find survey so unreliable that it was entitled to no weight), *aff'd*, 57 F.3d 1062 (2d Cir. 1995).

VII. Disclosure and Reporting

A. When Was Information About the Survey Methodology and Results Disclosed?

Objections to the definition of the relevant population, the method of selecting the sample, and the wording of questions generally are raised for the first time when the results of the survey are presented. By that time it is too late to correct methodological deficiencies that could have been addressed in the planning stages of the survey. The plaintiff in a trademark case¹⁴⁹ submitted a set of proposed survey questions to the trial judge, who ruled that the survey results would be admissible at trial while reserving the question of the weight the evidence would be given.¹⁵⁰ The court of appeals called this approach a commendable procedure and suggested that it would have been even more desirable if the parties had "attempt[ed] in good faith to agree upon the questions to be in such a survey."¹⁵¹

The *Manual for Complex Litigation, Second*, recommended that parties be required, "before conducting any poll, to provide other parties with an outline of the proposed form and methodology, including the particular questions that will be asked, the introductory statements or instructions that will be given, and other controls to be used in the interrogation process."¹⁵² The parties then were encouraged to attempt to resolve any methodological disagreements before the survey was conducted.¹⁵³ Although this passage in the second edition of the manual has been cited with apparent approval,¹⁵⁴ the prior agreement the manual recommends has occurred rarely and the *Manual for Complex Litigation, Third*, recommends, but does not advocate requiring, prior disclosure and discussion of survey plans.¹⁵⁵

Rule 26 of the Federal Rules of Civil Procedure requires extensive disclosure of the basis of opinions offered by testifying experts. However, these provisions may not produce disclosure of all survey materials, because parties are not obli-

149. *Union Carbide Corp. v. Ever-Ready, Inc.*, 392 F. Supp. 280 (N.D. Ill. 1975), *rev'd*, 531 F.2d 366 (7th Cir.), *cert. denied*, 429 U.S. 830 (1976).

150. Before trial, the presiding judge was appointed to the court of appeals, so the case was tried by another district court judge.

151. *Union Carbide*, 531 F.2d at 386. More recently, the Seventh Circuit recommended the filing of a motion *in limine*, asking the district court to determine the admissibility of a survey based on an examination of the survey questions and the results of a preliminary survey before the party undertakes the expense of conducting the actual survey. *Piper Aircraft Corp. v. Wag-Aero, Inc.*, 741 F.2d 925, 929 (7th Cir. 1984).

152. MCL 2d, *supra* note 15, § 21.484.

153. *Id.*

154. *E.g.*, *National Football League Properties, Inc. v. New Jersey Giants, Inc.*, 637 F. Supp. 507, 514 n.3 (D.N.J. 1986).

155. MCL 3d, *supra* note 15, § 21.493.

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gated to disclose information about nontestifying experts. Parties considering whether to commission or use a survey for litigation are not obligated to present a survey that produces unfavorable results. Prior disclosure of a proposed survey instrument places the party that ultimately would prefer not to present the survey in the position of presenting damaging results or leaving the impression that the results are not being presented because they were unfavorable. Anticipating such a situation, parties do not decide whether an expert will testify until after the results of the survey are available.

Nonetheless, courts are in a position to encourage early disclosure and discussion even if they do not lead to agreement between the parties. In *McNeilab, Inc. v. American Home Products Corp.*,¹⁵⁶ Judge William C. Conner encouraged the parties to submit their survey plans for court approval to ensure their evidentiary value; the plaintiff did so and altered its research plan based on Judge Conner's recommendations. Parties can anticipate that changes consistent with a judicial suggestion are likely to increase the weight given to, or at least the prospects of admissibility of, the survey.¹⁵⁷

B. Does the Survey Report Include Complete and Detailed Information on All Relevant Characteristics?

The completeness of the survey report is one indicator of the trustworthiness of the survey and the professionalism of the expert who is presenting the results of the survey. A survey report generally should provide in detail

1. the purpose of the survey;
2. a definition of the target population and a description of the population that was actually sampled;
3. a description of the sample design, including the method of selecting respondents, the method of interview, the number of callbacks, respondent eligibility or screening criteria, and other pertinent information;
4. a description of the results of sample implementation, including (a) the number of potential respondents contacted, (b) the number not reached, (c) the number of refusals, (d) the number of incomplete interviews or terminations, (e) the number of noneligibles, and (f) the number of completed interviews;
5. the exact wording of the questions used, including a copy of each version of the actual questionnaire, interviewer instructions, and visual exhibits;
6. a description of any special scoring (e.g., grouping of verbatim responses into broader categories);

156. 848 F.2d 34, 36 (2d Cir. 1988) (discussing with approval the actions of the district court).

157. Larry C. Jones, *Developing and Using Survey Evidence in Trademark Litigation*, 19 Memphis St. U. L. Rev. 471, 481 (1989).

7. estimates of the sampling error, where appropriate (i.e., in probability samples);
8. statistical tables clearly labeled and identified as to source of data, including the number of raw cases forming the base for each table, row, or column; and
9. copies of interviewer instructions, validation results, and code books.¹⁵⁸

A description of the procedures and results of pilot testing is not included on this list. Survey professionals generally do not describe pilot testing in their reports. The Federal Rules of Civil Procedure, however, may require that a testifying expert disclose pilot work that serves as a basis for the expert's opinion. The situation is more complicated when a nontestifying expert conducts the pilot work and the testifying expert learns about the pilot testing only indirectly through the attorney's advice about the relevant issues in the case. Some commentators suggest that attorneys are obligated to disclose such pilot work.¹⁵⁹

C. In Surveys of Individuals, What Measures Were Taken to Protect the Identities of Individual Respondents?

The respondents questioned in a survey generally do not testify in legal proceedings and are unavailable for cross-examination. Indeed, one of the advantages of a survey is that it avoids a repetitious and unrepresentative parade of witnesses. To verify that interviews occurred with qualified respondents, standard survey practice includes validation procedures,¹⁶⁰ the results of which should be included in the survey report.

Conflicts may arise when an opposing party asks for survey respondents' names and addresses in order to reinterview some respondents. The party introducing the survey or the survey organization that conducted the research generally resists supplying such information.¹⁶¹ Professional surveyors as a rule guarantee

158. These criteria were adapted from the Council of Am. Survey Res. Orgs., *supra* note 41, § III. B. Failure to supply this information substantially impairs a court's ability to evaluate a survey. *In re Prudential Ins. Co. of Am. Sales Practices Litig.*, 962 F. Supp. 450, 532 (D.N.J. 1997) (citing the first edition of this manual). *But see Florida Bar v. Went for It, Inc.*, 515 U.S. 618, 626–28 (1995), in which a majority of the Supreme Court relied on a summary of results prepared by the Florida Bar from a consumer survey purporting to show consumer objections to attorney solicitation by mail. In a strong dissent, Justice Kennedy, joined by three of his colleagues, found the survey inadequate based on the document available to the court, pointing out that the summary included “no actual surveys, few indications of sample size or selection procedures, no explanations of methodology, and no discussion of excluded results . . . no description of the statistical universe or scientific framework that permits any productive use of the information the so-called Summary of Record contains.” *Id.* at 640.

159. Yvonne C. Schroeder, *Pretesting Survey Questions*, 11 Am. J. Trial Advoc. 195, 197–201 (1987).

160. See *supra* § V.C.

161. See, e.g., *Alpo Petfoods, Inc. v. Rakston Purina Co.*, 720 F. Supp. 194 (D.D.C. 1989), *aff'd in part & vacated in part*, 913 F.2d 958 (D.C. Cir. 1990).

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confidentiality in an effort to increase participation rates and to encourage candid responses. Because failure to extend confidentiality may bias both the willingness of potential respondents to participate in a survey and their responses, the professional standards for survey researchers generally prohibit disclosure of respondents' identities. "The use of survey results in a legal proceeding does not relieve the Survey Research Organization of its ethical obligation to maintain in confidence all Respondent-identifiable information or lessen the importance of Respondent anonymity."¹⁶² Although no surveyor-respondent privilege currently is recognized, the need for surveys and the availability of other means to examine and ensure their trustworthiness argue for deference to legitimate claims for confidentiality in order to avoid seriously compromising the ability of surveys to produce accurate information.¹⁶³

Copies of all questionnaires should be made available upon request so that the opposing party has an opportunity to evaluate the raw data. All identifying information, such as the respondent's name, address, and telephone number, should be removed to ensure respondent confidentiality.

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162. Council of Am. Survey Res. Orgs., *supra* note 41, § 1.A.3.f. Similar provisions are contained in the By-Laws of the American Association for Public Opinion Research.

163. Litton Indus., Inc., No. 9123, 1979 FTC LEXIS 311, at *13 & n.12 (June 19, 1979) (Order Concerning the Identification of Individual Survey-Respondents with Their Questionnaires) (citing Frederick H. Boness & John F. Cordes, Note, *The Researcher-Subject Relationship: The Need for Protection and a Model Statute*, 62 Geo. L.J. 243, 253 (1973)). See also *Lampshire v. Procter & Gamble Co.*, 94 F.R.D. 58, 60 (N.D. Ga. 1982) (defendant denied access to personal identifying information about women involved in studies by the Centers for Disease Control based on Fed. R. Civ. P. 26(c) giving court the authority to enter "any order which justice requires to protect a party or persons from annoyance, embarrassment, oppression, or undue burden or expense.") (citation omitted).

Glossary of Terms

The following terms and definitions were adapted from a variety of sources, including Handbook of Survey Research (Peter H. Rossi et al. eds., 1983); 1 Environmental Protection Agency, Survey Management Handbook (1983); Measurement Errors in Surveys (Paul P. Biemer et al. eds., 1991); William E. Saris, Computer-Assisted Interviewing (1991); Seymour Sudman, Applied Sampling (1976).

branching. A questionnaire structure that uses the answers to earlier questions to determine which set of additional questions should be asked (e.g., citizens who report having served as jurors on a criminal case are asked different questions about their experiences than citizens who report having served as jurors on a civil case).

CAI (computer-assisted interviewing). A method of conducting interviews in which an interviewer asks questions and records the respondent's answer by following a computer-generated protocol.

CATI (computer-assisted telephone interviewing). A method of conducting telephone interviews in which an interviewer asks questions and records the respondent's answer by following a computer-generated protocol.

closed-ended question. A question that provides the respondent with a list of choices and asks the respondent to choose from among them.

cluster sampling. A sampling technique allowing for the selection of sample elements in groups or clusters, rather than on an individual basis; it may significantly reduce field costs and may increase sampling error if elements in the same cluster are more similar to one another than are elements in different clusters.

confidence interval. An indication of the probable range of error associated with a sample value obtained from a probability sample. Also, margin of error.

convenience sample. A sample of elements selected because they were readily available.

double-blind research. Research in which the respondent and the interviewer are not given information that will alert them to the anticipated or preferred pattern of response.

error score. The degree of measurement error in an observed score (see true score).

full-filter question. A question asked of respondents to screen out those who do not have an opinion on the issue under investigation before asking them the question proper.

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mall intercept survey. A survey conducted in a mall or shopping center in which potential respondents are approached by a recruiter (intercepted) and invited to participate in the survey.

multistage sampling design. A sampling design in which sampling takes place in several stages, beginning with larger units (e.g., cities) and then proceeding with smaller units (e.g., households or individuals within these units).

nonprobability sample. Any sample that does not qualify as a probability sample.

open-ended question. A question that requires the respondent to formulate his or her own response.

order effect. A tendency of respondents to choose an item based in part on the order in which it appears in the question, questionnaire, or interview (see primacy effect and recency effect); also referred to as a context effect because the context of the question influences the way the respondent perceives and answers it.

parameter. A summary measure of a characteristic of a population (e.g., average age, proportion of households in an area owning a computer). Statistics are estimates of parameters.

pilot test. A small field test replicating the field procedures planned for the full-scale survey; although the terms *pilot test* and *pretest* are sometimes used interchangeably, a pretest tests the questionnaire, whereas a pilot test generally tests proposed collection procedures as well.

population. The totality of elements (objects, individuals, or other social units) that have some common property of interest; the target population is the collection of elements that the researcher would like to study; the survey population is the population that is actually sampled and for which data may be obtained. Also, universe.

population value, population parameter. The actual value of some characteristic in the population (e.g., the average age); the population value is estimated by taking a random sample from the population and computing the corresponding sample value.

pretest. A small preliminary test of a survey questionnaire. See pilot test.

primacy effect. A tendency of respondents to choose early items from a list of choices; the opposite of a recency effect.

probability sample. A type of sample selected so that every element in the population has a known nonzero probability of being included in the sample; a simple random sample is a probability sample.

probe. A follow-up question that an interviewer asks to obtain a more complete answer from a respondent (e.g., "Anything else?" "What kind of medical problem do you mean?").

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quasi-filter question. A question that offers a "don't know" or "no opinion" option to respondents as part of a set of response alternatives; used to screen out respondents who may not have an opinion on the issue under investigation.

random sample. See simple random sample.

recency effect. A tendency of respondents to choose later items from a list of choices; the opposite of a primacy effect.

sample. A subset of a population or universe selected so as to yield information about the population as a whole.

sampling error. The estimated size of the difference between the result obtained from a sample study and the result that would be obtained by attempting a complete study of all units in the sampling frame from which the sample was selected in the same manner and with the same care.

sampling frame. The source or sources from which the objects, individuals, or other social units in a sample are drawn.

secondary meaning. A descriptive term that becomes protectable as a trademark if it signifies to the purchasing public that the product comes from a single producer or source.

simple random sample. The most basic type of probability sample; each unit in the population has an equal probability of being in the sample, and possible samples of a given size are equally likely to be selected.

skip pattern, skip sequence. A sequence of questions in which some should not be asked (should be skipped) based on the respondent's answer to a previous question (e.g., if the respondent indicates that he does not own a car, should not be asked what brand of car he owns).

stratified sampling. A sampling technique that permits the researcher to subdivide the population into mutually exclusive and exhaustive subpopulations, or strata; within these strata, separate samples are selected; results can be combined to form overall population estimates or used to report separate within-stratum estimates.

survey population. See population.

systematic sampling. A sampling technique that consists of a random starting point and the selection of every n th member of the population; it generally produces the same results as simple random sampling.

target population. See population.

trade dress. A distinctive and nonfunctional design of a package or product protected under state unfair competition law and the federal Lanham Act §43(a), 15 U.S.C. §1125(a) (1946) (amended 1992).

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true score. The underlying true value, which is unobservable because there is always some error in measurement; the observed score = true score + error score.

universe. See population.

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EXHIBIT C

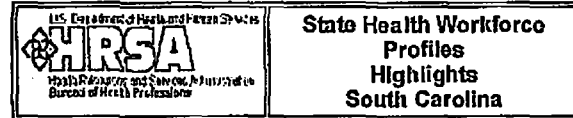
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National Center for Health Workforce Analysis

Alabama

The South Carolina Health Workforce: Highlights from the Health Workforce Profile



[Printer-friendly South Carolina Highlights \(PDF - 41 KB\)](#)

- There were more than 140,700 people employed in the health sector in South Carolina in 2000, 7.7% of South Carolina's total workforce. South Carolina ranked 40th among the states in per capita health services employment.
- Health services employment in South Carolina grew 81% between 1988 and 2000, while the state's population grew by 18%, resulting in a net per capita growth of 53% in health services sector employment. This was more than twice the national rate of per capita growth in the health services sector of 21%.
- The total population of South Carolina is projected to grow 12% between 2000 and 2020, while the population 65 and over is projected to grow 69% between 2000 and 2020.
- In 1999, South Carolina was above the national rates of deaths due to cancer, heart disease, and firearms.
- In 2000, South Carolina was slightly below the national rate in the number of hospital beds per 100,000 population.

Highlights of the findings about the health workforce in South Carolina are presented below.

Medicine

- There were more than 6,900 active patient care physicians in South Carolina in 2000. With 172 physicians per 100,000 population, South Carolina was below the national ratio of 198 physicians per 100,000. South Carolina ranked 32nd among states in physicians per capita.
- South Carolina had 56 active primary care physicians per 100,000 population in 2000, lower than the national rate of 69 per 100,000 for the entire country.
- Medical schools in South Carolina graduated 206 new physicians in 2000. South Carolina ranked 28th among the 46 states with medical schools in number of medical school graduates. On a per capita basis, South Carolina graduated less new physicians per 100,000 population (5.2) than did the entire United States (6.4) and ranked 28th among the 46 states in medical school graduates per capita.
- There were 260 physician assistants practicing in South Carolina in 2000. This was equal to 3.4 physician assistants per 100,000 population, less than half the national rate of 14.4.

Nursing

- There were more than 32,500 licensed registered nurses (RNs) in South Carolina in 2000; over 29,200 were employed in nursing. There were 728.3 RNs per 100,000 population in South Carolina in 2000, less than the national rate of 780.2.
- South Carolina ranked 26th among the states in the per capita employment of Licensed Practical/Vocational Nurses (LPNs), with 233.1 LPNs per 100,000 population as compared to the national rate of 240.8 per 100,000. South Carolina ranked 26th in the number of LPNs employed in 2000 with 9,380 workers.
- South Carolina had 1,223 nurse practitioners in 2000. This was equal to 30.4 nurse practitioners per 100,000 population, slightly below the national rate of 33.7.
- With 129 certified nurse midwives in 2000, South Carolina had 3.2 certified nurse midwives per 100,000 population, higher than the national rate of 2.9. South Carolina ranked 20th among states in certified nurse midwives per capita.
- With 625 certified registered nurse anesthetists in 2000, South Carolina had 15.5 nurse anesthetists per 100,000 population, higher than the national rate of 9.3.

Dentistry, Pharmacy and Mental Health

- There were 2,328 dentists, 1,410 dental hygienists, and 2,970 dental assistants practicing in South Carolina in 2000. There were 57.9 dentists per 100,000 population in South Carolina in 2000, below the national rate of 63.6. South Carolina ranked 25th in the nation in dentists per capita. The per capita ratio of dental hygienists was substantially lower than the national rate.
- The number of dentists in South Carolina increased by 71% between 1991 and 2000, while the state's population grew 13%. The result was a 52% increase in dentists per capita compared to a 16% increase nationwide.
- There were 2,720 pharmacists and 3,770 pharmacy technicians and aides practicing in South Carolina in 2000. South Carolina had 67.6 pharmacists and 93.7 pharmacy technicians and aides per 100,000 population in 2000, which ranked them 42nd and 16th, respectively, among the 50 states.
- There were 405 psychiatrists, 770 psychologists, and 5,310 social workers in South Carolina in 2000. This was equal to 10.5 psychiatrists, 19.1 psychologists, and 132 social workers per 100,000 population. South Carolina

ranked 22nd among states in psychiatrists per capita, 45th among states in psychologists per capita, and 35th among states in social workers per capita.

Aides

- There were 4,000 home health aides and 14,710 nursing aides, orderlies, and attendants working in South Carolina in 2000. South Carolina had 99.4 home health aides and 365.6 nursing aides, orderlies, and attendants per 100,000 population in 2000, which ranked 45th and 40th, respectively, among the 50 states.

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IN THE COURT OF COMMON PLEAS
FOR THE SEVENTH JUDICIAL CIRCUIT

CIVIL ACTION NO: 07-CP-42-1438

V.

Defendants.

**DEFENDANTS' MEMORANDUM OF LAW IN SUPPORT OF MOTION
FOR LEAVE TO DEPOSE A STATISTICALLY SIGNIFICANT
SAMPLE OF PRESCRIBING PHYSICIANS AND INSTITUTIONS**

Defendants Ortho-McNeil-Janssen Pharmaceuticals, Inc. (f/k/a Janssen Pharmaceutica Inc.) ("Janssen") and Johnson & Johnson (collectively "Defendants"), by and through their counsel, file this Memorandum of Law In Support of their Motion for Leave to Depose a Statistically Significant Sample of Prescribing Physicians and Institutions. Through the instant Motion, Defendants now seek an Order permitting them to take the depositions of 150 physicians and institutions that prescribed antipsychotic medicines to South Carolina Medicaid patients so that they may properly defend against Plaintiff's claims. The testimony expected to be gained is not duplicative of any of the discovery gathered to date and is not available from any other source.

I. STATEMENT OF FACTS

In this suit, Plaintiff alleges that Defendants have improperly marketed Risperdal®, its second-generation antipsychotic medication, and seeks damages on behalf of, *inter alia*, South Carolina's medical assistance program which, it claims, paid for unnecessary prescriptions and for the treatment of patient injuries resulting from Risperdal® use. Specifically, Plaintiff claims that Defendants "knowingly caused false claims for payment to the State's Medicaid program by intentionally promoting non-medically accepted indications and non-medically necessary uses of Risperdal to prescribing physicians," see Compl. at ¶ 90, that Defendants "fraudulently represented [to prescribing physicians] that Risperdal is safer and more effective than less expensive, first generation antipsychotics," see *id.* at ¶ 95, and that, due to Defendants' breach of its express and implied warranties, the "State spent significant sums of money . . . for medical treatment for those South Carolina citizens who developed serious side effects and/or adverse reactions after using Risperdal," see *id.* at ¶ 141.

To defend against these claims, Defendants should be permitted to take testimony from a statistically significant sample of prescribing physicians to inquire as to the discussions between the prescribing physicians and Defendants' sales representatives and to show that the representatives were not detailing for non-medically accepted or non-medically necessary uses. Further, depositions of the prescribing physicians will reveal their first-hand treatment experience with Risperdal, including the medicine's effectiveness for treatment of their patients' symptoms and its side effect profile. The depositions will also enable Defendants to explore whether or to what extent the physicians' patients developed serious side effects and/or adverse

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testified that "the more you look at, the more you know," but also explained that it is not necessary to depose more than 150 physicians: "You get great benefits from increasing from say fifty to a hundred, substantial benefits from a hundred to a hundred and fifty, but the benefits drop off as you move up." *Id.* at 44-45. Further, the number of depositions necessary for statistical significance does not change based on the overall size of the population. *Id.* at 45 (stating "if we were sampling from twenty-six hundred or twenty-six million, I would have probably still said one fifty"). Dr. Wecker explained that he randomly selected the names of the physicians to be deposed by using a computer system that acts, essentially, as a coin toss:

Your Honor will understand that I could not have said let's use a hundred and fifty. You lawyers pick them. That would not have worked because the lawyers could cherry pick by intent or by accident, the group that you got would not be representative of the whole if they are cherry picked. That's why I picked the one fifty.

Id. at 46. Having considered Dr. Wecker's testimony, Judge Hebert allowed Janssen to depose 150 prescribing physicians – a statistically significant sample of the relevant universe of prescribing physicians. *Id.* at 50.

Additionally, the process of identifying the prescribing physicians to be deposed could not be performed prior to February 9, 2009, the date on which Janssen was able to access the records from the Medicaid database.¹ Until that time, Defendant's expert could not review the data and make conclusions concerning the number and selection

¹ Plaintiff produced an electronic version of the Medicaid database on December 17, 2008. Unfortunately, Defendant encountered several technical issues with Plaintiff's production and could not process the data. The parties ultimately resolved the technical issues on or around February 9, 2009.

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of physicians whose depositions would enable him to conduct a statistical analysis. See Wecker Declaration, Ex. A.

II. ARGUMENT

The "discovery rules mandate full and fair disclosure to prevent a trial from becoming a guessing game or one of ambush for either party." *Scott v. Greenville Hous. Auth.*, 579 S.E. 2d 151, 158 (S.C. Ct. App. 2003). To that end, a party may take the testimony of any person by deposition upon oral examination. S.C. R. Civ. P. 30(a)(1). Unlike the Federal Rules of Civil Procedure, the South Carolina Rules of Civil Procedure do not limit the number of depositions that may be taken during discovery. *Cf. Fed. R. Civ. P. 30(a)(2)(A)(i)*.

Courts have held that the depositions of prescribing physicians may be useful — indeed necessary — to a defendant in order to develop evidence and defend against claims similar to those asserted here. In the Zyprexa multi-district litigation, reposed in the United States District Court for the Eastern District of New York, Magistrate Judge Roanne L. Mann ruled that defendant Eli Lilly was entitled to depose West Virginia prescribing physicians to, at a minimum, develop evidence regarding Eli Lilly's liability under West Virginia's Consumer Credit Protection Act. Unhappy with the ruling, West Virginia appealed the decision to the MDL judge, Senior District Judge Jack B. Weinstein. In affirming Magistrate Judge Mann's ruling, Judge Weinstein noted,

To the extent defendant is found liable, the depositions and data may well be necessary for defendant to develop evidence regarding the number of violations it committed under the CCPA and the civil penalty to be imposed for each violation in the discretion of a West Virginia court. Magistrate Mann's findings on the relevance and burden regarding the physicians' depositions and Medicaid database data are not inappropriate.

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See, e.g., *West Virginia v. Eli Lilly & Co.*, No. 06-CV-5826, 2008 WL 4186167 (E.D.N.Y. Sept. 10, 2008).²

Similarly, here, Defendants are entitled to defend against Plaintiff's claims that Defendants' sales representatives improperly promoted Risperdal to physicians and made certain warranties to them concerning Risperdal's safety profile. Additionally, Defendants should be permitted to explore the physicians' treatment experiences with Risperdal – both in terms of efficacy and safety, and with respect to incidence and treatment of other illnesses allegedly caused by the patients' use of Risperdal. These

² A similar issue was presented in the Zyprexa litigation when the MDL Court was asked to determine whether the defendants were entitled to discovery of patient medical records. See *In re Zyprexa Prods. Liab. Litig.*, 254 F.R.D. 50 (E.D.N.Y. Sept. 24, 2008) (Mann, U.S.M.J.), *aff'd* No. 04-MD-1596, slip op. at 6 (E.D.N.Y. Oct. 21, 2008) (Weinstein, U.S.D.J.). There, the Court repeated its earlier holding that "the medical records for Medicaid beneficiaries taking Zyprexa are relevant to Lilly's defense." *Id.* at 51. Accordingly, the plaintiff was ordered "to produce a randomly selected, statistically significant sample of [Medicaid] patient records" so that the defendant may prepare its defense against the plaintiff's claims because such records may "help explain information in the Medicaid databases." *Id.* at 51-52.

Once it was determined that a statistically significant sample of medical records would be produced, the court then considered the number of records that would constitute a statistically significant sample. *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2008 WL 4890588 (E.D. N.Y. Oct. 27, 2008). At that point, the defendants clarified that they intended to use the medical records to draw comparisons between atypical antipsychotics in order to defend against the plaintiff's claim that other antipsychotics were cheaper, safer and as or more effective than defendants' products. *Id.* at *2. Having reviewed the statements of experts for both sides, the Court ordered the plaintiff to produce a certain number of records per each subgroup (i.e., comparison between Zyprexa and Risperdal for treatment of schizophrenia, et cetera) implicated by the plaintiff's expert reports. *Id.* at *4. The Court also permitted the defendants to obtain patient records at the depositions of the prescribing physicians so that the defendants may "effectively question [prescribers] about their treatment experience." *Id.* at *3.

In reaching these decisions, the Court recognized that, though production of these records may be burdensome, "[i]f you make such huge claims, the defendants are going to defend, and they're entitled to defend, and we can't deny [them] due process." *Id.* at *2 (citing Transcript of Proceedings Held on Oct. 17, 2008, *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596 (JBW) (E.D.N.Y.), at 61-62).

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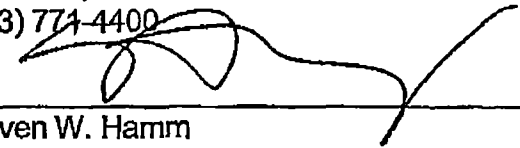
allegations form the backbone of Plaintiff's claims against Defendants and directly impact Plaintiff's assessment of damages. Obviously, Defendants cannot depose the entire population of approximately 2,800 doctors who prescribed antipsychotic medicines for ten or more Medicaid participants and prescribed Risperdal for one or more participants during the relevant time period. Accordingly, Defendants must be granted leave to take the depositions of a statistically significant sample of physicians and institutions that prescribed antipsychotic medicines to South Carolina Medicaid patients in order to test their factual validity and adequately defend against them.

III. CONCLUSION

For the reasons stated above, this Court should grant Defendants' Motion for Leave to Depose a Statistically Significant Sample of Prescribing Physicians and Institutions and permit Defendants to take the depositions of 150 physicians and institutions that prescribed antipsychotic medicines to South Carolina Medicaid patients. These Defendants pray for such other and further relief, both general and special, legal and equitable, to which they are justly entitled.

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Columbia, South Carolina 29202
(803) 771-4400

BY:


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JoAnne Wessinger Hill
Steven J. Pugh

-and-

Thomas F. Campion (admitted *pro hac vice*)
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INC., AND JOHNSON & JOHNSON

June 3, 2009
Columbia, South Carolina

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CERTIFICATE OF SERVICE

I, Vickie J. Storey, an employee of Richardson Plowden & Robinson, P.A., do hereby certify that I served the foregoing DEFENDANTS' MEMORANDUM OF LAW IN SUPPORT OF MOTION FOR LEAVE TO DEPOSE A STATISTICALLY SIGNIFICANT SAMPLE OF PRESCRIBING PHYSICIANS AND INSTITUTIONS on the undersigned counsel by causing a copy of same to be either mailed by United States Mail, Postage Prepaid, First Class, or hand-delivered as follows:

VIA U.S. MAIL:

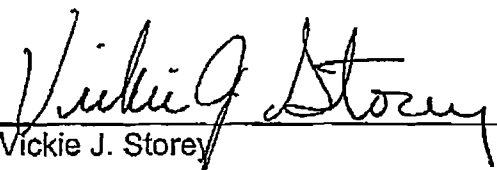
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Vickie J. Storey

June 3, 2009

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EXHIBIT A

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M. HOPE BLACKLEY

IN THE COURT OF COMMON PLEAS
STATE OF SOUTH CAROLINA
COUNTY OF SPARTANBURG

STATE OF SOUTH CAROLINA
ex rel. Henry McMaster, in his capacity
as Attorney General of the State of
South Carolina

Plaintiff,

v.

JANSSEN PHARMACEUTICA, INC.,
JANSSEN, LP and
JOHNSON & JOHNSON, INC.,

Defendant.

CIVIL ACTION NO.: 07-CP-42-1438

AFFIDAVIT OF WILLIAM E. WECKER, Ph.D.

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I, William E. Wecker, Ph.D., being first duly sworn according to law, do hereby testify from my own personal knowledge as follows:

1. I am a statistician and applied mathematician, and have conducted research in statistical theory, statistical methods and applied mathematics for more than 30 years. I received a Bachelor of Science degree from the United States Air Force Academy in 1963, a Master of Science degree from the University of Michigan in 1970, and a Ph.D. in statistics and management science from the University of Michigan in 1972. I have served on the faculties of the University of Chicago, the University of California at Davis, and Stanford University, where I taught

statistics and applied mathematics at the graduate level. I am a member of the American Statistical Association, the Institute of Mathematical Statistics, and the Society for Risk Analysis. I served as Associate Editor of the Journal of the American Statistical Association for 4 years and of the Journal of Business and Economic Statistics for 18 years. I am currently the president of William E. Wecker Associates, Inc. My qualifications and a list of my professional publications are shown in my curriculum vitae, a true and correct copy of which is attached hereto as Exhibit 1.

2. The purpose of this affidavit is two-fold: First, I will describe the relevance of obtaining testimony from the actual prescribers of Risperdal to patients in South Carolina. In this case, the testimony will come from depositions of doctors who prescribe Risperdal (and other antipsychotic medications) to patients under either the Medicaid Fee for Service program or the State Health Plan ("State Programs"). The second purpose of this affidavit is to describe what number of doctor depositions will be sufficient to reach reliable conclusions about the universe of such Risperdal prescribers.

3. I have been asked by counsel for Janssen to work with them to develop suitable questions covering both 1) the efficacy of patient treatment with Risperdal, and 2) Janssen's marketing and promotion of Risperdal. I anticipate that approximately 90 substantive questions will be asked of each doctor. In contrast to other sources of information which are useful but incomplete, such as the Medicaid claims database, the doctor depositions will yield direct evidence on relevant issues such as whether Janssen engaged in off-label marketing of Risperdal to doctors, whether doctors were influenced by Janssen sales representatives in their prescription decisions, whether

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Risperdal was effective in treating the positive and negative symptoms of schizophrenia, and whether Risperdal had more moderate side effects than first generation antipsychotics.

4. Moreover, to obtain this direct evidence on such issues, Janssen need not take the deposition of every Risperdal prescriber under the State Programs. While it would be prohibitively time-consuming and expensive to interview each such South Carolina prescriber of Risperdal, a properly representative sample of South Carolina doctors can provide an economically feasible, reasonably accurate approximation of the same information.

5. It is generally accepted among professional statisticians as well as scientists and scholars in related fields that statistical sampling is the only generally applicable, scientifically valid method for creating a representative sample from a universe that is too large to process exhaustively. By means of statistical sampling it is possible to produce unbiased, reasonably accurate approximations, having a known degree of potential error, to questions whose exact answers would be impracticably expensive or burdensome to obtain.

6. In this case, the sample need not be large to be adequate for this purpose. I have calculated that a sample of 150 doctors would be sufficient. I will explain how I determined the necessary sample size at a later point in this affidavit and the expected accuracy of estimates I expect to be able to derive from it.

7. I have proposed that the interviews of the statistically selected doctors take place as legal depositions, so that the doctors' responses are taken under oath with both the questions and answers recorded stenographically.

8. The following questions are illustrative of the questions that will be put to each of the selected doctors.

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Q: In your experience is Risperdal generally effective for treating the positive symptoms of schizophrenia?

Q: Has any Janssen sales representative ever promoted to you any off-label use of Risperdal in children?

9. With the assumption that each doctor will be asked approximately 90 substantive questions, I anticipate that the depositions will last approximately 90 minutes.

10. The population to be sampled consists of approximately 2,800 doctors who prescribed antipsychotic drugs for 10 or more participants and prescribed Risperdal for 1 or more participants in the State Programs during 2000–2007. The following table summarizes this population of prescribing doctors. They are grouped into three “strata” defined by the numbers of patients in the State Programs to whom they prescribed antipsychotic drugs.¹

Stratum	Number of Patients Prescribed To	Number of Prescribing Doctors (Population Size)	Percent of Prescribing Doctors
1	410 – 1,100	40	1.4%
2	100 – 409	305	10.9%
3	10 – 99	2,448	87.6%
Total		2,793	100.0%

11. Generally speaking, doctors who have prescribed antipsychotic drugs to greater numbers of patients can be expected to have more experience regarding the efficacy of Risperdal and more experience regarding marketing and promotional activities of Janssen than doctors with fewer such patients. I have grouped the doctors into strata accordingly. I have selected sample

¹ The population sizes shown for the strata are preliminary. I expect they will change somewhat as I resolve multiple ID numbers used by some prescribers and different prescriber ID systems used in the two State Programs.

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sizes as shown in the following table to insure coverage of these strata while allowing adequate accuracy of estimates.

Stratum	Number of Patients Prescribed To	Number of Prescribing Doctors (Population Size)	Percent of Prescribing Doctors	Sample Size
1	410 - 1,100	40	1.4%	40
2	100 - 409	305	10.9%	55
3	10 - 99	2,448	87.6%	55
Total		2,793	100.0%	150

12. These sample sizes allow for 100 percent coverage of the doctors with the highest level of prescribing activity, so results from this stratum are not subject to sampling variability. The proportion of doctors in the population in the second and third strata who would answer "yes" (for example) to a particular question if asked will be estimated from the results of the sample. Using the sample sizes shown above, the margin of error of these estimates is anticipated to be plus-or-minus 12.0 and 13.1 percentage points or less for strata 2 and 3, respectively.²

13. Based on my experience with sample surveys, I anticipate that many doctors may give the same answers to the same deposition questions for at least a portion of the direct examination. This does not mean that those depositions are unnecessary or redundant for my purpose. They are necessary for the purpose of extrapolating the sample results to those that

² These margins of error are for a "worst case" where 50 percent of the doctors in the sample respond "yes" to a question. For percentages closer to 0 or 100 percent, the margins of error for the population estimates would be smaller. For example, if 20 percent of doctors in the sample responded "yes" the margins of error for the population estimates would be plus-or-minus 9.6 and 10.5 percentage points for the second and third strata, respectively.

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would be achieved for the entire population, if the entire population were deposited, because the accuracy of the extrapolation depends importantly on the size of the sample.

14. A sample of less than 150 would result in somewhat less accurate estimates. For example, given a sample of 100, I would alter the stratum definitions and sample sizes as shown in the following table.

Stratum	Number of Patients Prescribed To	Number of Prescribing Doctors	Percent of Prescribing Doctors	Sample Size
1	500 - 1,100	20	0.7%	20
2	100 - 499	325	11.6%	40
3	10 - 99	2,448	87.6%	40
Total		2,793	100.0%	100

15. These reduced sample sizes would allow for 100 percent coverage of the doctors in the stratum with the highest level of prescribing activity, here reduced to 20 in size. The proportion of doctors in the population in the second and third strata who would answer "yes" to a particular question if asked would be estimated from the results of the sample with a margin of error of plus-or-minus 14.5 and 15.4 percentage points or less, respectively.

Executed on June 1st, 2009.

W^u Wecker
 William E. Wecker, Ph.D.

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CALIFORNIA JURAT WITH AFFIANT STATEMENT

- ☒ See Attached Document (Notary to cross out lines 1-6 below)
☐ See Statement Below (Lines 1-5 to be completed only by document signer[s], *not* Notary)

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Signature of Document Signer No. 1 _____ Signature of Document Signer No. 2 (if any) _____

State of California

County of Marin

Subscribed and sworn to (or affirmed) before me on this

1 day of June, 2009, by
Date Month Year
 (1) William Earl Wecker
Name of Signer

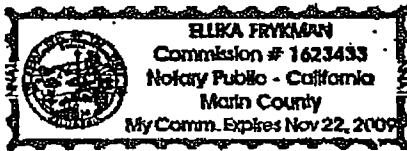
proved to me on the basis of satisfactory evidence to be the person who appeared before me (or)

(and

(2) _____
Name of Signer

proved to me on the basis of satisfactory evidence to be the person who appeared before me.)

Signature [Signature] [Signature]
Signature of Notary Public



Place Notary Seal Above

OPTIONAL

Though the information below is not required by law, it may prove valuable to persons relying on the document and could prevent fraudulent removal and reattachment of this form to another document.

Further Description of Any Attached Document

Title or Type of Document: Affidavit of William E. Wecker

Document Date: 6/1/09 Number of Pages: 6

Signer(s) Other Than Named Above: _____

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RIGHT THUMBPRINT OF SIGNER #2
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Exhibit 1

Curriculum Vitae of William E. Wecker

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May, 2009

WILLIAM E. WECKER

505 San Marin Drive
Novato, California 94945

Telephone: (415) 898-2255
Fax: (415) 898-2260
E-Mail: wecker@wecker.com

EDUCATION

B.S. (Basic Science) (1963), USAF Academy
M.S. (Operations Research) (1970), University of Michigan
Ph.D. (Statistics and Management Science) (1972), University of Michigan

EMPLOYMENT

1963-1967 Fighter pilot, USAF
1968-1969 Chief of Protocol, USAF, Berlin, Germany
1970-1972 Graduate Student, University of Michigan
1973-1976 Assistant Professor, Graduate School of Business, University of Chicago
1977-1983 Associate Professor, Graduate School of Business, University of Chicago
1984-1985 Associate Professor, Graduate School of Management, University of California, Davis
1985-1989 Professor, Graduate School of Management, University of California, Davis
1994-1998 Consulting Professor of Law, School of Law, Stanford University
1990- President, William E. Wecker Associates, Inc.

ACTIVITIES

1977-1981 Associate Editor (Theory and Methods), Journal of the American Statistical Association
1981-1999 Associate Editor, Journal of Business and Economic Statistics
1990-1992 Management Committee, Journal of Business and Economic Statistics
1976-1994 Seminar Leader, NSF/NBER Seminar on Time Series Analysis
1993-1994 National Advisory Council on Environmental Policy and Technology
(Lead Subcommittee)
Member of: American Association for the Advancement of Science
American Statistical Association
Institute of Mathematical Statistics
Society for Risk Analysis

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PUBLICATIONS

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"Statistical Estimation of Incremental Cost from Accounting Data" (with R. Weil), Handbook of Litigation Services for Accountants and Lawyers, John Wiley & Sons, 1990.

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EXHIBIT B

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IN THE TWENTY-SEVENTH JUDICIAL DISTRICT COURT
IN AND FOR THE PARISH OF ST. LANDRY
STATE OF LOUISIANA

CHARLES C. FOTI, JR. ET AL
VERSUS CRIMINAL DOCKET NO. 04-3967-D
JANSSEN PHARMACEUTICA ET AL

TRANSCRIPT OF MOTION TO EXCLUDE DEPOSING
OF 50 WITNESSES AND STATUS CONFERENCE

PROCEEDINGS had in the above entitled and numbered
cause at Opelousas, Louisiana, before, His Honor, DONALD W.
HEBERT, Judge of the 27th Judicial District Court in and for
the Parish of St. Landry, State of Louisiana on this 10th
day of October 2008.

APPEARANCES:

MR. PATRICK C. MORROW AND
MR. JEFFERY M. BASSETT
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MR. TOM CAMPION
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MR. JAMES B. IRWIN AND
MS. MONIQUE GARSAUD
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Counsel for the Defendants; and

M. HOPE BLACKLEY

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MR. JAMES GUGLIELMO
P.O. Drawer 1329
Opelousas, Louisiana 70571
Counsel for the Defendants,

REPORTED BY PATSY J. JONES,
Official Court Reporter, in
and for the Parish of St. Landry,
State of Louisiana.

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ST. LANDRY PARISH, LOUISIANA

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M. HOPE BLACKLEY

THE COURT: Good morning. Please be seated. It's nice to see everyone. Let's start with the important stuff. Mr. Perrin, you survived Ike and Gustav?

MR. PERRIN: I survived Ike, Your Honor and Gustav left me alone. I know that wasn't the case around all parts here, but we're back and running. I appreciate the Court's indulgence in September. We were without our office for about a week and getting back up was a little bit rigorous but that's not between anybody here.

THE COURT: We had our own problems here with Gustav, nonetheless it's good to see you here.

MR. PERRIN: Thank you.

THE COURT: The second most important bit of business is everyone, this is my new law clerk, Mr. Blake Altazan. What is much more important on this date is he just got the news that he took the bar and passed it. So congratulations. That's why I'm in a good mood. Okay, let's see, where are my notes? Last we were here after the interruptions of various and sundry hurricanes—oh, and I must ask everyone, I'm assuming everybody in here is selling short right?

MR. MORROW: You're so funny, Judge.

THE COURT: Because if you're not, we're in big trouble. Alright, you had discrete discovery requests that were going to be made by September 3rd, Mr. Perrin.

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MR. PERRIN: Yes, Your Honor, those were filed shortly before September 3rd. Ms. Garsaud and I have been in regular communication on that. I granted them an extension and then I gave them another extension until Friday of next week, just because of the volume that they said they were putting together, so I'm assuming there will be some objections. We may need to come back before the Court but I haven't received their responses yet, so that's proceeding on that schedule.

THE COURT: Outstanding. I got some good news yesterday from Mr. Juneau that you folks have gotten the case management order ready.

MR. PERRIN: We have, Your Honor.

THE COURT: And if I can give you the dates you seek so far as the trial date, which I think is February 8th, Mr. Juneau?

MR. JUNEAU: That's correct. February 8, 2010.

THE COURT: I can do that, and we're going to do that. The amended pleadings were filed as required.

MR. PERRIN: Yes, Your Honor.

THE COURT: And an answer was filed as well. I think I saw Mr. Guglielmo's answer hit my desk at some point. So we're all on the same page on everything. The privilege log is still being looked at. At some point Mr. Juneau's going to have to figure out a way for us to look at all of

M. HOPE BLACKLEY

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this in camera stuff and if we have to do that, that's fine. So that leaves me with, at least for today---let me tell you that I'm extremely pleased that you were able to come to some workable case management order without me having to fumble through it and mess it up, and who better to do it than the two sides, so congratulations and I appreciate the good work on that.

MR. PERRIN: Well, thank you, Your Honor.

THE COURT: We've got a Motion to Discontinue the Fifty Remaining Depositions.

MR. PERRIN: That's correct, Your Honor.

THE COURT: And I believe that's your motion?

MR. PERRIN: It is. Mr. Bassett will argue that today, Your Honor.

THE COURT: Mr. Bassett, note of evidence is open, sir.

MR. BASSETT: Thank you, Judge. May It Please The Court: Your Honor, in the August 13, 2007 order there was a provision in that order that said, "After 100 depositions have been taken by Defendant Janssen, Plaintiff may bring a motion before the Court seeking to prevent additional depositions from occurring pursuant to this Consent Judgment if Plaintiff believes that additional depositions are unwarranted by the discovery needs of this action. Defendant shall have the right to oppose the motion..." So pursuant to that order we're bringing a motion to

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terminate the depositions. As the Judge knows, we didn't think the depositions were necessary in the first place, but that's water under the bridge. The Judge ordered that they could take one fifty subject to this, limiting one hundred article that has us here, and we don't have really clear guidance as to what the criteria would be for us to terminate or for them to continue because your order doesn't speak to that, so we're just going to resort to principles, I guess of jurisprudence, equity and common sense.

THE COURT: Now let's do this. First of all the stipulation, I'm assuming there's a stipulation, roughly a hundred depositions have been reached. Is that right, Mr. Campion?

MR. CAMPION: Right. Ms. Garsaud is going to speak for us, Judge.

THE COURT: Ms. Garsaud.

MS. GARSAUD: Your Honor, we're just shy of a hundred. We're about I believe at ninety-five or ninety-six, we're close to a hundred.

THE COURT: So are you going to complain about them bringing the motion now ninety-five as opposed to a hundred?

MS. GARSAUD: No indeed not, no.

THE COURT: Then we'll stipulate so we'll have something in evidence for me to consider that we've reached the threshold and now you have

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the right to issue your complaint and request to discontinue. Okay.

MR. BASSETT: Judge, we looked at all of the jurisprudence for all the Louisiana cases where they have a hundred depositions set and limits of a hundred fifty and as the Court might suspect, there are none, so we really don't have any jurisprudential guidelines other than the Court has great discretion in discovery matters. We looked at the equity and the common sense argument and from our standpoint they've taken the depositions. They've taken a hundred supposedly random depositions. We don't agree that they're random; we think that they handpick them, but that's something we can argue about later. And we said that the depositions have gotten repetitive. So the basis of our--the basis of our motion is number one, we think that they've gotten--whatever it was they wanted to get they've gotten. The information that's coming out of the depositions is repetitive for the most part and whatever benefit there is to get from these depositions is outweighed by the financial burden it places on the plaintiffs. Now we know that we filed a suit and we're prepared to proceed with the depositions if the Court orders, but these are expensive depositions. We hire and contract lawyers to do it, it's money out of our pocket to do it and if the Court orders it, so be

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it. In most major--in a lot of these types of complex litigation cases the deposition turns if they have them are more like each side gets twenty-five or something like that. So a hundred is a lot. A hundred and fifty is a lot. Now Judge, when you ordered a hundred and fifty there was no scientific evidence that you heard, or nobody came here and said Judge, this is the sample size that we go on and our experts say that a statistically significant sample is a hundred and fifty, we just said, if they want to do a hundred and fifty and it was some kind of arbitrary random number that was just kind of put out there, at least from our standpoint, or whatever. So in our brief we said that it was repetitive and in the--there were five briefs, the Janssen's response was, "Plaintiff's indication that testimony from the healthcare providers 'is for the most part repetitive' is correct." So we don't have any argument there. They want us to stipulate that a hundred would be a statistically significant sample, just as one hundred and fifty, can't do that. We have--we don't think that the sample that they're using and the method that they're using, we don't agree with any method that they're using. As a matter of fact in some document that we just got a couple of days ago about their expert's presentation or whatever, it says that the gold

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standard is clinical trials. So for example, for the first time we hear one of the things they may want to model, they said one of the questions they asked to the provider is, "In your experience, does Risperdal have a more moderate side effect profile than first generation antipsychotics?" Alright, well Judge, the gold standard tests that they talk about are out there. Clinical studies where they actually give the drugs to people and give blind studies, and they do that. There's the CATY and there's a study for the National Institute of Mental Health that was in the Dallas--front page of *Dallas Morning News* a couple of weeks ago where they actually are giving the drugs to the people and testing them, the older generation versus the new generation. So this type of observational study where they asked Dr. Glowacki what his experience is or what he thinks without knowing--without really asking him how many people has he prescribed it to, how many older generation, what types, what type of newer generations, has he looked at the files or anything, just this question out of the blue, we think it has limited effect in the first place. But the question is this, is a hundred enough, and it says here in their memorandum, "To be sure, Janssen's expert can draw reliable conclusions about the entire prescribing population from 100 depositions."

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That's what they say. So they say they've got enough. They want to preclude us from some point arguing later that it should have been a hundred and fifty or two hundred, or whatever, well I met with our experts to kind of--today, to kind of understand how this thing works and there's all kinds of variables that go into this. There's the sample size, there's the type of question they ask, Judge, there's power calculations that help you get to the sample size, and we're not in a position to stipulate to anything. We have no idea how they arrived or what they want to do with their model. All we know is that whatever benefit they've gotten out of it, they admit it's repetitive. They admit in their brief that they can model from the hundred. So Judge, if you kind of do a balancing act, the expense to both sides, keep in mind these people have a lot of money. It's a big pharmaceutical company and again, we're not whining, we took them on, we understand that, but we shouldn't be--we shouldn't go take a whole bunch of depositions if they say that they've got enough for their model just because they're worried we might complain about their number. If they do one fifty we're probably going to complain about that, Judge, because we don't--the way their study is constructed we have a lot of complaints about it and I'm sure they have a complaint about our studies. So in summary,

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Judge, you didn't really give us a guideline, but I think if we resort to equity and common sense, it's getting repetitive, everybody admits it, they say they've got enough for their study and we think that a hundred was a lot.

THE COURT: Okay, before you take off, I guess the first thing I want to mention, and I'll give you the opportunity to respond to is, I didn't set that hundred and fifty number. I signed the order with concurrence of both sides who simply handed it to me *fait accompli*, which I'm very happy with every time you do that. So I just want to note for the record that I didn't put any conditions in it because nobody asked for them. Y'all agreed that they'd take a hundred and fifty and after a hundred y'all could come in and complain. You say you've got an expert who says all kind of things. There's a chair, there's a witness stand. You arguing it doesn't make it so.

MR. BASSETT: Right.

THE COURT: I don't know. All I have right now before me in evidence to consider as a Court is that you have reached the threshold of a hundred and you take issue with it, for whatever reason, because you think it doesn't work with your construct and your statistical expert says this or that. How do I know that? That's one problem that I have. The last thing I want to tell you, then I'll give you the opportunity

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again to tell you the note of evidence is opened if you want to put evidence in, I'm not here to do a balancing act. I've said repeatedly throughout these proceedings I don't know how the plaintiffs are going to try their case. I got an indication earlier on that it was going to be by statistical modeling only. Then we kind of got, well, maybe so, maybe not. Now it appears we're back on statistical modeling, and what I said from day one is you try your case the way you choose to try your case. That's your right. Their right is the same. You may disagree with the construct, but to tell me that I should stop another fifty depositions, I guess another five hundred, the question becomes to me, is it relevant? Is it material? Does it lead to admissible evidence? Now there is a cost factor that I think I must consider at some point and as you indicate you've got a company that's a big company with a lot of money, Johnson & Johnson and Janssen, or whatever the heck they are. But by the same token, you're plaintiffs. You wanted to come here and you knew what you--you knew the hole you were digging that you had to fill up and so I do think it's whining.

MR. BASSETT: May I respond, Judge?

THE COURT: Sure.

MR. BASSETT: Judge, the uh--historically Judge, the order that was signed, Your Honor had

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made it pretty clear that Your Honor was going to let them take as many doctors--was going to let them take a lot of doctors depositions, or as many as they wanted and try their case and we had made it pretty clear in advance of that order that we didn't think that was the way to try the case.

THE COURT: I acknowledge that historical reference.

MR. BASSETT: And so there was a bit of arm-twisting that went into the order, trying to not require the Judge to solve that for us and knowing what the Judge's ruling would be. And they can try the case the way they want it. I understand your logic there, Judge, but that doesn't mean that they could come in and say, we want to do a thousand depositions. From your test right there, well, is it relevant, is it this, is it this, well they could do--basically say Judge, we want to do six thousand depositions, we want to depose every single doctor because that's the statistical sample we want, and that wouldn't be fair and that wouldn't be equitable and that wouldn't be the way most cases are done. And in all cases, not just in this case, in lots of cases where complex litigation is involved, the Courts limit the numbers of depositions and the limit isn't just the test that you said, Judge, is it relevant, the limit's also is it

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repetitive, what's fair, what makes sense, because we can't just let litigation run wild and everybody do whatever they want, thousands of depositions, the guy with the most money gets to drive the show, or whatever. So I think that if there's any burden here today, it should be on them because I think it's extraordinary Judge for someone to take a hundred depositions in a legal action. I think that you've given them great leeway through that order and I think that the order had that built-in part where we could come in and say enough is enough. They say it's enough. They say in their brief that that's enough for our model. They say it's repetitive. So if anybody should bear the burden, Judge, why should it be us? I'm not going to put on any experts. The burden should be on them because what's extraordinary is the number of depositions that they're taking. What's not extraordinary is us saying a hundred depositions in a case is too many, particularly when they have agreed it's repetitive and it's enough for their model. So that's the only response I have, Your Honor.

THE COURT: I want to do one more bit of arm-twisting. We've got one million two hundred and fifty thousand claims as I understand it, or thereabouts, in the rough vicinity. That's a lot of claims about the prescriptions that were rendered. And to sit here and tell me that the

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number one fifty borders on the outrageous, which is pretty much what I'm hearing, when you've got one million two hundred and fifty thousand claims is to me disingenuous. Now again, when you set the hundred and fifty between you, I acknowledge--I acknowledge arm-twisting. I acknowledge everything that you referenced historically and like good lawyers you saw the practical effect of let's not get in the Judge's way now. Let's try to do the best we can. And I understand that and I understand what I did. I did it on purpose because somebody--and I think I exercised my judicial discretion by saying that you're not going to run this case. Plaintiffs don't get to file a suit and then call the rules on how we're going to try it. That's all I tried to say. I'm not going to bend over backwards to help Mr. Campion over there or you. So with that, I didn't hear one single shred of evidence as to what--why even one medical doctor deposition was necessary. Still my understanding of this case is that it's off label marketing that's off putting to the plaintiffs. So I guess the position is, and I've never been corrected one way or the other is, you issued prescriptions for off label, non-FDA approved uses of this medication. Whether the doctor--why he did it is irrelevant. You weren't supposed to do it. That was--and I don't know if that's right or wrong, but I'm telling

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you today that I still don't have any evidence to tell me why they needed the first hundred, why they need another fifty, or why you think they didn't and why they shouldn't. I still only got Mr. Bassett's argument and the stipulation that they've reached the threshold of a hundred. If that's what y'all want me to decide on, it doesn't give me much, is my whole point. And I'll give you the opportunity to again, after Ms. Garsaud speaks, to see if you want to put any evidence in. Ms. Garsaud, the note of evidence is still open for you.

MS. GARSAUD: Thank you, Your Honor. For now what I would just like to do is address some of the questions and issues raised by you and Mr. Bassett. I think if--I don't know if you've had a chance to look at the most recent filed petition, the Fourth and Supplemental Amending Petition but it is--the plaintiffs have injected throughout this petition what we have done--what Janssen has done in relation to the physicians. We've misled them, we have fraudulently misrepresented information, we have promoted the product off label to them and that the physicians relied on all of this erroneous and false information in making these decisions. So I think when you start with the petition and look at the allegations regarding Janssen and their relation to the physicians that what the physicians do and

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what the physicians say is very relevant. So who do you go to, to get the information? You go to the physicians. And I think that when you go to the physicians as you've discussed there's over a million claims, prescriptions made, our data suggests from the Medicaid database there are approximately I think twenty-six hundred prescribers of this product at the time period that we're looking at.

THE COURT: Twenty-six hundred what?

MS. GARSAUD: Prescribers.

THE COURT: Okay.

MS. GARSAUD: Different doctors throughout the state that have written these prescriptions.

THE COURT: Okay.

MS. GARSAUD: The reality is of course we would love to interview and depose whenever, each prescriber, but we can't. We realize that that is not a good use of resources for anyone, so what do we do? We say we need to find a statistically relevant sample, a statistically significant sample, and Your Honor, that is something that does come from the experts, and I think you will hear all that when they put on their presentations.

THE COURT: Well then why are we not hearing it now as part of this evidentiary ruling that I have to make?

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MR. GARSAUD: Well, if you'd like--I'd be more than happy--

THE COURT: It's not what I'd like. Let me tell y'all this. Let me just say this real quick, Ms. Garsaud. I'm going to tell both sides this, I make a decision when y'all finish. One of you is not going to be happy with it. Presumably you take a Writ, it goes up to the Third Circuit. My colleagues of the Third Circuit who incidentally, along with six of the seven in the Supreme Court said I'm dead wrong on the Medical Privacy Act, so now they want us to do six thousand contradictory hearings. My point is this, when you get up to the Court of Appeals my understanding of their review is they're going to look and see whether I had evidence which allowed me to make this decision. All I'm going to have in evidence is a stipulation that you reached the threshold of one hundred depositions. Now I guess I could get a sign and put it in neon and make it blink to tell you that--I'm trying to tell you that somebody needs to put some evidence on if y'all want my betters to overrule me again, or do whatever they're going to do with me, but I'm not hearing any evidence. I'm hearing great lawyer arguments. I think I've said this in here a bunch of times. Lawyer arguments at every jury I have ever presided over, I've told the jury, lawyers' statements are not evidence. Last time I looked

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that's still Hornbook Law. So what do I have in evidence? Now I don't know how else to say it more persuasively. Finish your argument, put some evidence on. If you're not, I'm ready to rule.

MS. GARSAUD: Okay, can I just confer real briefly with Mr. Campion and Mr. Brody?

THE COURT: Sure.

MS. GARSAUD: Judge, for now I'm not going to present any evidence. I'd just like to add though, even without the evidence if you look at your discretion in discovery, we came to you with a consent judgment, whether it's arm-twisting or not, that said a hundred and fifty and they could come and stop us at a hundred. That's what they've done. We're here saying we still need the one hundred and fifty. And now that our experts, I think, will testify, and I am going to ask him to get on the stand and testify why we need the one hundred and fifty, if that is okay. I know I just told you I was not going to but I believe that we have changed our minds.

THE COURT: And that's okay. That's fine. Actually it's going to make me a little bit happier, I guess, that at least they'll have something to review when they decide whether I was right or wrong. You mention in your brief that pretty much it's repetitive. They say the same thing every time.

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MS. GARSAUD: Well, Your Honor, we're seeing that they're saying the same thing every time and what they're saying is yes, the medication is safe and effective. No, I do not get promoted off label, I was not asked to use the medication off label, but nevertheless, what our statistician has--the information he's provided us that in order to get the statistically significant sample that the plaintiffs have begun injecting into this litigation is this whole statistical evidence issue, is that I need to look at a hundred and fifty. That is how I will be able to get the most credible and valuable information to me as a statistician to come up with my recommendation.

THE COURT: That could be, so I glean from your comments, and I'm going to come back to Mr. Bassett in a second, that everybody agrees, and I think although it's never been stated for the record that we are likely going to try this case by statistical model, in the main. That's the first thing I want to say. Second thing is you saying it doesn't make it so.

MS. GARSAUD: You're right.

THE COURT: Mr. Bassett, do you have any evidence you wish to present?

MR. BASSETT: Yes, sir. I'd like to offer, file and introduce, which is already in the record, the brief on behalf of Janssen, which

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says, "To be sure, Janssen's expert can draw reliable conclusions about the entire prescribing population from 100 depositions."

THE COURT: Any objection to that being presented?

MS. GARSAUD: No, Your Honor, we have no objection.

THE COURT: We accept that as Plaintiff #1 in this hearing. Anything else, Mr. Bassett?

MR. BASSETT: No, Your Honor.

THE COURT: Okay. Now Ms. Garsaud, do you have any evidence you wish to present?

MS. GARSAUD: Yes, if I could call our statistician, statistical expert, Dr. William Wecker.

THE COURT: Come on up and be sworn please, Dr. Wecker. And I've been remiss. We've got Dr. Solanky here who is the Court's statistical expert that I'd like to introduce to everyone. He's going to be listening at least to tell me what's what. If you'd be sworn, please sir.

THE CLERK: Raise your right hand. Do you solemnly swear the testimony you're about to give shall be the truth, the whole truth, and nothing but the truth, so help you God?

DR. WECKER: I do.

MS. GARSAUD: Your Honor, I'm going to defer to Mr. Brody to question Dr. Wecker.

THE COURT: Go ahead.

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MR. BRODY: Good morning, Your Honor. Dr. Wecker has a somewhat broader presentation that we had created that was geared towards the issues that are going to be confronting the Court as we move forward through the discovery process towards trial. I want to focus right now for the note of evidence on this motion with a very focus question to the relevance of the motion. We would also like him later to talk through the presentation because there's something we felt was going to be important but I'll just focus on what we need for the motion at this time.

DR. WILLIAM WECKER

called as a witness, being duly sworn;
was examined and testified as follows:

DIRECT EXAMINATION

(ON QUALIFICATIONS)

BY MR. BRODY:

Q. Dr. Wecker, could you state your name for the record, please?

A. William E. Wecker.

Q. And what is your profession?

A. I'm a statistician.

Q. Can you briefly describe for the Court your educational background in statistics?

A. I have a Bachelor of Science Degree from the United States Air Force Academy in 1963 and then after a period of

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military service I returned to the University of Michigan where I got the Master of Science and PhD Degree in Statistics and Applied Mathematics.

Q. And after you left the University of Michigan with your PhD, what was your next professional position?

A. I moved to the University of Chicago where I was assistant professor and later associate professor teaching Statistics and Applied Mathematics at the graduate level.

Q. How long did you stay at the University of Chicago?

A. Twelve or thirteen years.

Q. And in terms of roughly--what year would that take us up to?

A. Mid 80's.

Q. Okay. At that point what was your next professional position?

A. I accepted an appointment at the University of California at Davis where I became a full professor and did the same kind of work, Statistics and Applied mathematics.

Q. And how long did you remain at the University of California at Davis?

A. I've got a Vitae here but I'll give you my best recollection, around 1990.

Q. And when you left U.C. Davis what was your next professional position?

A. Two really. I started a consulting company, which I continue today. We are consultants in Statistics and Applied Mathematics to clients all over the world. I also continue to teach from time to time at Stanford and the University of Chicago.

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Q. Can you tell the Court a little bit about the statistical work that your company you started does?

A. Statistics is very broad in fields of application so we have clients that range from airlines to automobile companies, to banks, to governments, including governments outside the United States.

Q. And just to give the Court a little bit of a flavor, what types of questions and what types of statistical problems do you have experience looking at for your company?

A. It's every imaginable kind. It includes mergers of railroads, sometimes epidemiological questions relating to human health, and sometimes more appropriate issues here relating to medications and their efficacy and how to assess those kinds of questions. But that's not a special focus for us. We engage in statistical questions of all kinds.

Q. Have you published in the field of statistics?

A. Yes.

Q. And are you a member of any professional associations in the field of Statistics?

A. Yes, American Statistical Association, the Institute for Mathematical Statistics and a couple of others.

Q. Have you ever been qualified by a Court as an expert in Statistics?

A. Yes, sir.

Q. You ever--I figure I can probably cut it off there if there's--

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MR. BRODY: Your Honor, I'd like you to recognize Dr. Wecker as an expert in the field of Statistics.

THE COURT: Mr. Bassett?

MR. BASSETT: Your Honor, we don't have any questions for Dr. Wecker at this time. I'd just like to note that we are not prepared to cross-examine him on his qualifications because we never had the opportunity to take his deposition. We just became aware of what he might say by something that was overnighted to us. We got it October 8th. The fact that he might testify was not mentioned in brief by counsel, or whatever, so Your Honor can accept or not accept him, but we just don't want to be precluded from challenging his qualifications after we've had our right to take his deposition, investigate his qualifications and take a proper deposition. So we just don't want any ruling today to preclude us from objecting to his qualifications at the trial or at a later date.

THE COURT: I'm not going to make any decisions on what my decision today--I'm going to tell you this, you've been at this for four years, both sides, and to sit here and tell me, well I didn't know and they didn't tell me, well they do have discovery devices that allow you to find that out. But if you choose not to question him I'm going to accept him as an expert in the

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field of statistics and statistical modeling.

What else do you offer him in?

MR. BRODY: That's what we are offering him in for today's purposes.

THE COURT: Alright. Let's proceed.

DIRECT EXAMINATION

BY MR. BRODY:

Q. Dr. Wecker, are you familiar with the physician deposition process that's been going on in this case?

A. Yes, I designed it.

Q. And can you tell the Court--why don't you explain to the Court what the--just in general if you could explain the physician deposition process as it's been going on through these first--what we've stipulated to as being a hundred depositions?

A. Yes. It begins with the population of prescribing physicians, which numbers approximately twenty-six hundred. I have the exact numbers if it's important. I should explain where those physician names come from. Later today I understand I'll be describing a Medicaid database that has roughly a hundred and twenty million records in it, some of which are pharmacy records. And when an anti-psychotic prescription is Medicaid claim as a pharmacy record, there is nearly always a name of the prescribing physician. So I collected those names and found approximately twenty-six hundred. Then counsel for Janssen posed a question to me as to how could we learn what answers those twenty-six hundred physicians would give if

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they were asked questions of the kind that I can show you at some point today, the questions that usually begin, "In your experience..." and then continue on. And I explained that it is not necessary to look at all twenty-six hundred to know the answer. It is possible to have conclusions that are reliable about the answers all twenty-six hundred would give if you look at only a small portion of them. But you have to choose the ones you look at in a special statistical way. And I explained I'll do that for you. And so I designed the sample of a hundred and fifty in a--I'll mention a technical word, it's a stratified random sample and that's the design that is common for this kind of work. It uses essentially coin-flipping methods to determine who gets the deposition and who doesn't. And then I designed with the help of counsel, a script, so that all of the deponents would be asked exactly the same questions in exactly the same order. It's very much like sample survey interviews with the additional favorable feature from my point of view, that you actually have a transcript so that you can know exactly what was said. I then said when you're finished with that process I'll collect up the data and I will make certain statistical calculations and make statements not only about the one fifty but about all twenty-six hundred. What they would say if the process had continued for twenty-six hundred times instead of a hundred and fifty times, that's the design.

Q. And if you could explain to the Court how is it that you can draw conclusions--what is it that makes you able to

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draw conclusions about all twenty-six hundred from a sample size like a hundred and fifty?

A. Well, it's all aspects of the implementation as well because it's possible to gum up a process like this, but I'll leave aside simple blundering and go to the key thing, it's the effect of random sampling so that a coin--we don't use coins, we do this with computers, but to draw the analogy, a coin plays no favorites, and so by selecting the people to be deposed essentially by coin flips implemented by computer, then we can be assured that the group that we interview or depose is a representative of the larger group and the conclusions we reach can be generalized. If we--on the other hand we were to just take the A's and the B's from the last name, then people like me would be here testifying, you cannot generalize that.

Q. Now I want to focus on the issue that is before the Court on plaintiff's motion today, and that's the sample size, a hundred versus a hundred and fifty. Can you explain to the Court what the difference is for this process, with the physician group we have between stopping at a hundred depositions and continuing on to a hundred and fifty?

A. Well, there are a couple of differences. One is I designed this thing for a hundred and fifty and if you're a purist here in the statistical world, I've got a fixed sample size of a hundred and fifty and I'm counting now, I suppose I could try backing and filling and approximating but normally the statistical design does not include concepts of the hearings coming in and then the process stopping, but perhaps I could deal with that, but I'd

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rather not. The hundred and fifty is the design that would be much better evidence, I think, without complication if we just did what was design. The other thing is that although I heard earlier that the answers are repetitive and in some cases they are, nearly every time the answer is no, no one has ever suggested off-label use. I can read the exact question later. And those could be called repetitive because of the seventy that I've had a chance to look at so far lag from the hundred just not reaching me yet, Your Honor. Nearly everyone is saying the same thing but that's not true for every question. There are seventy-two substantive questions and those are split more--some of those are split more evenly. And so with as many answers as I have and as many different kinds of prescribing physicians, some who prescribe a great many more than a thousand, some who specialize in treating schizophrenic patients, some who do not, hence the stratification that I imposed at the beginning. I did not feel comfortable. If I would have thought a hundred would do it, I would have picked a hundred. A hundred and fifty in my judgment is going to be what's needed here in order to come up with statistically reliable results.

Q. Now in terms of the--from a statistical perspective, the confidence with which results can be--from a hundred can be extrapolated to twenty-six hundred as opposed to results from a hundred and fifty being extrapolated to twenty-six hundred, can you--does that make any difference in terms of what your ultimate result is that you're reporting?

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A. Yes, the results of a hundred and fifty will be more accurate and I think sufficiently accurate for--it's a judgment call. I can't be sure what issues will come up in the future and what question that was asked out of the seventy-two will turn out to be essential to the case and so I have to anticipate those things as best I can. But there's no question the hundred and fifty will be substantially more accurate than the one hundred. And what a waste it would be to have a hundred and find out that the statistical variation is such that you really can't learn what you had hoped to learn, whereas if you had a hundred and fifty you could.

MR. BRODY: Thank you, Dr. Wecker. I appreciate you taking your time to explain it and as part of the note of evidence on the motion.

THE COURT: Mr. Bassett?

MR. BASSETT: Judge, first of all, and we're not arguing with Your Honor, just to respond to something the Judge said. Judge, on experts the first opportunity to look at experts to see the case management order when they produce reports and then his report's not due until April and we got some presentation thing that we got in the mail a couple of days ago, so there really hasn't been an opportunity to cross-examine this expert. It's not been through a lack of due diligence on our part. We have interrogatories outstanding as to who the experts will be, or whatever, but I just want to let the Court know that I know the

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litigation is old but we really haven't had an opportunity to cross-examine this expert yet and it's not because we haven't wanted to, we're just finding out the things he was going to testify about in a document that was delivered to us two days ago. But I just want to respond to that, Judge.

THE COURT: It wasn't my intent to hurt your feelings.

MR. BASSETT: Well, they did, Judge.

THE COURT: But it was my intent to point out that in fact this is the evidence that we knew when you filed your request that they discontinue that something of this nature would occur. And I understand that we haven't reached any point--today is the first day we're going to have experts. So I wasn't trying to be facetious today. I was trying to say I think it was expectable that some type of testimony from a gentleman such as Dr. Wecker would occur. That's all I'm saying. So please accept my apologies if in fact you were offended.

MR. BASSETT: Judge, it's not so much that my feelings are hurt as I just don't want to be precluded from challenging this doctor's qualifications to testify in whatever field he's being qualified in until we've had a chance to properly cross-examine him.

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THE COURT: And I haven't ruled that you will be precluded, but I'm also not ruling that you won't be. That's a matter for another day.

MR. BASSETT: Thank you, Judge.

THE COURT: Okay.

CROSS-EXAMINATION

BY MR. BASSETT:

Q. Dr. Wecker, what we got in advance of this hearing before we got your report here or the presentation, what we got was a brief from counsel, and it said, "To be sure, Janssen's experts can draw reliable conclusions about the entire prescribing population from a hundred depositions." Is that not true, sir?

A. I think I can draw reliable conclusions but not as reliable as if I have a hundred and fifty. Not as accurate.

Q. You can draw on the basis of the hundred depositions that you have today you can draw reliable conclusions?

A. Yes, it's a reliable conclusion to report that I cannot determine anything because at least I'm giving you scientifically correct statement. So yes, I will not be precluded from making scientifically correct statements that I can defend, but they may not be as useful as they would be if I had enough data to speak to the issues.

Q. In your presentation you say that the gold standard is randomized clinical trials?

A. Yes, but I think you're on a different subject, but I agree with that.

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Q. Well, if we ask the question like in the brief that we have, it says the question that you asked the doctors, "In your experience, does Risperdal typically have a more moderate side effect profile in first generation anti-psychotics?" That's a question that--in your sample that you're asking the doctors in Louisiana, right?

A. Yes. The question begins with "In your experience, doctor..."

Q. Right. And what is that, some sort of observational study? What would you call that?

A. I would prefer to call it a reporting of what the doctors have to say in response to that question.

Q. There are clinical trials out there that the National Institute of Mental Health has done that examine that exact issue, are there not?

A. No. You may have clinical trials but they are not clinical trials of Louisiana Medicaid patients and they do not tell you what the experience is of a doctor treating Louisiana Medicaid patients.

Q. But there are clinical trials that tell us if Risperdal has more serious side effects than the older generation drugs. That's what you're asking the doctors here, right?

A. I think there's a difference. First I'm not conversant with the clinical trials. I know they exist and I know a little bit about them, but that's not the same--they do not give the answer to the question what do physician treaters of Louisiana Medicaid patients have in the way of

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experience with these drugs. I don't think you can infer one from the other.

Q. Well, aren't you in your study, unless I don't understand how all this works, is it the doctors--say, if these doctors say, in our experience we haven't seen that the new generations cause more serious side effects than the old generations, aren't you to come to court and kind of use that as evidence in front of the Judge to say is Risperdal safer than the older generations? Isn't that what this is about?

A. If asked I would come to say something more limited than that. I would come to say that the hundred and fifty that have had this question asked are representative of the twenty-six hundred. This is the question, these were the answers and then I'd down.

Q. Well, given that there are--are you familiar with the CATIE Study?

A. Only generally. I haven't dived into it.

Q. Are you familiar with the study in Great Britain?

A. No.

Q. Are you familiar with the recent study that just came out by the National Institute of Mental Health?

A. I don't know those studies.

Q. You've never heard of that study?

A. I've heard of them but I don't want to pretend that I'm expert in them. Perhaps I will be when I see you again, but I'm not today.

Q. Are you familiar with those studies? Have you read those studies? Have you read articles on those studies?

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A. I've read a little about the CATIE Study but that's not been something I've been assigned to do. My assignment had to do with these depositions.

Q. I understand. Are you familiar with the other study, the recent one by the National Mental Health? Have you read about it?

A. No.

Q. Would you agree that according to what you're presenting us here that those types of clinical studies would be the gold standard and that they would be superior to this type of study where you kind of randomly go ask doctors in Louisiana?

A. No, I cannot agree with that. First kind of go randomly if it's allowed in this court to have one's feelings hurt, everyone who is a statistician would get hurt by that one. That's what we're supposed to do. It's not a weakness. So the fact that we went to these doctors with a randomization method, that's the good thing. Second, to continue answering your question, no the clinical studies cannot tell us what these doctors will answer to these questions and to the extent that what doctors in Louisiana who treat Medicaid patients in Louisiana have to say, and the way to answer these questions, if the Court finds that to be relevant information then I've provided a means by which they can get information without having to talk to twenty-six hundred people.

Q. Well doctor, the reason I'm asking that question is because my understanding is that you want to model things and the reason that y'all need to do this hundred, and one

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of the reasons that you need to do a hundred and fifty depositions is you want to ask questions to show that the Risperdol is safer. This is example that's used in counsel's brief, that Risperdal is safer than the older generation drug and I'm just asking if you really needed to do all that since you say the gold standard is clinical studies, and there are several clinical studies out there. It's my understanding the only difference is is that you think somehow with the Louisiana population it's going to be different than the populations in these clinical studies?

A. Well, there's no question of that. They are different, and I know from experience that Medicaid populations are quite different in terms of risk factors and conclusions from the general populations don't automatically carry over to special populations. That's true and I could defend that if required. I'm starting to see with some clarity now where I can be helpful on the issue that is before the Court here. I think the issue is simply not a statistical issue. The issue is whether or not the Court is going to be interested in what Louisiana physicians who prescribe these anti-psychotics have to say in the answer to these questions. That's really not a statistical question. It's a question perhaps of evidence and relevance but it hinges not on statistics, it hinges on whether it's interesting to the Court to know what these doctors have to say. It's as simple as that.

Q. Are you aware that some doctors' depositions have been scheduled and they cancel and not reschedule?

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A. I understand there have been some scheduling problems but mainly not, and with my urging they're continuing to pursue everyone I selected.

Q. Are there--is there any reason you're aware of why certain doctors' depositions were scheduled then cancelled and then not rescheduled? Are those doctors being eliminated from the study?

A. I don't know why the scheduling and rescheduling. I have no knowledge on that and no one has talked to me about eliminating anyone, and depending on the call, if it ever comes, I will have an answer, but most likely my answer is don't eliminate them because you choose to. If they died, they're eliminated. They will not be answering questions. That does not pose a problem to me as a statistician. They are simply non-responsive and that doesn't pose a problem. But if the lawyers decide that they now don't want to go to fifty doctors of their choosing, that's terrible to the integrity of the process statistically.

Q. So you would think that the depositions that have been cancelled so far of doctors--strike that. Let me ask this in a different way, Dr. Wecker. We really didn't know what your--how these doctors were selected. Still really don't, but what you're saying is you selected each and every one of these one hundred and fifty doctors?

A. Yes sir, I did.

Q. And it's your expectation that all of them would be deposed, not selectively?

A. That's the goal. In a practical world, sometimes that doesn't happen, but I would urge that they do everything

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that they can to get all hundred and fifty, and if they can't, then I need to understand why they can't and do something about it.

Q. You wouldn't approve of a system whereby they selectively cancel some and don't reschedule those?

MR. BRODY: Your Honor, I'm going to object.

This is well beyond the scope of direct examination and I don't think it's relevant to the issue that was framed for the Court today.

THE COURT: The scope of cross-examination is unlimited. That objection is overruled. Answer the question.

A. Yes, sir. It would depend on the reason for the rescheduling or the lack of rescheduling and I'd have to hear it out, but generally I would not approve. If the deposition is accomplished I don't care very much about the date and so rescheduling by itself is not a problem. But failure to take the deposition would not be good.

Q. Are you an expert in designing surveys?

A. I've done that many times, yes.

Q. Have you been qualified as an expert in designing surveys?

A. I'd have to look at the records probably, but I've been at this business now for thirty years, so I don't have a recollection off hand.

Q. Can you explain what the method of randomized response is in survey research?

A. I'd have to hear more of the context but--so I'm not sure. I'd have to hear more of what that has--

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Q. But as we sit here today you're not able to answer that question. You don't know what the method of randomized response is?

A. I know the two words but if you put the two together I'd have to hear--if a colleague talked to me about that I'd say, explain to me what you mean.

Q. Alright. So as we sit here today those words have no meaning to you though?

A. The two words do, but normally you don't think of the response as being randomized, you think of the subject as being the subject of randomization. The response belongs to the respondent.

Q. You didn't use the method of randomized response in your survey?

A. No, I used a very basic method, simply a stratified random sample of the twenty-six hundred.

Q. And you don't know if randomized response would be a better way to get more accurate information from your survey?

A. It doesn't occur to me that it's a better way, no. But my survey information, if I might continue briefly, would be available for everyone and if there's a better way to analyze it than what I've analyzed, they're welcome to analyze it as they choose.

Q. Well, are the survey questions that you're giving out randomized in any way?

A. No. They are in strict order. They're always asked in the same order.

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Q. Why might that be a useful thing to do if you think it would be to randomize it?

A. Well, sometimes, in fact often in interview work, depending on the response to one question, you might then proceed down a different branch in a tree here of questions, and so that that person gets different questions and if they had answered differently. That's just a way to do sampling. It wasn't necessary here. It's a complication that wasn't needed.

Q. Did you use some mathematical component to arrive at your survey number of one fifty?

A. No, it's not a number that can be calculated precisely and I did not calculate it precisely. After all it's a nice round number, so it's obvious I picked it. I know from experience how to do those calculations, then I could see from experience that if I wanted it at the end of this work to have results that differed between two comparison groups to be termed statistically significant, which means not confused by the sampling fluctuations that are inherent in any sampling, that a number of about a hundred and fifty would be really the least that I was comfortable with.

Q. But their mathematical formulas that were at your disposal would determine what the correct sample size would have been?

A. Not really. Those formulas, which I am familiar with, are--have inputs to them, the requirements that can't possibly be known before you start the sampling so you have to make some judgment as to what you think you're going to see as you proceed. And if you already knew that you

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wouldn't have the sample in the first place. So they're sort of a guide but they're not precise.

Q. So you've never used mathematical formulas in determining sample size?

A. I use them all the time, but only as a general guide.

Q. Did you do it in this case?

A. No, because they're all in my head. I've done them so many hundreds of times, I sort of know how they come out.

Q. Alright, but you're—so the number one fifty you could have used—you could have sat down with a pen and paper and you could have used some mathematical formula to get us to that number, but you just kind of picked it out of your head, some random number that you thought was good from your experience?

A. No, no, I'm saying the opposite. There is no formula that you can apply to a situation as complicated as we have here that will say choose a hundred and fifty. There are formulas that would guide you on a question-by-question basis and tell you if you're willing to assume something about how the results come in, what degree of accuracy can be achieved. There are formulas like that. But since there are seventy-two substantive questions and you have a different formula answer for each one and you don't really know how the answers are going to come, the formulas aren't of that much use, not for precise calculation.

Q. So just to make sure I understand it, sometimes you use these formulas and sometimes you don't, but the reason you didn't do it in this case is you didn't think the formulas would be useful because you ask so many questions?

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Did I say that right?

A. That's part of it and part of it is that the costs were not strongly at issue. In some surveys there's—I don't mean to undervalue your concern about the costs of this whole enterprise, but there are some situations, say if you're interviewing people in neighborhoods that it becomes less expensive if you speak to one person to go to the next door neighbor and the next door neighbor after that because you don't have to travel as much. Well, that reduces the cost of the exercise but it has a downside in terms of statistical accuracy because you get what's called a cluster sample. Nothing wrong with a cluster sample but it's just not as accurate as some others. So then you can start balancing the costs against the accuracy and formulas come into play at that time. But our situation just doesn't seem to call for that.

Q. I'm sorry doctor, I didn't follow that. Are you saying that--what was your cost concern exactly in this case?

A. I didn't bring it in, in this case. I was saying that in response to your question about formulas there's something called Neyman allocation, N-e-y-m-a-n, but that has to do with saving money, that doesn't have to do with statistical accuracy, per se. But maybe half the time you do sampling costs are a big factor and if you can do some designs for ten percent of the costs of other designs at only a small penalty and accuracy and you like to do calculations on that. I really didn't see those issues coming up here.

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Q. If cost was a factor in this one, the sample size would have been smaller?

A. I don't know. It's a hypothetical that didn't happen.

Q. But really the number--the one fifty is just kind of an eyeball number for you, right?

A. It's an experience judgment number and if I had to deal with a hundred I'd be uneasy about the outcomes. We'll know when the results are over and I have opinions that don't have the specificity that I had wished to have if I'm restricted.

Q. What is the role of power in sample size computations?

A. That's another calculation that one can make that deals with the question of discriminating between say two situations that are hypothetically put. Once again it would have to be a hypothetical calculation in this work and I normally don't do power calculations in advance of a sample design, but sometimes I do afterwards.

Q. Excuse me, Dr. Wecker, I have one--let me confer with counsel on that.

(MR. BASSETT CONFERS WITH COUNSEL AT THIS POINT.)

MR. BASSETT: Thank you, Dr. Wecker, that's all I have.

DR. WECKER: Thank you, sir.

MR. BRODY: Your Honor, I just have two follow-up questions.

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RE-DIRECT EXAMINATION

BY MR. BRODY:

Q. Dr. Wecker, are you aware of any randomized clinical trial anti-psychotic medications involving the Louisiana Medicaid population?

A. No.

Q. One more question, are all clinical trials conclusive?

A. Not necessarily no, it depends on a lot of things, like sample sizes and outcomes.

MR. BRODY: Thank you.

BY THE COURT:

Q. How did you pick the hundred and fifty names, doctor?

A. I have done that, yes Your Honor.

Q. How?

A. Essentially by means of coin flips, although computers programs do it, that's why I use the SAS statistical software for random number generation and I saved all the results and prepared to disclose them should anybody want them.

Q. Okay, you said that a hundred would be useful and reliable but a hundred and fifty would be I guess more useful and more reliable. Is it because of the sheer numbers?

A. Yes, Your Honor. It's as simple as that. The more you look at, the more you know.

Q. So if you did less than a full sample, if you did thirteen hundred of the twenty-six hundred you would be more comfortable in your result?

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A. Not much more though, Your Honor, because the rewards of increasing sample size diminish as you go to increasing numbers. You get great benefits for increasing from say fifty to a hundred substantial benefits from a hundred to a hundred and fifty, but the benefits drop off as you move up.

Q. Does it matter what your overall size that you're sampling is?

A. From the size of the population, you mean?

Q. Yes.

A. Well that's something that almost no one but statisticians understands.

Q. I don't want to understand it, all I want you to do is tell me.

A. It doesn't matter. It doesn't really matter. There's a tiny term and some formulas but it can be neglected, so if we were sampling from twenty-six hundred or twenty-six million, I would have probably still said one fifty.

Q. Okay, the last thing I have to at least help me is if you do a hundred it will be useful--it will be reliable. Let's see, you said to reduce it from a hundred and fifty to a hundred would be terrible to the integrity of the process. How much would the integrity be affected by reducing from one fifty to a hundred?

A. If one is a purist about it, it would mean that one couldn't generalize at all to the population because I would have to study which one hundred were actually done. Your Honor will understand that I could not have said let's use a hundred and fifty. You lawyers pick them. That would

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not have worked because the lawyers could cherry pick by intent or by accident, the group that you got would not be representative of the whole if they are cherry picked. That's why I picked the one fifty. Now if I pick one fifty and say if you do these one fifty I can promise you that they will represent the whole, and instead you say, well let me cherry pick a hundred, that does great violence to the integrity of the process.

Q. I understand that. You didn't use a subjective process to select these one hundred and fifty prescribers, you used a random coin flip by computer?

A. Yes, Your Honor.

Q. How much is the accuracy affected by reducing the sample size from one fifty to a hundred, even though both are useful and reliable?

A. I'd have to do a calculation to answer that, but I can approximate it. Maybe twenty percent.

Q. Suppose you went up to two hundred for your sample size, would it increase the accuracy?

A. Not by that much because the benefits drop off as you go from one fifty to two hundred.

Q. Alright. Assume that I know nothing about statistics. How fast does it have to grow before it drops off where it doesn't count much anymore? A percent, two percent.

A. It's like a ski slope, Your Honor. At the top of the slope the benefits are great as you increase the sample size and it just keeps getting less steep as you keep going on out. You can always get a gain. It's always beneficial to look at more, but the benefits of accuracy peter out

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after a hundred and fifty to a hundred. But if I may, Your Honor, there's another element. Why would anyone look at fifteen hundred, and people frequently do, like the CATIE Study, is because sub groups turn out to be important. And so you may think you have fifteen hundred but if you want to look only at the males or only at the older people, now the sample size is whittled down substantially, so they start with a larger group. So if they know they can look at sub groups where the study of the data starts to suggest something special to be learned. So that's the reason sometimes that people pick larger samples.

Q. Okay. A hundred and fifty is whatever percentage of twenty-six hundred that it is. One hears every day, one sees--particularly every day we see about twenty polls and they're presumably taking a nationwide poll and they do it with eight hundred people. Why do we need a hundred and fifty on a twenty-six hundred population when they do eight hundred on a three hundred million population?

A. There are two parts to the answer, Your Honor. First the size of the population is essentially of no importance. So whether the fact that it's twenty-six hundred versus twenty-six million or two hundred million doesn't have much to do with accuracy, but it is true that eight hundred is more accurate than a hundred and fifty. And so we know from watching the poll results on television that they'll say within a margin of error, plus or minus two percent. That's with eight hundred sir. Well, I'm not going to be that accurate with a hundred and fifty. So I will not be able to discriminate small differences in efficacy that are--

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well, in answers to questions really, small differences in answers to questions because I only have a hundred and fifty. The large differences in answers to questions I can discriminate and say that they're not a fluke of sampling, they're real, and if you continue this process twenty-six hundred times you would see that all the rest of the people were answering similarly. But if it's a close call and we have say fifty-three percent answering one way and forty-seven the other way, I can't promise you that if this process were continued that it wouldn't reverse very much like an election poll.

THE COURT: Okay. I think I've gone to the extent of what I can understand so I'm going to quit. Mr. Bassett, you have any questions on what I've covered?

MR. BASSETT: No, Your Honor.

THE COURT: Ms. Garsaud?

MS. GARSAUD: No.

THE COURT: Mr. Brody. I'm sorry.

MR. BRODY: No, Your Honor. No additional questions.

THE COURT: You may step down doctor, thank you. Any other evidence you wish to present, Mr. Brody, or Ms. Garsaud?

MS. GARSAUD: No, Your Honor.

THE COURT: Mr. Bassett, any rebuttal?

MR. BASSETT: No, Your Honor.

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THE COURT: Okay, note of evidence is closed. I'll hear you, Mr. Bassett, if you have anything further to say.

MR. BASSETT: Judge, it would just be repeating the arguments I've already made. I've heard him to say--it sounded to me like it was a fairly arbitrary number he picked, that he could make do with a hundred. I think that there are mathematical formulas that he said that were out there, that could have got to the sample size. He just picked this one out there. Their brief said that they could do with a hundred. He wants do the extra fifty, I don't see the big difference except for the cost or whatever, so those are the arguments we have, Your Honor.

THE COURT: Thank you. Ms. Garsaud?

MS. GARSAUD: Your Honor, just in conclusion I think this case about Louisiana. There's allegations about Louisiana doctors and the best place to go look for that information is through the depositions of the Louisiana doctors. And based on everything that Dr. Wecker just testified to, a hundred and fifty is the best number to achieve that. Thank you.

THE COURT: With regard to the mathematical formulas, Dr. Wecker said he didn't think he needed them. He's the only expert I heard testify. I understand that it's burdensome to take another fifty depositions. The other thing

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he said was he was more comfortable. The efficacy would increase from a hundred to a hundred and fifty. It incrementally reduces as I understand it with the sample size that you're taking and that in his expert opinion he needed a hundred and fifty to do what he set out to do without doing something terrible to the integrity of the process. I'm going to deny the request to discontinue the fifty and allow the fifty to continue, at the cost of the plaintiffs. Okay, now we're going to take a very short recess. I have to make a call or two, then we're going to go into our status conference and hopefully we can finish up before too long.

(COURT STANDS IN RECESS AT THIS POINT.)

THE COURT: Patsy, we're on the record now for the status conference. The first thing we're going to do is accept the case management order compiled by both parties.

MR. CAMPION: There are two copies, Your Honor.

THE COURT: Thank you. I'm going to say that since you guys crafted this I'm pretty well satisfied that you're both satisfied with it, so all I have to look for is the dates that actually acknowledge the trial date and then everything falls back from there, right?

MR. CAMPION: That's correct, Your Honor.

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THE COURT: Alright, February 8th. Where is my calendar? I think I'm pretty good on that. I did look.

MR. IRWIN: Your Honor, we picked the time for the pre-trial conference also, or a date for the pre-trial conference, but we have not included a time in there.

THE COURT: Okay.

MR. IRWIN: For the pre-trial conference. You may want to look for that.

THE COURT: Looks like y'all have the--I haven't set anything in 2010 because I like to keep my docket in less than a year if possible because I never know how much longer I'm going to be here and so I like to think that what I start I'm going to get to finish. Okay, the pre-trial date, you have a date but not a time?

MR. PERRIN: I think we put down February 1 as the pretrial date.

MR. IRWIN: That's correct, Your Honor.

THE COURT: It's awful late for a pretrial, don't you think folks?

MR. PERRIN: That's the final pretrial, Your Honor. We have a series of deadlines that start actually in the summer of next year going forward, and I certainly don't mean to preclude any other conferences the Court may wish to have.

THE COURT: How can I twist your arms only a week before the trial?

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MR. PERRIN: I'm sorry?

THE COURT: How am I going to twist your arms with only a week before the trial? That would pretty much be nothing. It'll be ineffectual.

MR. PERRIN: Judge, I have been here--

MR. IRWIN: There are motion hearings coming up before then that you'll be seeing us, you'll be twisting our arms and beating us up in the head with our arms at the motion hearings. And we can adjust the pre-trial date, Your Honor, if that's the Court's preference.

THE COURT: I'm going to tell you that other than Mr. Juneau sitting over there the only governor that I have on me is that I'm overwhelmed. I just can't fathom the length of the trial we're going to have, so I'm happy that y'all have reached this part. Whenever I feel particularly gloomy I call Mr. Juneau and say, you got a handle on this? And I know he does, so then I can say okay, I'm happy with the case management order. Nine o'clock?

MR. PERRIN: That's fine, Your Honor.

THE COURT: Okay, then I'm going to accept the case management order and adopt it as the order of the Court, date it today's date, which is the 10th. Pat, did they give you a copy yet?

MR. JUNEAU: No, sir. But I knew about it because I talked to Mr. Perrin and Mr. Champion joined in. I knew it would be presented today.

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THE COURT: Also, before we get started on the more, I guess substantive portion of the status conference, I got a call from our I.T. guy during the week saying we want to do something to put on your computer, and so he called me and I said I don't know what you're talking about.

MR. CAMPION: Judge, we had hoped that maybe Dr. Gordis could be tied in and we were trying to find out if the facilities here were such that we could make a telephone--a television connection.

THE COURT: And were they?

MS. GARSAUD: Yes, they were. Unfortunately Dr. Gordis though was out of the country, so that precluded us from--

THE COURT: Okay, Yom Kippur is now over, right? He's back in the country?

MR. BRODY: My understanding is he's back next week.

MR. JUNEAU: Next week, I think, Your Honor.

THE COURT: Okay. So Pat, you're going to get him whatever we do today to at least apprise him?

MR. JUNEAU: Yes, I personally talked to him on the phone and I will get to him materials. He knows about this conference, what's going on and I'm going to fully brief him on that.

THE COURT: Okay, as I told you earlier this is Dr. Solanky from the University of New Orleans. He is our court expert. What I asked you guys to do today, first of all you've already

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done the majority of it. You got the case management order done. That's outstanding. Now we can move toward a definitive date. I should tell you all that I--whenever they call for scheduling conferences, either myself, or my clerk is instructed to tell the lawyers that I give only first fixings. You get a continuance if you are on your deathbed and have your tombstone with you. I do not grant continuances. I mean it's very rare, and the reason I do so is that if you hold their feet to the fire we have our trials and my docket moves. So I'm telling you now, don't come back and ask me to move it. Don't ask me to continue it. We're going forward. Again, I'm very happy with that, so we can get it done. Now, I had asked you, knowing that it would probably be problematical; I'm not sure how far could push an envelope, to bring your, at least experts here so we could speak in generalities, so that this gentleman and Dr. Gordis could then tell me whether it make sense. What I'm going to shoot for, everything you've both sent me indicates that the construct of the model is-- controls everything. I want to shoot right down the middle. I want a fair presentation so that when a jury hears this, that it's reliable, it's useful, it's accurate, it's fair to both sides. That's why I've asked you to have your experts here today. I received during the week, very

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recently, something from Mr. Brody indicating that there would be a presentation of sorts by Dr. Wecker. I am given to believe that there is some umbrage taken by that.

MR. MORROW: Yes sir, Your Honor. When the Court ordered the parties to bring their experts, it was specifically asked whether or not we would have to render a report, make a presentation. The Court said no, we just want them here. Two days before this hearing we get an overnight mail from Mr. Brody and for the first time we learned about Mr. Wecker. And that was the reason why Mr. Bassett was unable to cross him, Your Honor, because forty-eight hours is insufficient for us to go in and critique his Curriculum Vitae. And then now they want to give you a presentation of their side of the case without the opportunity for the plaintiffs to cross-examine Mr. Wecker, to get a report from him. And Judge, you told us not to come to make any type of presentation and forty-eight hours before this hearing they come up and give us a report, this is what our expert is going to say and present to the Court? It's not fair, Judge. It's not right. And we object to any presentation at this juncture in this case. We have a right to confront Mr. Wecker and any other experts that come forward, just as they have a right to confront any and all experts. But to send us something within forty-eight hours,

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Judge, and say this is what my expert is going to say, that's not right Judge, and that was not contemplated by the Judge's order, the plaintiffs do not feel that when the Court ordered the parties to bring their experts. Had we known that the Judge would entertain, you know, reports--I mean, presentations, Judge we could have presented you a two or three hour presentation on the plaintiff's concept of this case, but that is not what the Court told us, and we object. We strenuously object to the defendant attempting to put on in this status conference any type of presentation. You know, we don't have a right to cross-examine him and we certainly disagree just in looking at this thing with a lot of things that he's saying. Give us the opportunity to go take his deposition and cross-examine him, Your Honor, before he puts forth their position unbridled before this Court. So we strongly object to the presentation.

THE COURT: Mr. Campion.

MR. CAMPION: Yes, Your Honor. The transcript obviously will control, but I do not recall you having said anything to the effect of what Mr. Morrow has just said.

THE COURT: I'm reading the transcript as we speak to see if I can find any. Okay, let's assume it doesn't say that.

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MR. CAMPION: Right. I had the following in mind, it did not occur to me that you were asking these people to come here so they could stand up and be viewed, because otherwise we could have brought photographs, and otherwise you wouldn't have brought the expert to look at the photograph. So we had the impression, I think a fair one, that you wanted to have some general impression, general presentation, not even subject to cross-examination, and therefore we did what we had to do. To the extent they believe that they are not prepared to move today, why don't you arrange for the next hearing where their people can do exactly what Mr. Wecker did in the document he gave you and the presentation he's prepared to make? Thank you.

THE COURT: What's wrong with that, Mr. Morrow?

MR. MORROW: Well, first of all why did he wait till less than forty-eight hours to send this to me, you know? If he had all of that, if that was their impression from two or three months ago, why wait forty-eight hours to send it to me?

MR. CAMPION: Because that's when it got done.

MR. MORROW: Oh--

THE COURT: Anything else, Mr. Morrow?

MR. MORROW: Yes, sir. We strongly object.

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THE COURT: I understand you strongly object. What I don't understand is what you strongly object to. If you object to me making you bring your experts here and saying anything at all, you both have the right to do that, and I know I'm overstepping my bounds in that regard. When I'm looking at my transcript, which everyone here seems so happy to do, and underline my verbiage, what I said was that we've reached the point where if I've got experts and we're finished with the broad discovery, it's time to start moving to trial. So I want your experts here, or at least your lead expert so we can start some discussion. I'm going to get out of your way after they're here and you're going to--if you don't want to divulge to one another, you don't have to. That was your prerogative. Then I'll make some decisions and go forward. What I was--what I've been concerned about from the beginning and what I just said, I believe to me it's important that the construct of the model be done correctly. At the end of the day you're both going to have ideas. At least now I think you both agree that we're going to do a statistical model of some sort. Then it's going to be incumbent upon me to choose what I find is the fairest construct, which is why Dr. Solanky is here to aid me. Now I'm not certain as to--I don't know that I understand the objection or the strenuousness of

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it, Mr. Morrow. Do you feel that if they make a presentation that I am somehow going to be tainted? And if you think that, I understand, but I don't understand the objection.

MR. MORROW: The objection is very simple, Your Honor. The plaintiffs were under the impression that you wanted the experts here without rendering any type of report, etc., because we--the Court will recall we said Judge, why do we need to bring our experts here when the defendants have not finished giving us or responding to our discovery. So how can we--

THE COURT: I don't see that anywhere in the transcript.

MR. MORROW: We had talked about that in prior--you know, in prior status conferences, Your Honor, so we were somewhat confused as to why we're bringing our experts here if we're not rendering any reports, and that was the understanding that the plaintiffs had.

THE COURT: Tell me what your understanding was as to what your expert was going to do?

MR. MORROW: I don't know. The Court said bring them here. And we told the Judge, we don't have any expert reports to give you because discovery has not been completed. The Court said, bring your experts here. So we have the experts here. And had--

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THE COURT: Alright, I'm--I'm sorry, I don't mean to interrupt you. Go ahead.

MR. MORROW: And had we known that this Court would entertain presentations, we would have presented them to the Court today, but that was not the impression of the plaintiffs when we left here the last time and the time before that, Your Honor, and I don't know if whatever--if the Court allows this presentation, is that evidence? Is it being recorded? I don't know. We object to it as--number one it being going forward. Number two, that it be recorded because this is merely a presentation. We don't have the right to cross-examine, you know?

THE COURT: I don't think—I think I can assuage some of your concerns.

MR. MORROW: Okay.

THE COURT: I'm not going to record it. I'm going to leave.

MR. MORROW: Okay.

THE COURT: I'm going in my office and do some work.

MR. MORROW: Okay.

THE COURT: What I wanted your experts here for, and I thought, of course I always think I'm plain and probably I wasn't, was I wanted to get some handle for my expert on which direction you guys are going. Now I am befuddled that you thought that—I just can't believe you thought

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that I wanted you to bring your expert so I could look at him and see if he had a Brooks Brother's suit or not. I mean it's just amazing to me. What did you think was going to happen?

MR. MORROW: I did not know, Your Honor, and the plaintiffs, we talked about that. The Judge wants us to have our experts here but yet he is not expecting any type of expert report simply because the discovery had not been completed.

THE COURT: What did you think I meant when I said that we were going to have an initial "verbatim" (Court making reference to verbatim reading of prior transcript) discussion between the experts so that we could get a handle on which direction we're going. What did you think that meant?

MR. MORROW: I don't know, Your Honor. I don't know. I truly did not understand the Court's directive. Had we understood that, yes we would be--we would have our expert prepared to render some type of general--

THE COURT: I am not trying to put you at a disadvantage in any way, shape, or form. What I was trying to do, and I knew as I said I was overstepping, but we needed to get started. Well, one thing it's done, we got a case management order with a trial date now. So we're moving forward. We at least get to eyeball, if nothing else, your expert, the lead expert

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statistician, Mr. Campion's lead expert
statistician, and you get to meet Dr. Solanky,
but more than that, I didn't want to just have
them come here and make a trip for nothing. What
I wanted, and what I intend to do, if it will
help you any, is I'm going to leave. You don't
have to say a word if you choose not to, but what
I wanted them to do is give at least in
generalities, which is what I thought I said, to
Dr. Solanky so he can begin to prepare me on an
understanding of what you guys are going to be
doing. I don't need a report today. There's no
cross-examination. You're not bound by anything
you present, but I'm assuming that you folks,
I've said this a hundred times, you guys are the
crème de la crème in your profession. To sit here
and tell me that you didn't understand, then my
response is this, and I did say this last time,
the last time I looked we had a new invention on
the planet, it was called a telephone or an e-
mail, and say Judge, could we get a conference
call, and what did you mean? Nobody did that. Why
are we doing that today?

MR. MORROW: Judge, our experts will be more
than happy to meet with Dr. Solanky and talk to
him about their methodology. Sure, we can do
that.

THE COURT: And if y'all want to do it
separate that's okay with me. I'm going to tell

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JULIA S. COOPER

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you this, at the end of the day, he's going to tell me what either side told him. I mean, it's going to happen because I have to know because I meant what I said when Dr. Wecker was on the stand, that I had gone to the extent of my knowledge, which wasn't real far. So I'm going to need some help.

MR. MORROW: Sure.

THE COURT: So how do I solve this dilemma today?

MR. MORROW: Well, if the Court will allow the experts to meet with the court-appointed experts, then we can, either jointly or separately tell them in generalities what our respective positions are. I think that's a good remedy, Your Honor.

THE COURT: Mr. Campion, how much at a disadvantage have you been placed if Dr. Wecker comes in and he's pretty much telling them what he's going to do?

MR. CAMPION: No disadvantage, Your Honor.

THE COURT: I'm sorry?

MR. CAMPION: No disadvantage, Your Honor. We're prepared to do anything today.

THE COURT: Okay, then I'm going in my office. Besides the case management order, oh, privilege log, when are we going to do something with that?

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MR. PERRIN: Your Honor, Mr. Irwin and a gentleman named Chad Reed from Mr. Campion's office, I believe Philadelphia office, if I recall correctly, we've had a number of conference calls. We are meeting in New Orleans on October 29th and 30th in Mr. Irwin's office to try to narrow the focus or issues of legal disputes and possibly some factual disputes that would reduce the number of remaining documents that might be ripe for an in camera review. Our anticipation was, and let me say this, we have stated that's our intentions. We will then report to Mr. Juneau on where we are and we'll try to move that ball down the field. That obviously needs to be done before we even try to conclude discovery. So we--1:30:59

THE COURT: That's my point. We've got a case management order, but this privilege log still looms out there and I don't see how we can really do anything with any degree of assurance that we're not going to have to redo something until we deal with this privilege log. Having said that, from the last hearing you might have gleaned that while I have great respect for my colleagues across the juridical landscape, I understand you're following Judge Fallon's model. I don't know what that is. I'm not going to guarantee you that I'm going to agree with him. I hold him in high esteem with the utmost respect,

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but I'm going to tell you that I'm going to reserve my right to make a decision on what I think the--so when you get to fussing and/or disagreeing in whatever fashion, when you come here don't expect to have a puppet Judge Fallon, or Judge Couch. So that's my job. With that, other than the privilege log, what else, Mr. Morrow?

MR. PERRIN: Judge, two things.

THE COURT: Okay, I'm sorry.

MR. PERRIN: I believe that we continued our discussions about the privilege log in view of the pointed question you put to me on the telephone conference during the hurricane recess I believe was did I expect you to review twenty-five thousand documents, or Mr. Juneau, something like that.

THE COURT: Two hundred fifty thousand, I believe.

MR. PERRIN: Whatever it is. I don't remember the number. I get confused on zero sometimes, but we took that as perhaps a--we should have an enlightened view to continue our discussions and see if maybe our polar opposites were not as far apart as they might seem, hence the continued discussions and the meeting in two weeks. Secondly, Mr. Campion and I had a conversation earlier this week about the contradictory hearing issue that was raised in January when the

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insurance company, the nursing homes and others, you remember we had several hearings in here, telephone and all that, and I'll let Mr. Campion speak to that. I don't want to speak for him.

MR. CAMPION: We are mindful of what the appellate court said. Janssen will not be seeking the contradictory hearings of which the appellate court has spoken. So that aspect of the case is over.

THE COURT: That's a relief since I don't know when we would have had time to do six thousand contradictory hearings, nonetheless I got spanked pretty good and that happens sometimes. Okay, what else, Mr. Perrin?

MR. PERRIN: That's all I'm aware of today, Your Honor.

MR. CAMPION: Date for the next hearing, Your Honor.

THE COURT: Okay, let's see, I need calendars for next month and the month after. While they're doing that, Mr. Morrow, you had risen and--

MR. MORROW: I know I was going to address the issue of the six thousand hearings.

THE COURT: Mr. Juneau, am I leaving anything out before I leave?

MR. JUNEAU: No, sir.

THE COURT: We'll get the calendar in a second. Patsy, you can go off now.

(COURT STANDS IN RECESS AT THIS POINT.)

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THE COURT: We're going to set our status conference for January 7, 2009 at 9:00 a.m. and I'll see what you bring me then. And I also accept and place into the record the seventeenth periodic status report. I'll note that we've effectively handled number three, which was to set a trial date and case management order. With that, is there anything else I could foul hook before I leave?

MR. JUNEAU: I don't believe so, Your Honor.

THE COURT: Alright, it's good seeing you guys. Good luck everyone.

MR. CAMPION: Thank you, Your Honor.

THE COURT: Dr. Solanky, before you leave, you and Mr. Juneau would you please visit with me? Give me two minutes with Mr. Juneau and Dr. Solanky and then y'all do what you need to do and if you don't want to do anything look, I understand. I can't make you do this. I'm just trying to get where we're going.

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STANISLAUS COUNTY

STATE OF LOUISIANA

PARISH OF ST. LANDRY

I, PATSY J. JONES, Official Court Reporter, Twenty-Seventh Judicial District Court, do hereby certify that the above and foregoing pages constitute a true and correct transcript of my stenographic notes and recording taken in the above captioned matter at the time and place set forth herein.

Opelousas, Louisiana, on this 5th day of November,

2008.



Patsy J. Jones
PATSY J. JONES, OFFICIAL COURT REPORTER

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EXHIBIT E

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STATE OF SOUTH CAROLINA

COURT OF COMMON PLEAS

COUNTY OF SPARTANBURG

2007-CP-42-1438

Ex Rel HENRY MCMASTER, in his capacity
as ATTORNEY GENERAL of THE STATE of
SOUTH CAROLINA,

Plaintiff,

-vs-

JANSSEN PHARMACEUTICA, INC., JANSSEN,
LP, and JOHNSON & JOHNSON, INC.,

Defendants.

TRANSCRIPT OF RECORD

May 4, 2009

Spartanburg, South Carolina

Ordered: May 4, 2009

Delivered: May 8, 2009

B E F O R E:

THE HONORABLE ROGER E. COUCH, Presiding Judge.

Pamela Faucette
Circuit Court Reporter

PAMELA FAUCETTE, CVR - (864) 574-9534 or (336) 260-2864

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1 MR. TRAMMELL: Sure.

2 THE COURT: As to whether or not -- he'll -- he'll go
3 over the Lily procedure with you. And, if that works, fine.
4 If not, then, I would get involved then and see if we can't
5 resolve it.

6 MR. TRAMMELL: And just to be clear, I said, what I want
7 him to do was respond to my question, which he did. So, I --
8 I needed to get a response to my motion. And I think this is
9 the -- I'll talk -- talk about the procedure with him, but I
10 think this is the way forward.

11 THE COURT: All right. Let's -- let's see if that can't
12 be resolved in that fashion. And -- and I think it's a
13 workable solution. It wasn't all my idea, but it seems to
14 working.

15 (Brief Pause)

16 THE COURT: All right. Now, there's apparently
17 Janssen's proposed stipulated order governing discovery from
18 prescribing physicians?

19 MR. MURPHY: That's correct, Your Honor.

20 THE COURT: Yes, sir.

21 MR. MURPHY: We had -- I had had sent to Mr. Trammell a
22 proposed protocol for taking depositions of one hundred and
23 fifty (150) prescribers in the State of South Carolina.

24 THE COURT: Yes, sir.

25 MR. MURPHY: You'll recall, when we initially appeared

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1 before you, we explained how we brought kind of towards --
2 would seek to move forward in regard to statistics -

3 THE COURT: Uh-huh (affirmative).

4 MR. MURPHY: --- atypical statistics and the like and we
5 identified that procedure.

6 Mr. Trammell responded, or his office responded, in a
7 -- in about ten (10) days with a counter proposal. And where
8 I proposed one hundred and fifty (150), they proposed ten
9 (10).

10 That, however, just isn't going to work. In -- in the
11 State of South Carolina, there are not less than seventy-eight
12 hundred (7,800) prescribers of atypicals in the fee-for-
13 service Medicaid program, another twenty-five hundred (2,500)
14 in the -- the State Health Plan.

15 And, so, that is even greater -- that's even a greater
16 pool than what we've seen in Louisiana.

17 But, still our experts says, "I won't need any more than
18 one hundred, fifty (150)." Now -

19 THE COURT: Well, let me -- let me hear what Mr.
20 Trammell has to say about the -

21 MR. MURPHY: Sure.

22 MR. TRAMMELL: Well, this again is an area where I
23 think will benefit from our experience in the Lily case.

24 If you recall, the first hearing probably -- well, maybe
25 the first hearing in the Zyprexa case before the board, I

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PAMELA FAUCETTE

1 talked for hours about what would happen when you launch into
2 a discovery program like this.

3 And the Lily program was based on the program Janssen got
4 in Louisiana, where they got to do a hundred and fifty (150)
5 doctors' depositions.

6 They got a bunch of medical records. And they convinced
7 the judge to do that and the judge ended up getting reversed
8 twice.

9 So, then, they desisted and they said, "Well, we don't --
10 we don't want to do that anymore." So, what they've asked to
11 do here is go depose a bunch of these doctors for reasons I
12 can't imagine.

13 I've acknowledged to the Court and to the Defendant that
14 to the extent they want to get some testimony from doctors
15 about, you know, what information doctors consider when they
16 prescribe drugs, what do they think of Risperdal, what kinds
17 of patients it's good for, to play for a jury, I think that's
18 fine.

19 It becomes cumulative very quickly. Lily asked for I'm
20 sure as many as -- as Janssen has asked for. Lily has noticed
21 zero and all fact -- fact deposition cut off is in five (5)
22 weeks.

23 So, they're obviously prepared to go to trial not having
24 done any of those depositions. And I think the reason is,
25 when they know there are real deadlines, and when the case is

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SPRING LAKE COUNTY
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MARJORIE BLACKLEY

EXHIBIT F

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SPARTANBURG COUNTY
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Transcript of the Testimony of **TRIAL DAY 9** **JANSSEN**

Date: October 12, 2010
Volume: 1

Case:

Printed On: 10/18/2010

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TWENTY-SEVENTH JUDICIAL DISTRICT COURT

FOR THE PARISH OF ST. LANDRY
STATE OF LOUISIANA

CHARLES FOTI, ATTORNEY GENERAL
EX REL, STATE OF LOUISIANA

CIVIL DOCKET
NO. 04-C-3967-D

VERSUS

JANSSEN PHARMACEUTICA, INC., ET AL

--- CONSOLIDATED WITH ---

CHARLES FOTI, ATTORNEY GENERAL
EX REL, STATE OF LOUISIANA

NO. 04-3977-D

VERSUS

JANSSEN PHARMACEUTICA, INC., ET AL

* * *

UNOFFICIAL TRANSCRIPT OF THE

PROCEEDINGS HELD BEFORE THE HONORABLE DONALD W.
HEBERT in the 27th Judicial District Court,
Division D, Opelousas, Louisiana, on October
12th, 2010.

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ST. LANDRY COUNTY
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M. HOPE BLACKLEY

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1 THE COURT: 2 Which I pretty much bought, 3 except that Judge Wienstien, I think, 4 in "Hood" kind of had left himself a 5 very, very, very narrow opening, and 6 evidently that went up in smoke. So 7 all of the efforts that this Court 8 utilized to understand this 9 statistical modeling stuff, I'm going 10 to tell you I got a pretty good handle 11 on statistics. But I don't think my 12 handle on statistics -- nobody here is 13 questioning Dr. Wecker's expertise in 14 the field of statistics and 15 statistical modeling. That's not the 16 question. 17 The question is what opinion is 18 he going to give to me with regard to 19 the facts that are relevant to this 20 case? 21 MR. BRODY: 22 The opinion that he's going to 23 give to you as to the facts that are 24 relevant in this case, first, is the 25 only way to draw conclusions about an	1 tell you what the opinions are and the 2 numbers of the opinions of other 3 people, but my opinion on whether the 4 letter was misleading, 5 misrepresentative, was there an 6 attempt to defraud or an attempt to 7 obtain payment, he's not going to have 8 an opinion on any of that. 9 MR. BRODY: 10 No, he's not. He's merely going 11 to report what the results of the 12 survey were and what the experience of 13 Louisiana doctors, of the hundred and 14 fifty that were part of the survey, 15 allows him to say about the population 16 as a whole through a population 17 estimate, which is a common 18 statistical tool. This is what 19 statisticians do. 20 THE COURT: 21 I understand this is what 22 statisticians do. That's not the 23 issue before me. I understand the 24 validity of statistical. 25 Regardless, they are accurate. I
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1 entire population of individuals when 2 the population is too large to talk to 3 every single person is through the 4 statistical tool of statistical 5 sampling that allows us to do it. And 6 he's going to talk about how the 7 survey was designed, why the results 8 are reliable and how he can take the 9 responses to the survey questions. 10 Just as, you know, the Gallop 11 organization does when they give 12 projections of how likely voters are 13 going to vote in an upcoming 14 presidential election. 15 THE COURT: 16 I understand the concept. 17 MR. BRODY: 18 And he's going to say, here are 19 the statistical tools that we have to 20 do that, and using those statistical 21 tools, here is, based on the responses 22 we got, based on the number of 23 prescriptions those doctors wrote -- 24 THE COURT: 25 Based on what we did, I'm going	1 was amazed at how an algorithm can be 2 created to perform a statistical 3 operation which will pretty much tell 4 you the answer to almost any human 5 question that comes up. 6 That's not the question. The 7 question is, does it meet the 8 exception as to hearsay created by 9 Article 703 of the Code of Evidence? 10 MR. BRODY: 11 And the answer is that it does, 12 Your Honor. 13 THE COURT: 14 Okay. 15 Close, Mr. Ryan. Don't close 16 long. 17 MR. RYAN: 18 It's a conduit. He's parroting 19 the opinions of others. And it's 20 not -- it's not, um -- the type of 21 evidence, um -- that's referenced in 22 703. 23 THE COURT: 24 Okay. I'm going to tell you that 25 I did go back and I read, because

9 (Pages 30 to 33)

Page 34	Page 36
1 that's what I'm supposed to do, and 2 the McDaniel case written by Judge 3 Cooks, basically says, Fabian Patin's 4 testimony should have been allowed, it 5 was clear error to not allow it. But 6 he was a forensic architect rendering 7 an opinion on what the industry 8 standard was, and the industry 9 standard was certainly relevant as 10 to -- in his opinion was certainly 11 relevant as to what the industry 12 standard was because he was an 13 architect. Now, whether he's a 14 forensic architect I'm not even sure 15 what that is, but evidently there's 16 such a field. 17 In this particular instance, this 18 Court finds that what we've got is a 19 gentleman who is unparalleled in the 20 field of statistics, there is no doubt 21 in my mind, but he is not going to 22 render any opinion that has any 23 relevance to this case with reference 24 to his expertise. He's going to give 25 us, by what I'm understanding, his	1 opinions entering upon the subject, 2 the facts or data with regard to this 3 case -- not his opinion, he is merely 4 acting as a conduit to tell me what 5 others' opinions are. As a result, 6 I'm going to deny his testimony. 7 And I'll give you the opportunity 8 to then refocus your case. I'll note 9 your objection to my ruling for the 10 record. 11 MR. BRODY: 12 Thank you, Your Honor. 13 THE COURT: 14 Okay. Y'all need some time to 15 prepare for what you're going to do 16 next? Or are you ready for another 17 witness? 18 MR. BRODY: 19 Do you have other objections to 20 the testimony that Dr. Wecker is going 21 to give about the data that can be 22 taken up in advance? 23 MR. RYAN: 24 Yes. There is one other -- There 25 is one other aspect of the -- of
Page 35	Page 37
1 understanding -- his expert 2 understanding on what 150 physicians' 3 opinions were. So all he is is he's 4 taking their opinions and saying, this 5 is what they said. 6 And I take issue with you saying, 7 well, there's no other way it could 8 have been presented. I recall going 9 up earlier where we were discussing 10 whether Louisiana's privacy laws were 11 beyond HIPAA. And I said, well, you 12 know what? I'm going to let her go, 13 because we can't have six thousand 14 contradictory hearings. And my court 15 of appeals sent me back with a slap on 16 the hand and said, you can't do that. 17 Six thousand? You may have to 18 have that. Right now, our law doesn't 19 allow anything else. 20 Based on all of that, and 21 primarily based upon the fact that I 22 find the gentleman is not going to be 23 giving us an opinion of the type 24 reasonably relied upon by experts in 25 the particular field in forming	1 Mr. Wecker's testimony that has not 2 yet been discussed, Your Honor. 3 THE COURT: 4 Okay. 5 MR. RYAN: 6 Your Honor, it's my understanding 7 that Dr. Wecker, who is a 8 statistician. 9 THE COURT: 10 I may be getting the gentleman's 11 name wrong, and I apologize if I am. 12 It is Wecker? 13 MR. BRODY: 14 Wecker. Yes, sir. 15 THE COURT: 16 Dr. Wecker. 17 MR. BRODY: 18 Yes, sir. 19 THE COURT: 20 Okay. 21 MR. RYAN: 22 That as part of his analysis in 23 his report, that he took data from 24 1995, um -- and actually, through the 25 year 2007, and did what we perceive to

10 (Pages 34 to 37)

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1 close to lunch time so I can't be too long.
 2 A. Good morning, sir.
 3 Q. All right. And you're not a medical
 4 doctor? Correct?
 5 A. I'm not.
 6 Q. You're not a pharmacist; right?
 7 A. I am not.
 8 Q. You have never prescribed Risperdal;
 9 right?
 10 A. Correct.
 11 Q. And as you just described to us, one
 12 of the things that you did is you looked at
 13 the claims, you examined all claims in the 36
 14 months after the first antipsychotic drug
 15 prescription for a diagnosis to indicate an
 16 alleged side effect. Is that correct?
 17 A. I did that.
 18 Q. All right. So you have looked at
 19 diagnoses in the Medicaid data to make the
 20 conclusions that you have made to the jury in
 21 part; correct?
 22 A. Yes.
 23 Q. All right. Have you ever criticized
 24 the use of the Medicaid claims database
 25 before?

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1 A. I can't think of it.
 2 Q. Okay. Do you recall giving a report
 3 in this case?
 4 A. Yes.
 5 Q. Do you have it in front of you?
 6 A. Yes.
 7 Q. All right. Could you turn to page
 8 28 of your report, please?
 9 A. I have it.
 10 Q. Could we go to the Elmo, please? Do
 11 you have this report?
 12 MR. BRODY:
 13 Your Honor, I'm going to raise an
 14 objection to this.
 15 (Bench conference).
 16 MR. RYAN:
 17 May I proceed, Your Honor?
 18 THE COURT:
 19 Please.
 20 EXAMINATION BY MR. RYAN:
 21 Q. Okay. At page 28 of your report, do
 22 you, without mentioning the names of anybody's
 23 analysis that you're talking about, do you
 24 agree that you -- that in talking about the
 25 Medicaid claims database that you stated that

1 it -- the Medicaid claims database does -- if
 2 -- medical patient diagnoses are not
 3 routinely and reliably recorded. The analysis
 4 of a diagnosis is not proof of what the
 5 unreported diagnosis is or is not? Do you
 6 recall making that statement?
 7 A. I haven't found it yet. What
 8 paragraph?
 9 Q. It's on page 28 at the bottom.
 10 A. Oh, I see.
 11 Q. It says -- talking about an
 12 analysis. And it says without --
 13 A. Just a moment, and I will read it.
 14 Yeah. What I read it says, "If
 15 the diagnoses are not routinely reliably
 16 recorded, then absence of diagnosis is not
 17 proof".
 18 Q. All right. But, Dr. Wecker, you
 19 just indicated that your opinions in this case
 20 are based on your review of medical diagnoses
 21 contained in the Medicaid data. Is that
 22 correct?
 23 A. Correct.
 24 Q. All right. And do you recall
 25 stating in your report -- Let's do it this

1 way. Is that, -- Look at the next -- the next
 2 page, page 29 in your report. You say that
 3 "There was no requirement that a diagnosis be
 4 recorded for prescription drug claims in the
 5 Medicaid claims database prior to August
 6 2005. Indeed, only 5.4 percent of Risperdal
 7 prescription claims in the Medicaid database
 8 have a diagnosis recorded in the period 1995
 9 to 2005." Do you see that?
 10 A. Sure.
 11 Q. Okay. I asked you before, have you
 12 ever criticized the database, the Medicaid
 13 database for any reason, and you say -- I
 14 understood you to say you couldn't recall. Is
 15 that correct?
 16 A. Yeah. I don't think this is a
 17 criticism of the database.
 18 Q. All right. How can you -- Do you
 19 agree that you're stating there that the
 20 Louisiana Medicaid database did not even have
 21 a requirement that somebody put in a diagnosis
 22 until the year 2005?
 23 A. No, that's not true at all. It says
 24 they didn't have a requirement they put it in
 25 the prescription record, but they had

25 (Pages 94 to 97)

EXHIBIT G

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For Opinion See 2004 WL 5049605 (Trial Order), 2004 WL 5049606 (Trial Order), 2004 WL 5751368 (Trial Order), 2004 WL 5049604 (Trial Order), 2004 WL 5751367 (Trial Order)

Superior Court of California.
San Diego County
Benetta BUELL-WILSON; Barry S. Wilson, Plaintiffs,

v.

FORD MOTOR COMPANY, a Delaware Corporation; Drew Ford, a California Corporation; and Does 1 to 50,
inclusive, Defendants.

Case No. GIC800836.

November 13, 2003.

No. 14 of 14

Plaintiffs' Motion in Limine to Exclude from Trial the Opinions of William Wecker, Ph.D.

Judge: Hon. Kevin A. Enright.

There are three kinds of lies: Lies, Damn Lies and Statistics.

Benjamin Disraeli (British Prime Minister 1868, 1874-1880)

I

INTRODUCTION

The opinions of William Wecker, Ph.D. should be excluded from trial. Dr. Wecker is a statistician retained by the defense to offer opinions regarding the comparative collision rates of the Ford Explorer versus other vehicles. Dr. Wecker's opinions, however, are irrelevant to whether the 1997 Ford Explorer, in which plaintiff Benetta Wilson suffered catastrophic injuries, was defective in design. Further, the data on which Dr. Wecker bases his opinions includes thousands of collisions which are dissimilar to Mrs. Wilson's on characteristics as fundamental as vehicle make and model, type of collision, type of injury and numerous other factors. Dr. Wecker's opinions, therefore, will confuse the issues, mislead the jury and waste valuable resources. For these reasons, plaintiffs respectfully request that this Court join other courts across the country and exclude from trial any evidence or opinions from Dr. Wecker.

II

FACTS

1. The 1997 Ford Explorer's Defective Design Elements Caused it to Rollover and its Roof to Crush, Which Resulted in Mrs. Wilson's Catastrophic Injuries.

On January 19, 2002, Mrs. Benetta Buell-Wilson suffered catastrophic injuries when her 1997 Ford Explorer 4-door, 4-wheel-drive lost control and rolled several times. That afternoon, Mrs. Wilson was driving westbound

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on Interstate 8, just west of Tavern Road. Suddenly, a large object, most likely a metal dolly, appeared in front of Mrs. Wilson's vehicle. She avoided the object by steering left, but the Explorer quickly went out of control on the highway. Mrs. Wilson could not regain control of the Explorer and, according to eye-witnesses, it began to fishtail. The Explorer's passenger side wheels lifted and the vehicle rolled violently. During the rolls, the Explorer's roof crushed in on Mrs. Wilson. As result of the collision, Mrs. Wilson suffered, among many other injuries, a significant displacement of her spinal cord at T-12. Mrs. Wilson is a complete paraplegic with no feeling or movement from her waist down.

Substantial evidence shows that the 1997 Ford Explorer has a defective design which results in several dangerous characteristics. The evidence will show that this model Explorer's limited track width and high center of gravity result in a dangerous propensity to rollover. Despite knowledge of its defective design, Ford continued to manufacture and distribute the Explorer because of its enormous profits. The evidence will also show that, in an effort to further increase profits, Ford diminished the Explorer's A and B pillars, which resulted in a marked decrease in roof strength. As a result, the Explorer's roof is too weak to withstand the all too frequent rollovers and has a propensity to crush the vehicle's occupant(s). The foreseeable results of these defective, and extremely dangerous, design elements converged in Mrs. Wilson's collision when the vehicle lost control, rolled several times and its roof crushed her. The Wilsons sued Ford Motor Company and Drew Ford on product liability theories, including a defective design and lack of adequate warnings.

2. Defense Expert William Wecker's Testimony is Intended to Divert Attention Away from the Explorer's Defective Design Elements.

Defendants designated William Wecker, Ph.D., a statistician, as an expert witness. Dr. Wecker is a high-priced (\$550/hour) defense expert with whose testimony defendants intend to confound and mislead the jury. Dr. Wecker has, in summary fashion, proffered 8 general opinions which purport to compare the Ford Explorer with other sport utility vehicles. (Arnell Declaration; ¶ 2, Ex. 1.) Dr. Wecker bases his opinions, however, on incomplete and unreliable data. He uses Federal Accident Reporting System ("FARS") data, which is a federal database of *fatal* collisions, as well as the collected collision data of several states, *not including California*. (Wecker DT; 85:12-16. Arnell Dec., ¶ 3, Ex. 2.) Dr. Wecker, however, has no information regarding the circumstances of Mrs. Wilson's collision. He has not reviewed any expert depositions and has almost no understanding of how the collision occurred. (Wecker DT; 21:20-22, 42:17 - 43:4. Arnell Dec., ¶ 3, Ex. 2.) Dr. Wecker has made little or no effort to identify the circumstances of collisions in the databases and has made no effort to utilize only those that are similar to the circumstances of Mrs. Wilson's collision. Moreover, it is uncontested that Mrs. Wilson's collision does not appear in any of the databases on which Dr. Wecker relies. As a result, Dr. Wecker's opinions are irrelevant to this case's disputed issues, lack reasonable bases and will only confuse and mislead the jury.

III

LEGAL ANALYSIS

1. Dr. Wecker's Opinions are Irrelevant Because Defective Design Analysis Does Not Include Comparison of Collision Data with Other Vehicles.

In *Barker v. Lull Engineering Co.* (1978) 20 Cal. 3rd 413, the California Supreme Court reviewed products liability cases and held:

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[W]e have concluded from this review that a product is defective in design either (1) if the product has failed to perform as safely as an ordinary consumer would expect when used in an intended or reasonably foreseeable manner, or (2) if, in light of the relevant factors discussed below, the benefits of the challenged design do not outweigh the risk of danger inherent in such design.

[This test reflects our continued adherence to the principle that, *in a product liability action, the trier of fact must focus on the product, not on the manufacturer's conduct, and that the plaintiff need not prove that the manufacturer acted unreasonably or negligently in order to prevail in such an action.*

Barker, supra, 20 Cal. 3rd at 418. (Emphasis added.) The California Supreme Court then set forth the factors relevant to the "risk-benefit" test:

A review of past cases indicates that in evaluating the adequacy of a product's design pursuant to this latter standard, a jury may consider, among other relevant factors, the gravity of the danger posed by the challenged design, the likelihood that such danger would occur, the mechanical feasibility of a safer alternative design, the financial cost of an improved design, and the adverse consequences to the product and to the consumer that would result from an alternative design.

Id., at 431. The new California Approved Jury Instruction reiterates the factors which the jury is to consider:

- (a) The gravity of the potential harm resulting from the use of the [product];
- (b) The likelihood that such harm would occur;
- (c) The feasibility of an alternative design;
- (d) The cost of an alternative design;
- (e) The disadvantages of an alternative design;
- (f) Other relevant factors.

California Approved Jury Instruction 1204. These factors omit any reference to a comparison of other vehicle collision rates. The California Supreme Court's holding, incorporated by the California Approved Jury Instruction, defines the parameters of evidence relevant to the "risk-benefit" analysis in a products liability case.

Evidence Code section 350 states, "No evidence is admissible except relevant evidence." Evidence Code section 210 defines relevant evidence as, "[E]vidence ... having any tendency in reason to prove or disprove any disputed fact that is of consequence to the determination of the action."

The California Supreme Court and the California Approved Jury Instructions omit collision rate comparisons because they are irrelevant to whether an automobile's design's risks outweigh its benefits. To address Dr. Wecker's proffered testimony, plaintiffs retained Richard Mensing, Ph.D., who holds Masters and Doctorate degrees in Statistics. Dr. Mensing candidly opined that a comparison does not provide any information regarding how safe products are, they only tell if the products are similar. (Mensing DT; 43:15 - 44:6. Arnell Dec., ¶4, Ex. 3.) A moments reflection leads a reasonable person to the same conclusion: The Explorer's collision rates, as compared to the other vehicles' collision rates, say nothing about the inherently dangerous characteristics of the Explorer's design. Dr. Wecker's comparisons are intended to foster the impermissible inference that the Explorer is, in some ill-defined way, comparable to other vehicles. The law, however, prohibits a product's manufacturer from relying on industry customs or standards to disprove a design defect. *Grinshaw v. Ford Motor Co.* (1981) 119 Cal. App. 3rd 757, 803 ("In a strict products liability case, industry custom or usage is irrelevant to the issue of defect.") Dr. Wecker's opinions regarding fatal vehicle rates, etc. are irrelevant and inadmissible.

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Analysis of two of Dr. Wecker's charts proves their irrelevance. Dr. Wecker's first chart (of more than 100 charts) is entitled "Fatal Vehicle Rates Two-Door Two-Wheel-Drive Compact Utility Vehicles." (Arnell Dec., Arnell Dec., ¶ 5, Ex. 4.) This chart is based solely on FARS data, which Dr. Wecker admits does not include Mrs. Wilson's collision, or any other collision that did not result in a fatality. Dr. Wecker makes absolutely no attempt to correlate the circumstances of the underlying collisions with the circumstances of Mrs. Wilson's collision. This is evidence from the chart's title: The data includes only collisions, of any type, involving two-door, two-wheel-drive vehicles that resulted in a fatality. This data says nothing about the Explorer's design. Another compelling example is Chart 93, which purports to depict, "Fatal or Major Injury Rollover Vehicle Rates in Single Vehicle Accidents Four-Door Four-Wheel-Drive Compact Utility Vehicles." (Arnell Dec., Arnell Dec., ¶ 6, Ex. 5.) The data underlying this chart is so meager, however, that it renders the chart irrelevant and immaterial. The underlying data relates to only 6 model years in 10 states, *not including California*. The data is presented in terms of rollovers per 10,000 vehicle years, which is derived from vehicle registrations, and does not consider the distance driven by any vehicle. (See, for example, Wecker DT; 48:23-49:3. Arnell Dec., ¶ 3, Ex. 2.) That is, a vehicle could be garaged the entire year, but if it was registered, it is included in the data comparison. Moreover, as Dr. Mensing explained, the data is devoid of any reference to the injured occupant's position in the vehicle or any discussion of the rollover's initiator, whether it was a tire blowout, contact with the median divider or an avoidance maneuver. (Mensing DT; 36:12 - 37:8. Arnell Dec., ¶ 4, Ex. 3.) Dr. Wecker, of course, does not know what initiated Mrs. Wilson's rollover. Simply put, comparing the collision rates of vehicle, with unknown mileage, in several states, excluding California, will tell the jury absolutely nothing about the Ford Explorer's design. Such evidence is irrelevant to this case's disputed issues and are inadmissible at trial.

2. The Collisions to Which Dr. Wecker Refers Are Inadmissible Because They Are Not Substantially Similar to Mrs. Wilson's Collision.

If defendants intend to proffer evidence of prior collisions, the law requires that the prior collisions be "substantially similar." In *Benson v. Honda Motor Co.* (1994) 26 Cal. App. 4th 1337, 1345, the court held: In a design defect case, an adequate foundation for admission of such evidence may be laid by proffering testimony concerning substantially similar machines used for a reasonable length of time under reasonably similar circumstances. [FN1]

FN1. Please note that the plaintiffs in *Benson* alleged a design defect under a negligence theory, as well as a strict liability theory. The *Benson* court found that the essential elements of a negligence claim justified the admission of the vehicle's safety-history, as long as it had the proper foundation. The Wilsons have not, however, alleged negligence and such evidence is irrelevant to their allegation of design defect under a strict liability theory. See *Barker v. Lull Engineering Co.* (1978) 20 Cal. 3rd 413. *infra*.

In *Ault v. International Harvester Co.* (1974) 13 Cal. 3rd 113, 121-122, the California Supreme Court stated: Evidence of other accidents is admissible to prove a defective condition, knowledge, or the cause of an accident, provided that the circumstances of the other accidents are similar and not too remote.

California courts have consistently upheld the rule requiring substantial similarity.

In *Brake v. Beech Aircraft Corp.* (1986) 184 Cal. App. 3rd 930, plaintiff, whose decedent died in a small aircraft crash, alleged theories of strict liability and negligence against the aircraft's manufacturer. The appellate court repeated the California Supreme Court's rule in *Ault*, *supra*, and upheld the trial court's exclusion of evidence of other crashes, in part, because:

[P]laintiffs failed to lay a foundation of similarity between the accidents discussed therein and the accident in this case. Descriptions of flight attitude, trim settings, engine power, loading, weather conditions, altitudes, feathering, etc., were widely varied. In addition, there are complex multiple hearsay problems in the documents. Plaintiffs cannot overcome these myriad problems by relying on similarity of airfoils or tail design. Similarly, there was no foundation laid to show similarity as to the accidents referred to in the NTSB documents.

Brake, supra, 184 Cal. App. 3rd at 937. Numerous California authorities hold that evidence of prior collisions must be substantially similar to the collision at issue in the trial. ^[FN2]

FN2. The *Brake* court suggested a more relaxed standard for introducing evidence of previous crashes on the sole issue of defendant's notice of a defect. *Brake v. Beech Aircraft Corp.* (1986) 184 Cal. App. 3rd 930, 938. "Despite the lack of foundation to show similarity, however, those prior accidents involving stall/spins of Beech Baron 58's could have been admitted for the limited purpose of showing that Beech had notice of a dangerous condition." However this limitation on the rule is irrelevant to Dr. Wecker's proffered opinions because he has not proffered testimony regarding defendants' notice of the Explorer's defective design.

Defendant Ford Motor Company and its counsel Snell & Wilmer, LLP previously cited the "substantially similar" rule in the case *Raimondi, et al. v. Ford Motor Company, et al.* They argued:

Under California law, evidence of other accidents is not admissible unless plaintiffs first show that the circumstances surrounding the other accidents are "substantially similar" to the facts in the case at bar.

Defendant Ford Motor Company's *Motion in Limine to Exclude Other Accident Statistics*; 2:19-21. ^[FN3] (Arnell Dec., ¶ 7, Ex. 6.) Defense counsel concurs that to be admissible, evidence of prior collisions must be substantially similar.

FN3. Plaintiffs respectfully request that this Court take judicial notice of defendant *Ford Motor Company's Motion in Limine to Exclude Other Accident Statistics* in the case *Raimondi, et al. v. Ford Motor Company, et al.* Evidence Code § 452(d).

Defendants have made no showing that the evidence of prior collisions, which form the bases of Dr. Wecker's opinions, are substantially similar to Mrs. Wilson's collision. He relies on the FARS data, a federal database of fatal collisions, and collected collision data of several states, not including California. Dr. Wecker, however, has made no attempt to cull from these databases collisions which are substantially similar to Mrs. Wilson's collision. In fact, Dr. Wecker has no information regarding the circumstances of Mrs. Wilson's collision. He has not reviewed any expert depositions and has almost no understanding of how the collision occurred. (Wecker DT; 21:20-22, 42:17 - 43:4. Arnell Dec., ¶ 3, Ex. 2.) The only reasonable inference is that Dr. Wecker has included in his analysis every reported collision that appears in the FARS and/or the state data, regardless of their circumstances. Dr. Wecker has made no attempt to limit the collisions on which he relies to Ford Explorers. On the contrary, his analysis includes reference to numerous types of utility vehicles, regardless of their unique design characteristics. Dr. Wecker has made no attempt to show that the collisions, or the involved vehicles, are substantially similar to Mrs. Wilson's collision. For these reasons, Dr. Wecker's opinions are inadmissible.

3. There Are No Reasonable Bases for Dr. Wecker's Opinions.

Evidence Code section 801 states in part:

If a witness is testifying as an expert, his testimony in the form of an opinion is limited to such an opinion as is:

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(b) Based on matter (including his special knowledge, skill, experience, training, and education) perceived by or personally known to the witness or made known to him at or before the hearing, whether or not admissible, *that is of a type that reasonably may be relied upon by an expert in forming an opinion upon the subject to which his testimony relates*, unless an expert is precluded by law from using such matter as a basis for his opinion.

The law requires that data must be reasonably reliable to support an expert's opinion.

The statistics Dr. Wecker uses to support his opinions are incomplete and unreliable. The FARS data includes only collisions in which at least one occupant died. This data does not account for the vehicle's mileage and does not include analysis of why the collision occurred. It is undisputed that the FARS data omits Mrs. Wilson's collision. (Wecker DT; 46:2-49:22. Arnell Dec., ¶ 3, Ex. 2.) Defense counsel have, themselves, argued that the FARS data is unreliable. In the case *Lajeunesse, et al. v. Ford Motor Co., et al.*, defendant Ford Motor Company and their counsel Snell & Wilmer, LLP argued:

As mentioned above, the report's authors rely upon the Fatal Accident reporting System ("FARS"), an automobile accident database compiled by the federal government from various police accident reports. The information contained within the accident reports upon which FARS relies is often obtained from unknown eyewitnesses by a police officer, as well as the officer's own observations. Someone else then interprets that information before it is input into the FARS database. Such hearsay upon hearsay is inadmissible.

Ford Motor Company's *Motion in Limine to Exclude the Insurance Institute for Highway Safety April 1992 Report and May 1993 Status Report*; 4:24 - 5:1. ^[FN4] (Arnell Dec., ¶ 8, Ex. 7.)

FN4. Plaintiffs respectfully request that this Court take judicial notice of defendant Ford Motor Company's *Motion in Limine to Exclude the Highway Insurance Institute for Highway Safety April 1992 Report and May 1993 Status Report* in the case *Lajeunesse, et al v. Ford Motor Co., et al.* Evidence Code § 452(d).

The FARS data is an unreliable and unreasonable basis for Dr. Wecker's opinions.

The state data on which Dr. Wecker relies suffers from the same limitations. The state data also omits Mrs. Wilson's collision. This is because Dr. Wecker has data from only 10 - 11 states. The state data, as Dr. Wecker presents it, does not account for varying numbers of vehicles among the states. The state data also does not account for the mileage on any reported vehicle. (Wecker DT; 87:14-16. Arnell Dec., ¶ 3, Ex. 2.) A vehicle could be driven 100,000 or 0 miles in a year and be included in the database. The state data also compares various vehicle makes and models, despite their unique design characteristics. Dr. Wecker makes no effort to correlate this data with the circumstances of Mrs. Wilson's collision. The data, therefore, says nothing about the Explorer's inherent stability problems or its defective design.

Further, the state data contains several levels of hearsay. Plaintiff is informed and believes that traffic collision reports, which are hearsay, are collected. Persons then extrapolate certain data and incorporate it into a database, which purports to compile and present the data. This is another level of hearsay. Dr. Wecker then purports to show the data in his graphs, which is yet another level of hearsay. These multiple levels of hearsay make the data uncertain and unreliable. Significantly, Dr. Wecker's graphs do not depict the data's uncertainty. (Mensing DT; 47:13 - 48:6. Arnell Dec., ¶ 4, Ex. 3.) This is essential for its fair presentation. The FARS and state data are unreliable and unreasonable bases for Dr. Wecker's opinions.

4. Dr. Wecker's Opinions are Misleading and Unduly Prejudicial.

Evidence Code section 352 states:

The court in its discretion may exclude evidence if its probative value is substantially outweighed by the probability that its admission will (a) necessitate undue consumption of time or (b) create substantial danger of undue prejudice, of confusing the issues, or of misleading the jury.

Dr. Wecker's opinions are misleading in light of this case's disputed issues. The California Supreme Court has held that the Wilsons, "[N]eed not prove that the manufacturer acted unreasonably or negligently in order to prevail in [a product liability] action." *Barker v. Lull Engineering Co.* (1978) 20 Cal. 3rd 413,418. Defendants' negligence is not an issue in this product liability case.

If admitted, Dr. Wecker's opinions will mislead the jury into considering the reasonableness of Ford's conduct in manufacturing the Explorer and placing it into the stream of commerce. Dr. Wecker's opinions invite the jury to compare the Explorer to other makes and models of utility vehicles. This invitation will suggest to jurors that, if this comparison is made, one will conclude that the Explorer has an average number of collisions and Ford was reasonable in manufacturing and selling it. This conclusion is incorrect. More importantly, this conclusion is irrelevant to the question of whether the 1997 Explorer is manufactured according to a defective design, the determinative factors of which the California Supreme Court and the California Jury Instructions have clearly described. Ford's motivation is clearly to suggest to the jury that, in order to find the Explorer defective in design, they will have to conclude that several other makes and models (most likely driven by the jury or their families) are also defective. Ford's suggestion to the jury to make an inference regarding the reasonableness of its conduct will distract and mislead the jury from its obligation to decide whether the Explorer is defective. The jury cannot be expected to parse this case's relevant issues when those issues are muddled by Dr. Wecker's inaccurate and misleading opinions.

Dr. Wecker's testimony will waste an inordinate amount of time. Plaintiffs cannot sit by idly while Dr. Wecker offers incorrect and irrelevant opinions that the Ford Explorer has "comparable" collision and fatality rates. Plaintiffs will be forced to submit evidence on several major issues in order to refute his testimony. For example, plaintiffs would be forced to attack the data underlying Dr. Wecker's opinions, including its compilation and presentation, to prove that the comparative vehicles are not substantially similar to the Ford Explorer. Plaintiffs would also be forced to distinguish the mechanisms of the collisions in each of the underlying collisions/ fatalities and/or to prove that the comparative vehicles are also defective. This is an overwhelming and unreasonable burden to place on plaintiffs. The end result would be the same: The law would require the Court to strike Dr. Wecker's testimony because the other collisions/fatalities are dissimilar to Mrs. Wilson's collision. The cost to arrive at this conclusion, however, would be overwhelming to Plaintiffs.

Dr. Wecker's opinions would also be unduly prejudicial. As the California Supreme Court stated in *People v. Collins* (1968) 68 Cal. 2nd 319, 330:

Confronted with an equation which purports to yield a numerical index of probable guilt, few juries could resist the temptation to accord disproportionate weight to that index.

In *Collins*, the California Supreme Court reversed a robbery conviction because the State relied on inaccurate and unreliable statistics. The Court continued:

Undoubtedly the jurors were unduly impressed by the mystique of the mathematical demonstration but were unable to assess its relevancy or value.

under the circumstances the "trial by mathematics" so distorted the role of the jury and so disadvantaged counsel

for the defense, as to constitute in itself a miscarriage of justice.

Collins, supra, 68 Cal. 2nd at 332.

As Prime Minister Disraeli suggested, and the California Supreme Court and Dr. Mensing reiterated, people are likely to afford undue weight to statistics. (Mensing DT; 37:20 - 38:25. Arnell Dec., ¶ 4, Ex. 3.) Their deceptive simplicity would offer simple, although inaccurate, conclusions to jurors in this case facing the difficult task of considering complex design issues. Fairness demands that the Court not provide the jurors with an easy means to avoid the relevant question of the Explorer's defects and retreat to the comparatively simple, but irrelevant, question of whether Ford's actions were reasonable. For these reasons, Evidence Code section 352 militates for the exclusion from evidence of Dr. Wecker's opinions.

5. Numerous Other Courts Have Excluded Dr. Wecker's Testimony.

Significantly, numerous courts across the United States have excluded from trial Dr. Wecker's opinions:

- In January 2002, the San Diego Superior Court excluded from trial Dr. Wecker's opinions in the case *Lajeunesse, et al v. Ford Motor Co., et al.*^[FN5] (Arnell Dec., ¶9, Ex. 8, pg. 2, ¶ 6);

FN5. Plaintiffs respectfully request that this Court take judicial notice of the Court's order in the case *Lajeunesse, et al v. Ford Motor Co., et al.* Evidence Code § 452(d).

- The United States District Court for the Middle District of Georgia, in the case *Howard, et al. v. Ford Motor Co.*, excluded Dr. Wecker's opinions for several reasons, including "the danger of confusion of the issues and misleading the jury...."^[FN6] (Arnell Dec., ¶ 10, Ex. 9, pg. 7, ¶ 3.);

FN6. Plaintiffs respectfully request that this Court take judicial notice of the Court's Order in the case *Howard, et al v. Ford Motor Co.* Evidence Code § 452(d).

- The Bulloch County, Georgia Superior Court, in the case *Stewart, et a. v. Ford Motor Company, et al.* excluded from trial Dr. Wecker's opinions because the collisions underlying his statistical data were not substantially similar.^[FN7] (Arnell Dec., ¶ 11, Ex. 10, pg. 2, ¶ 5.);

FN7. Plaintiffs respectfully request that this Court take judicial notice of the Court's Order in the case *Stewart, et al. v. Ford Motor Company, et al.* Evidence Code § 452(d).

- In the case *Harsh, at al. v. General Motors Corporation, et a.*, the Pennsylvania Court of Common Pleas precluded Dr. Wecker from testifying at trial.^[FN8] (Arnell Dec., ¶ 12, Ex. 11.)

FN8. Plaintiffs respectfully request that this Court take judicial notice of the Court's Order in the case *Harsh, et al., v. General Motors Corporation, et al.* Evidence Code § 452(d).

The Honorable Judge Ronald Gardner, of the Orange County Superior Court, provided perhaps the most powerful statement of reasons for excluding Dr. Wecker's opinions at trial. In the case *Wagner, et al. v. General Motors Corp., et al.* (No. 60 06 02), the Honorable Judge Gardner ruled emphatically on plaintiffs counsel's motion to strike Dr. Wecker's testimony:

It is pure garbage plus. Motion granted. I will tell the jury to ignore all of this with pleasure.

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I consider the last 45 minutes of testimony the biggest waste of time I have listened to in almost 60 years as a trial judge and trial attorney. I refuse to impose this kind of - and I use advisedly - garbage on intelligent jurors. I will advise the jury to ignore everything they have heard.

Reporters Daily Transcript; 1652:14 - 16 and 1653:22 - 1654:1. ^[FN9] (Arnell Dec., ¶ 13, Ex. 12.) The numerous courts that have excluded Dr. Wecker's opinions have recognized the unfair prejudice that his misleading statistics would cause plaintiffs to suffer. The Wilsons respectfully request that this Court also recognize the unfair prejudice likely precipitated by his opinions and exclude them from trial.

FN9. Plaintiffs respectfully request that this Court take judicial notice of the Court's Order in the case *Wagner, et al. v. General Motors Corp., et al.*, pgs. 1652:14 - 16 and 1653:22 - 1654:1 Evidence Code § 452(d).

III

CONCLUSION

As analyzed above, Dr. Wecker's opinions are inadmissible at trial. Dr. Wecker's opinions are irrelevant to the issue of the Explorer's design. He bases his opinions on data from collisions that are not substantially similar to Mrs. Wilson's collision. This data, therefore, does not provide reasonable bases for his opinions. Dr. Wecker's opinions will significantly prejudice plaintiffs' case, confuse the issues, mislead the jury and waste valuable time and money. For these reasons, the Wilsons respectfully request that this Court exclude from trial Dr. Wecker's opinions as well as any related reference or evidence.

Benetta BUELL-WILSON; Barry S. Wilson, Plaintiffs, v. FORD MOTOR COMPANY, a Delaware Corporation; Drew Ford, a California Corporation; and Does 1 to 50, inclusive, Defendants.
2003 WL 25322208 (Cal.Superior) (Trial Motion, Memorandum and Affidavit)

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EXHIBIT H

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SC v. Eli Lilly & Company, Inc.
Civil Action No.: 2007-CP-42-1855
August 31, 2009 Hearing Questions from Judge Couch

- 1. For the Plaintiff State of SC: Is the state making claims for reimbursement of Medicaid funds for patients within the DMH system?**

No. DMH offers two services at issue. First, DMH funded Inpatient hospitals house patients who are institutionalized. Second, DMH doctors employed at DMH Community Mental Health Centers see patients on an outpatient basis. The Community Mental Health Center side of DMH is no different than a patient who seeks treatment with doctors in a private psychiatric practice. Medicaid patients have been institutionalized at DMH Inpatient hospitals, and Medicaid patients have been treated by DMH doctors at DMH Community Mental Health Centers. When patients are institutionalized in a DMH Inpatient hospital, DMH pays for all aspects of the treatment (including pharmacy and medical) while the patient is institutionalized, not Medicaid. When patients see DMH doctors at DMH Community Mental Health Centers on an outpatient basis and are written prescriptions for Zyprexa, DMH pays for the consultation with a DMH doctor, and Medicaid pays for the Zyprexa prescription that the patient fills at any pharmacy in the State. The State is not seeking to recover DMH's costs of institutionalizing Medicaid patients or any other costs incurred by DMH, including the cost for a DMH doctor to see a Medicaid patient at a DMH Community Mental Health Center. The State is only seeking recovery of the costs of filling Zyprexa prescriptions for Medicaid participants, regardless of whether a DMH doctor or non-DMH doctor wrote the prescription.

- 2. For the Plaintiff State of SC: Can the data be cross referenced in order to track the patient expenditures for those patients who were simultaneously treated through the in-patient and out-patient DMH systems?**

Yes, with limitation. Patient expenditures may be tracked within the DMH for medical and pharmacy in-patient services and for out-patient medical services. As explained in response to item 1, for all patients (including those patients who are Medicaid participants) DMH covers the medical and pharmacy costs for treatment in an in-patient hospital. DMH covers the medical costs for the doctor visit at the out-patient Community Mental Health Center; however, Medicaid covers the costs associated with DMH out-patient pharmacy prescriptions (i.e., when a Medicaid participant receives a prescription at a DMH Community Mental Health Center and fills that prescription at a pharmacy outside of DMH). The in-patient expenditures and out-patient medical expenditures may be tracked within DMH. The out-patient pharmacy expenditures for Medicaid patients may only be determined by reference to the Medicaid data. There is no cross walk between the Medicaid data and the DMH data.

Patients are not necessarily simultaneously treated through the in-patient and out-patient DMH systems. A patient who sees a private psychiatrist may be institutionalized at one of the DMH inpatient hospitals, and when that patient is released from the DMH inpatient hospital, that patient resumes care with the private psychiatrist, not at a DMH Community Mental Health Center. There are also patients who see a DMH psychiatrist at a DMH Community Mental Health Center who have never been institutionalized at a DMH inpatient hospital. A patient can

also be institutionalized yet never seek outpatient treatment. There is no baseline assumption that all Medicaid patients seen by a DMH psychiatrist at a DMH Community Mental Health Center have also been institutionalized and vice versa.

3. For the Defendant Eli Lilly: What is a record layout and what purpose does it serve?
(referenced on p. 3, Report to the Court re: Claims Data from DMH, August 18, 2009).

A record layout explains and provides context to the data sets produced by the State. If you import the data into an excel spreadsheet for example, there would be numerous columns of information. The record layout explains the significance of the data in each column. The record layout is necessary to interpret the data. We have already provided the record layout of the data produced (but Lilly says it does not match up.) If the data is relevant, then the record layout is relevant.

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EXHIBIT I

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1 State of South Carolina) Court of Common Pleas
 2 County of Spartanburg) Seventh Judicial Circuit
 3 No.: 2007-CP-42-1438

4 Ex rel. Henry McMaster,)
 5 in his Capacity as)
 6 Attorney General of the)
 7 State of South Carolina,)

8 Plaintiff,)

9 vs.)

10 Janssen Pharmaceutica,)
 11 Inc. Janssen, L.P. and)
 12 Johnson & Johnson, Inc.,)

13 Defendant.)

Videotape
 Deposition of
 MARY ROBERTS

September 26, 2008

14 Videotape Deposition on oral examination of
 15 Mary Roberts, reported by Jeffrey M. Thomas,
 16 Registered Professional Reporter and Notary Public
 17 in and for the State of South Carolina; said
 18 deposition taken pursuant to agreement and in
 19 accordance with the South Carolina Rules of Civil
 20 Procedure, at the Offices of Richardson Plowden &
 21 Robinson, P.A., 1900 Barnwell Street, Columbia,
 22 South Carolina, on September 26, 2008, at the hour
 23 of 10:00 a.m.

24 GARBER REPORTING SERVICE, INC.
 25 POST OFFICE BOX 12348
 COLUMBIA, SOUTH CAROLINA 29211
 (803) 256-4500

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MARY ROBERTS

1 regarding the deposition process so that you and I
2 are clear.

3 A. Okay.

4 Q. And we can go forward. The first thing
5 that I would ask is that you keep all of your
6 responses to my questions verbal. Shrugs of the
7 shoulder, nods of the head, are difficult for the
8 court reporter to capture even though it may be
9 picked up on the video.

10 Also if at any point you don't understand
11 a question that I'm giving to you, you are not quite
12 sure what I mean, let me know and I'll do my best to
13 rephrase it.

14 A. Okay.

15 Q. Next, I would ask that you allow me to
16 finish a question before you start to respond even
17 if you anticipate what I'm going to ask you. It
18 makes for a much cleaner record. I'll give you the
19 same courtesy and wait until you finish before I ask
20 the next question. Fair enough?

21 A. Fair enough.

22 Q. Okay. And if at any point you need to
23 take a break for any reason just let me know and
24 we'll accommodate you. Okay?

25 A. Okay.

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R. 8083

MARY ROBERTS

1 Q. All right. Ms. Roberts, where do you
2 reside?

3 A. You want my full address or --

4 Q. Yes, ma'am.

5 A. 104 Morning Shore Court, Lexington, South
6 Carolina.

7 Q. Okay. And presently by whom are you
8 employed?

9 A. First Health Services Corporation.

10 Q. And what is your title or your duty at
11 First Health Services Corporation?

12 A. I am the director of clinical services for
13 the First Health Services Corporation. And I am the
14 clinical manager for the South Carolina Medicaid
15 contract.

16 Q. How long have you been director of
17 clinical services?

18 A. Since November of '07.

19 Q. Before you were director of clinical
20 services, what title did you hold at First Health,
21 if any?

22 A. Then I was just the clinical manager for
23 South Carolina Medicaid.

24 Q. Okay. And how long have you had
25 responsibility as clinical manager of South Carolina

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MARY ROBERTS

1 Medicaid?

2 A. Since December of 2002.

3 Q. We'll come back to that in a minute. I
4 see that you have what appears to be a resume or
5 C.V.; is that correct?

6 A. I do.

7 Q. All right. You graduated from the
8 University of South Carolina in 1986?

9 A. Correct.

10 Q. With a B.S. in Pharmacy, correct?

11 A. Yes.

12 Q. And have you achieved any graduate
13 degrees?

14 A. No.

15 Q. I'm sure you can tell me quicker than I
16 can find it in here, but what year did you begin
17 your employment with First Health?

18 A. December 2002.

19 Q. So your first job with First Health was
20 clinical manager of South Carolina Medicaid?

21 A. That's correct.

22 Q. Now, as the clinical manager of South
23 Carolina Medicaid what are your duties and
24 responsibilities?

25 A. I'm the direct client liaison between

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MARY ROBERTS

1 First Health Services and South Carolina Medicaid,
2 specifically the pharmacy program. I help them
3 administer their pharmacy benefit to the Medicaid
4 recipients by determining -- helping them determine
5 plan rules, plan design, those types of things.

6 First Health Services does the claims
7 adjudication for the pharmacy claims. So I help
8 anything that needs to make that happen for the
9 recipients and the pharmacists.

10 Q. Are there any people at First Health who
11 report directly to you?

12 A. Yes.

13 Q. How many?

14 A. I need a cheat sheet. I'll guesstimate
15 10.

16 Q. And with regard to your responsibilities
17 as manager of the South Carolina Medicaid contract,
18 to whom do you report at First Health?

19 A. I report to Pete Quinn, chief operating
20 officer.

21 Q. And is Mr. Quinn located in South Carolina
22 or elsewhere?

23 A. He's located in Richmond, Virginia.

24 Q. Now, do you know the date on which First
25 Health initially became the pharmacy benefits

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SOUTH CAROLINA COUNTY

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MARY ROBERTS

1 manager for South Carolina Medicaid?

2 A. I believe it was towards the end of the
3 year 2000.

4 Q. Before you were the manager?

5 A. Clinical manager.

6 Q. Pardon me?

7 A. Clinical manager.

8 Q. Before you were clinical manager of the
9 South Carolina Medicaid contract who held that
10 position?

11 A. David Pinkston.

12 Q. Did Mr. Pinkston no longer with First
13 Health or did he move to some other position?

14 A. He is currently with First Health as
15 account manager for the South Carolina Medicaid
16 account. That is why I clarified clinical -- there
17 are two manager roles in this account; one is the
18 account manager and one is the clinical manager. He
19 is the account manager for South Carolina Medicaid.
20 He's also the director of account management.

21 Q. How do his duties as account manager
22 differ from yours as clinical manager of the South
23 Carolina Medicaid contract?

24 A. He's responsible for the contractual
25 requirements, the business side of our relationship

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MARY ROBERTS

1 least 90-plus of claims are sent to us point of
2 sale, real time.

3 A pharmacist presents -- a patient
4 presents the pharmacist with their prescription.
5 The pharmacist enters it into their computer just
6 like they would your or my prescription, anyone's
7 prescription.

8 Their software system, they have that
9 patient identified in their system as South Carolina
10 Medicaid. And there are all sorts of things that
11 they have to program in to tell it how to send it to
12 us, but the short version, their system is
13 programmed. This is a Medicaid patient. We send it
14 through to First Health Services.

15 The claim comes to us electronically. It
16 goes through our claims adjudication engine where we
17 verify the patient's eligibility, the pharmacist is
18 actually a provider in the South Carolina Medicaid
19 network.

20 We verify plan rules. And if everything
21 check out, the claim pays to the pharmacist. What
22 we do after that point is once a week we compile a
23 claims extract where we take all the information off
24 of all the claims that were submitted to us on
25 behalf of South Carolina Medicaid. And we send

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R. 8088

MARY ROBERTS

1 those claims over to Clemson who is their M.M.I.S.
2 vendor. And Clemson is the one who takes it from
3 there to get the checks out.

4 Q. So the check or the compensation actually
5 comes directly from Clemson or --

6 A. I think they probably send it to D.H.H.S.

7 Q. Okay. But Clemson utilizes data provided
8 by First Health to determine what level of
9 compensation is owed to a pharmacist?

10 A. Yes.

11 Q. Now, in the course of your answer you
12 stated that there are various items of information
13 that are input by the pharmacy or the pharmacist in
14 the course of fulfilling the prescription. My question to you is does the pharmacy or the
15 pharmacist input any information regarding
16 indication?
17

18 A. No. Let me qualify that.

19 Q. Sure.

20 A. Recently we have put in an edit where for
21 a certain set of patients and a certain set of drugs
22 they are required to put in the I.C.D. 9 code which
23 is the diagnosis code provided by the doctor, but
24 it's a very limited number of claims. And it's been
25 in effect six or eight months.

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CLAY COUNTY

GARBER REPORTING SERVICE

R. 8089

MARY ROBERTS

1 Q. And for what class of drugs or what
2 medicines?

3 A. These are patients who are members of the
4 family planning waiver which normally provides them
5 family planning services only. Their benefit has
6 been expanded to include antibiotic therapy for
7 sexually transmitted diseases.

8 So if it's a patient who is in this waiver
9 group -- normally we wouldn't pay an antibiotic. If
10 the pharmacist -- if it's one of the approved
11 antibiotics and one of the approved diagnoses and
12 they put the correct I.C.D. 9 on there the claim
13 will pay. Otherwise it will deny as this is not a
14 service for this patient.

15 Q. Yes, ma'am. And other than that group,
16 there any other --

17 A. No.

18 Q. -- group of patients or any other
19 medicines that are subject to --

20 A. No.

21 Q. -- that edit? Okay. Now, with regard to
22 the prescribing habits, prescribing trends that
23 occur over a period of time, and again I'm speaking
24 with regard to South Carolina Medicaid, is that
25 something that First Health evaluates, tracks, or

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MARY ROBERTS

1 monitors; that is, how certain medicines or how
2 often, how frequently, which type of specialty areas
3 are prescribing that medication? Is that one of the
4 things that First Health evaluates or monitors on
5 behalf of H.H.S.?

6 A. We evaluate how often certain types of
7 drugs are prescribed. And really it's how many
8 prescriptions does Medicaid pay for and how much
9 money for those groups of drugs. We do evaluate
10 that.

11 We do not have specialty data necessarily
12 for the docs. So we don't break it down by this
13 group of docs under this specialty prescribed
14 bunch of this drug, but we do look at doctors who
15 are high frequency prescribers, overall number of
16 claims or overall dollars prescribed, but we don't
17 really break it down further.

18 The Retro DUR program does look at
19 specific criteria. For example, we recently looked
20 at doctors who were prescribing an asthma drug that
21 is used for emergency situations, but didn't have
22 the asthma drug that was for maintenance therapy in
23 the patient's history.

24 And so we lettered those targeted doctors,
25 you know, are you aware this patient is getting this

GARBER REPORTING SERVICE

R. 8091

Common Pleas
Clerk : M Hope Blackley
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(864) 596-2591

Received From: White, John Belton Jr.
Harrison White Smith & Coggins, PC
Spartanburg, SC 29304

Date : 1/13/2011
RECEIPT # 40269
Clerk: kflerning

Paying for: State Of South Carolina,

Transaction Type: Payment

Payment Type: Check \$25.00

Reference # 51938

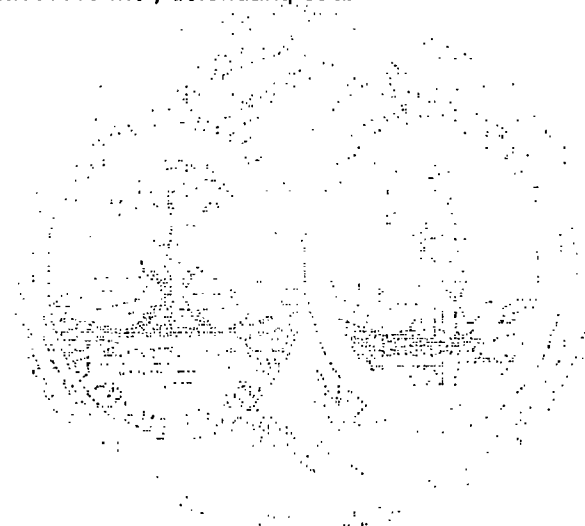
Comment: MOTION

Total Paid \$25.00

Total Received \$25.00

Change Due \$0.00

<u>Case #</u>	<u>Caption</u>	<u>Previous Balance</u>	<u>Amount Paid</u>	<u>Balance Due</u>
2007CP4201438	State Of South Carolina , plaintiff, et al VS Janssen Pharmaceutica Inc , defendant, et al	\$25.00	\$25.00	\$0.00



Total Cases:	1	\$25.00	\$25.00	\$0.00

STATE OF SOUTH CAROLINA
COUNTY OF SPARTANBURG

IN THE COURT OF COMMON PLEAS
FOR THE SEVENTH JUDICIAL CIRCUIT

STATE OF SOUTH CAROLINA, ex rel.
Alan Wilson, in his capacity as
Attorney General of the State of South
Carolina,

Civil Action No.: 2007-CP-42-1438

PLAINTIFF,

PLAINTIFF THE STATE OF SOUTH
CAROLINA'S RESPONSE
IN OPPOSITION TO

v.

DEFENDANTS' MOTION *IN LIMINE*
TO PRECLUDE THE INTRODUCTION
INTO EVIDENCE OF THE APRIL 19, 2004
DDMAC LETTER AND ANY EVIDENCE
OF OR REFERENCE TO THE LETTER
AT TRIAL

ORTHO-McNEIL-JANSSEN
PHARMACEUTICALS, INC. f/k/a
JANSSEN PHARMACEUTICA, INC.
and/or JANSSEN, LP, AND JOHNSON
& JOHNSON, INC.,

DEFENDANTS.

TO: STEVEN J. PUGH AND KENNETH A. MURPHY, ATTORNEYS FOR
DEFENDANTS

Plaintiff the State of South Carolina, ex rel. Alan Wilson,¹ in his capacity as Attorney General of the State of South Carolina (the "State"), hereby responds in opposition to the Memorandum of Law in Support of Defendants' Motion *in Limine* (the "Motion") to Preclude the Introduction Into Evidence of the April 19, 2004 DDMAC Letter and any Evidence of or Reference to the Letter at Trial (the "Memorandum") filed by the above-captioned "Defendants," and would respectfully show the Court as follows:

¹ Pursuant to South Carolina Rule of Civil Procedure 25(d)(1), the Honorable Alan Wilson has been substituted for the Honorable Henry McMaster as Attorney General for the State of South Carolina.

I.
SUMMARY OF RESPONSE

Defendants wrongly seek the Court's exclusion on hearsay and unfair prejudice grounds of an April 2004 "Warning Letter" (the "April 2004 Warning Letter") issued by the federal Food & Drug Administration ("FDA") Division of Drug Marketing, Advertising, and Communications ("DDMAC") to one or more of the Defendants that declared Defendants' November 10, 2003 "Dear Doctor" Letter (the "November 10, 2003 Letter") violated the Federal Food, Drug, and Cosmetic Act (the "FFDCA"). But, the April 2004 Warning Letter is not hearsay, or, in the alternative, the April 2004 Warning Letter is subject to an exception to the hearsay rule and should be admitted. Moreover, the April 2004 Warning Letter constitutes valid, effective enforcement action by the FDA against Defendants' "false and misleading" representations about Risperdal, and its admission will not cause the Defendants to suffer "undue prejudice." The Court should deny Defendants' Motion.

II.
ARGUMENT & AUTHORITIES

A. Standard

The admission or exclusion of evidence is left to the sound discretion of the trial judge, whose decision will not be reversed on appeal absent an abuse of discretion. *See State v. Tucker*, 462 S.E.2d 263, 265 (S.C. 1995). "'Hearsay' is a statement, other than one made by the declarant while testifying at the trial or hearing, offered in evidence to prove the truth of the matter asserted." S.C.R. Evid. 801(c). "The rule against hearsay prohibits the admission of evidence of an out-of-court statement to prove the truth of the matter asserted unless an exception to the rule applies." *Simpkins v. State*, 401 S.E.2d 142, 143 (S.C. 1991); *see* S.C.R. Evid. 803. "'An out of court statement is not hearsay if it is offered for the limited purpose of

explaining why a government investigation was undertaken.” *State v. Thompson*, 575 S.E.2d 77, 81 (S.C. Ct. App. 2003) (quoting *State v. Brown*, 451 S.E.2d 888, 893-94 (S.C. 1994)), quoted in *State v. Weaver*, 602 S.E.2d 786, 793 (S.C. Ct. App. 2004); see *State v. Rice*, 652 S.E.2d 409, 420 (S.C. Ct. App. 2007) (same). Further, “[p]roof of a statement introduced to show a party heard and acted upon information is not objectionable hearsay.” *Fields v. Reg’l Med. Ctr.*, 609 S.E.2d 506, 512 (S.C. 2005) (quoting and affirming in relevant part *Fields v. Reg’l Med. Ctr.*, 581 S.E.2d 489, 492-93 (S.C. Ct. App 2003) (citing *Webb v. Elrod*, 418 S.E.2d 559, 562 (S.C. Ct. App. 1992) and 31A C.J.S. *Evidence* § 259 (1996) (“Testimony is not hearsay where it *relates to* what the witness himself did in reliance on, or in response to, a statement, facts upon which action was taken, personal observations, explanation of conduct, the effect of statements on the listener, the fact that something was said, or identifying what was said.” (emphasis added))).

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Additionally, the South Carolina Rules of Evidence provide certain exceptions allowing for the admission of hearsay evidence in particular situations. Rule 803(8) exempts “Public Records and Reports” from the hearsay rule, which includes “[r]ecords, reports, statements, or data compilations, in any form, of public offices or agencies, setting forth (A) the activities of the office or agency, or (B) matters observed pursuant to duty imposed by law as to which matters there was a duty to report” S.C.R. Evid. 803(8).

Lastly, South Carolina Rule of Evidence 403 provides for the exclusion of evidence that is, among other things, unfairly prejudicial. “Unfair prejudice means an *undue* tendency to suggest a decision on an improper basis.” *State v. Stokes*, 673 S.E.2d 434, 443 (S.C. 2009) (emphasis added). “[T]he determination of prejudice must be based on the entire record, and the result will generally turn on the facts of each case.” *Id.*

B. The April 2004 Warning Letter Is Not Hearsay Because It Is Not Offered to Prove the Truth of the Matter Asserted.

Defendants incorrectly argue that the State offers the April 2004 Warning Letter to prove the truth of the matter asserted—i.e., “that Janssen’s November 10, 2003 “Dear Doctor” Letter was ‘false and misleading’” as a matter of law. (Defs.’ Mem. at 5.) Indeed, it is not the State’s position that because the FDA deemed the November 10, 2003 letter false and misleading, it is therefore “deceptive” as a matter of law under SCUTPA, contrary to Defendants’ assumption in its memorandum (at 4-5). That ultimate question is for the jury to determine based upon all the evidence presented. Whether its conclusions are right or wrong, the April 2004 Warning Letter is offered only to show that the FDA had undertaken a review of the November 10, 2003 “Dear Doctor” Letter, why the FDA engaged in such a review, and the official conclusions that the FDA reached. *See, e.g., Thompson*, 575 S.E.2d at 81. Defendants, of course, are free to offer admissible evidence countering those facts and conclusions, including many of the arguments they set forth in their Memorandum. (*See, e.g.,* Defs.’ Mem. at 5 (arguing that the April 2004 Warning Letter contains only the “author’s ‘opinions, judgments, and conclusions’”); *id.* at 7 (contending that the April 2004 Warning Letter “does not prove actual wrongdoing”).

The April 2004 Warning Letter is also offered by the State for another non-hearsay purpose: to put into context Defendants’ reaction to the April 2004 Warning Letter in issuing a subsequent July 2004 Dear Doctor Letter. *Fields*, 609 S.E.2d at 512. Because Defendants will undoubtedly seek to introduce the July 2004 Dear Doctor Letter into evidence, it is crucial that the jury also be permitted to consider that Defendants issued that letter “in reliance on, or in response to, a statement” by the FDA, as well as to understand that the April 2004 Dear Doctor Letter provides “facts upon which action was taken . . .” by Defendants. *Id.*

Because the April 2004 Warning Letter is not introduced to prove the truth of the matter asserted, it should not be excluded on hearsay grounds.

C. Assuming *Arguendo* the April 2004 Warning Letter Is Hearsay, It Falls Within the Public Records and Reports Exception to the Hearsay Rule, S.C.R. Evid. 803(8).

Even if the Court views the April 2004 Warning Letter as hearsay—which it is not for the reasons already stated—Defendants cannot avoid the governing “Public Records and Reports” exception to the hearsay rule. *See* S.C.R. Evid. 803(8). That exception specifically exempts the “[r]ecords, reports, statements, or data compilations, in any form, of public offices or agencies, setting forth (A) the activities of the office or agency, or (B) matters observed pursuant to duty imposed by law as to which matters there was a duty to report” *See, e.g., State v. Cutro*, 618 S.E.2d 890, 896 (S.C. 2005) (ruling that Rule 803(8) excepts, for example, autopsy reports generated pursuant to law). Plainly, the April 2004 Warning Letter constitutes a record, report or statement by a public office or agency (the FDA) and sets forth the activities the FDA undertook relative to the November 2003 Dear Doctor Letter, as well as discusses matters observed pursuant to the FDA’s legally authorized mission to police prescription drug labeling, including communications to doctors about prescription drugs. *See* 21 U.S.C. § 352 (governing authority under which FDA regulates prescription drug labeling).

Defendants hope to avoid the above result by mischaracterizing the April 2004 Warning Letter as merely the “author’s opinions, judgments, and conclusions,” which they argue are not covered by the Rule 803(8) exception. (*See* Defs.’ Mem. at 6 (“The April [2004 Warning Letter] contains *an FDA employee’s application and analysis* of highly technical federal regulations”) (emphasis added).) In another contemporaneously filed motion, Defendants cast the April 2004 Warning Letter as “express[ing] *the writer’s opinion* that the November 10, 2003 letter was “false or misleading”” (*See* Defs’ Mot. Summ. J. as to Pl.’s Unfair Trade Practices Claim

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Based on the Nov. 10, 2003 Mailing (filed Jan. 13, 2011) at 5 (emphasis added).) But, Defendants trip over their own mischaracterizations of the April 2004 Warning Letter in subsequently admitting in their Memorandum on this issue that the Letter “communicates *the agency’s position* on a matter.” (Defs.’ Mem. at 7 (citing *Regulatory Procedures Manual: Advisory Actions* at 2 (Exhibit C to Defs.’ Mem.)).)

Indeed, the FDA *Regulatory Procedures Manual* Defendants cite makes clear that a lone-wolf FDA employee cannot unilaterally issue Warning Letters. “Center concurrence is required prior to issuing Warning Letters in the areas” of “[a]ll labeling violations” and “[p]roduct advertising violations” (Defs.’ Mem. Exhibit C at 4-6)—meaning that Warning Letters in those instances may not “be issued at the discretion of the district director without center concurrence” (e.g., concurrence of the Center for Drug Evaluation and Research or “CDER,” for example) (*Id.* at 4-4.) Additionally, since March 2002, all Warning Letters must be submitted to FDA’s Office of Chief Counsel “prior to their issuance so that they can be reviewed for sufficiency and consistency with agency policy.” (*Id.* at 4-30.) And, in any event, Rule 803(b)(3)’s limitation as to “opinions, judgments, and conclusions” expressly applies only to “investigative notes,” not to an agency conclusion, as here.

Defendants’ reliance on the inapposite *Culbreath v. Investors Syndicate* and *State v. Morris* cases does not change the above analysis. In *Culbreath*, the inadmissible letters at issue in that 67-year-old decision consisted of responses to inquiries made by the *appellant’s counsel* to the *appellee corporation*—written years after the stock transactions underlying the lawsuit had occurred—setting forth the corporation’s history of stock sales, corporate earnings, and other data. 26 S.E.2d 809, 813 (S.C. 1943). Thus, the privately written and issued *Culbreath* letters—effectively *discovery responses*—evinced none of the confrontation safeguards and admissibility

indicia that render public records and reports admissible under Rule 803(8). Further, the excluded bankruptcy examiner's report in *State v. Morris* was not the equivalent of an "agency's position"—there was no imprimatur of a public authority or agency, as presented here—but instead constituted the lone examiner's "investigative opinions, legal analysis, and *potential* conclusions" that fell outside the express parameters of Rule 803(8). *Morris*, 656 S.E.2d 359, 368-69 (S.C. 2008) (emphasis added). For that reason, the Supreme Court excluded the examiner's report as hearsay not falling with the Rule 803(8) exception.

Thus, should the Court deem the April 2004 Warning Letter to be hearsay, it falls within the exception of Rule 803(8) and should be admitted.

D. Admission of the April 2004 Warning Letter Is Not Unfairly Prejudicial.

Lastly, Defendants argue that the April 2004 Warning Letter is not a final agency action and, therefore, it should be withheld from the jury. That position is, of course, expressly contradicted by Defendants' own Memorandum, which (as noted above) acknowledges that the April 2004 Warning Letter constitutes the "agency's position" on the issue (Defs.' Mem. at 7 (citing *Regulatory Procedures Manual: Advisory Actions* at 2 (Exhibit C to Defs.' Mem.))), as well as by the *conclusions* the FDA reached in the April 2004 Warning Letter itself—e.g., "[f]ailure to correct the violations . . . may result in FDA regulatory action, including seizure of injunction, *without further notice*"; "DDMAC has concluded that the [November 10, 2003 Letter] is false or misleading in violation of Sections 502(a) and 201(n) of the [FFDCA] (21 U.S.C. 352(a) and 321 (n)); and "DDMAC has concluded that these materials are false, misleading, and/or lacking in fair balance, and in violation of the [FFDCA]" (Defs.' Mem. Exhibit B at 1, 5.) The *Regulatory Procedures Manual* attached to Defendants' Memorandum (at Exhibit C) further clarifies that the "Warning Letter was developed *to correct violations of the statutes or regulations*" and "are based on the expectation that most individuals and firms

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will voluntarily *comply with the law*” as set forth in the Warning Letter. (*Id.* at 4-1 to 4-2 (emphases added).) There is simply no basis for Defendants to argue that the April 2004 Warning Letter is not valid, effective FDA enforcement action of regulatory violations as determined by that agency.

In any event, Defendants most certainly will offer—if the Court permits—their own expert’s opinion as to the weight and significance of the April 2004 Warning Letter, which the jury may then consider along with the State’s expert’s testimony and opinions. The jury may then decide—in light of all the evidence discussed above—whether the April 2004 Warning Letter lends support to, or detracts from, the State’s claimed SCUTPA violation. But, there is simply no undue prejudice inuring to Defendants as a result of the Court’s admission of the April 2004 Warning Letter under those circumstances. *See Stokes*, 673 S.E.2d at 443.

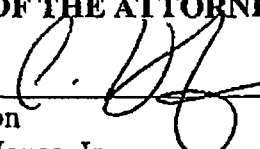
III. CONCLUSION

The State does not intend to argue that the FDA’s April 2004 Warning Letter constitutes conclusive evidence of Defendants’ SCUTPA violation. Therefore, the April 2004 Warning Letter is not offered for the truth of the matter asserted and is not hearsay. Should the Court decide the April 2004 Warning Letter is hearsay, it is nevertheless admissible under the “Public Records and Reports” exception of Rule 803(8). Finally, despite Defendants’ mischaracterizations of the April 2004 Warning Letter as merely the “author’s opinions” and an “advisory” “opinion” that the Defendants were free to ignore, the express language of the April 2004 Warning Letter itself and the regulations governing its issuance demonstrate its force and effect, and there will be no “undue” prejudice stemming from its admission. The State, therefore, respectfully requests the Court to deny Defendants’ Motion.

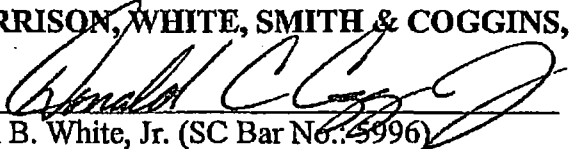
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STATE OF SOUTH CAROLINA
COUNTY OF SPARTANBURG

IN THE COURT OF COMMON PLEAS
FOR THE SEVENTH JUDICIAL CIRCUIT

STATE OF SOUTH CAROLINA ex rel.
Alan Wilson, in his capacity as
Attorney General of the State of South
Carolina,

Civil Action No. 2007-CP-42-1438

Plaintiff,

v.

ORTHO-McNEIL-JANSSEN
PHARMACEUTICALS, INC., f/k/a
JANSSEN PHARMACEUTICA INC.,
and/or JANSSEN, L.P. and
JOHNSON & JOHNSON, INC.,

Defendants.

**DEFENDANTS' MEMORANDUM OF LAW
IN OPPOSITION TO
PLAINTIFF'S MOTION TO EXCLUDE THE
TESTIMONY OF CERTAIN RISPERDAL
PRESCRIBERS AT TRIAL**

Defendants, Ortho-McNeil-Janssen Pharmaceuticals, Inc. ("Janssen" and Johnson & Johnson (erroneously named as Johnson & Johnson, Inc.), by and through their undersigned counsel, hereby submit this Memorandum of Law in Opposition to Plaintiff's Motion To Exclude The Testimony Of Certain Risperdal Prescribers At Trial ("Pl.'s Motion").

I. INTRODUCTION

Plaintiff attempts to preclude Defendants from presenting the testimony of "certain" South Carolina physicians who prescribed Risperdal®. The Motion is vague and unclear; Plaintiff does not even identify the prescribers to whose testimony it objects. Moreover, the Motion is not well-founded – evidence about what prescribers knew, and about their experiences with Risperdal and other antipsychotics, is relevant and admissible. This Court should deny Plaintiff's Motion.

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II. ARGUMENTS AND AUTHORITIES

A. Applicable Standard.

The admission or exclusion of evidence is within the sound discretion of the trial court and will not be reversed absent an abuse of discretion. *See, e.g., Jamison v. Ford Motor Co.*, 373 S.C. 248, 269, 644 S.E.2d 755, 766 (Ct. App. 2007). Evidence may be admitted at trial if it is relevant. *See* Rule 402, SCRE. Relevant evidence is “any evidence having any tendency to make the existence of any fact that is of consequence to the determination of the action more probable or less probable than it would be without the evidence.” Rule 401, SCRE. Relevant evidence may be excluded only if the court finds its “probative value is substantially outweighed by the danger of unfair prejudice, confusion of the issues, or misleading the jury, or by considerations of undue delay, waste of time, or needless presentation of cumulative evidence.” Rule 403, SCRE.

B. The Court Should Deny Plaintiff’s Motion.

1. Plaintiff Does Not Even Identify The “Certain Prescribers” Whose Testimony It Seeks To Preclude.

Plaintiff’s Motion seeks an Order excluding the testimony of “certain Risperdal prescribers.” But it is not clear which ones. There are two possibilities: (1) the twenty randomly-selected South Carolina prescribers whose responses to a deposition-based survey form the basis for some of Dr. William E. Wecker’s expert opinions, and (2) six other South Carolina physicians who responded to an Alert Letter from South Carolina’s Department of Health and Human Services (“the DHHS Alert Letter”) concerning

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metabolic risks associated with atypical antipsychotics.¹ As Defendants demonstrate below, testimony from either group is relevant to Plaintiff's claim. Indeed, it might ultimately prove to be dispositive of that claim. But, as a preliminary matter, Plaintiff's Motion should be denied because Plaintiff fails to either set forth with sufficient clarity the relief that it seeks or to explain, except in the most general and conclusory way, what it contends to be the evidentiary basis for its requested relief.

2. The Knowledge and Understanding of South Carolina Prescribers Is Relevant.

Plaintiff's Motion is premised on the notion that what South Carolina physician-prescribers knew and understood about the benefits and risks of antipsychotics is relevant only to a "learned intermediary" defense – a defense which, it says, is not available in a "penalties-only" claim under the South Carolina Unfair Trade Practices Act ("SCUTPA"). Pl.'s Motion at 5-7. That is not so. What prescribers knew – the basis for their prescribing decisions – is undeniably relevant to the "deception" element of Plaintiff's SCUTPA claim.

In its Motion, as in its Second Amended Complaint, Plaintiff contends that Defendants "'willfully engaged in a . . . *deceptive* . . . course of conduct in violation of SCUTPA' through its 'labeling of Risperdal, which . . . *deceptively* . . . minimized, misrepresented, and/or concealed the drug's dangerous side effects.'" Pl.'s Motion at 3 (quoting Second Am. Compl. ¶¶ 8, 13) (emphasis added). And, Plaintiff says, Defendants "'made, and continue[] to make . . . *deceptive* representations.'" *Id.* (quoting

¹ Defendants may call other physicians who held senior positions with State agencies and also practiced medicine. Defendants do not understand Plaintiff's Motion as an effort to exclude the testimony of those "prescribers".

Second Am. Compl. ¶ 58) (emphasis added). To recover, Plaintiff must show, in the first instance, that the Risperdal package insert and/or the November 2003 mailing were "deceptive" – i.e., that they were likely to deceive.

Whether a particular act or practice is likely to deceive "depends upon the surrounding facts and the impact of the transaction on the marketplace." *deBondt v. Carlton Motorcars, Inc.*, 342 S.C. 254, 269, 536 S.E.2d 399, 407 (Ct. App. 2000). Thus, in deciding whether a particular statement is "deceptive" for purposes of SCUTPA, the fact finder must consider the knowledge and sophistication of the intended audience. See 2 Fed. Trade Comm'n App. D-2 (2009) ("By the same token, a practice or representation directed to a well-educated group, *such as a prescription drug advertisement to doctors*, would be judged in light of the knowledge and sophistication of that group." (emphasis added)); see generally *Plowman v. Bagnal*, 316 S.C. 283, 287, 450 S.E.2d 36, 38 (1994) ("In section 39-5-20(b), the Legislature specifically instructs state courts to be guided by the decisions of the Federal Trade Commission (FTC) and the Federal Courts construing the Federal Trade Commission Act, 15 U.S.C. [§] 45(a)(1), in interpreting section 39-5-20(a)[.]").

South Carolina prescribers are the relevant, intended audience for the materials Plaintiff says were "deceptive". The November 2003 mailing was sent to prescribers; likewise, the Risperdal package insert was written for prescribers. See November 2003 mailing (Ex. 1) ("Dear Healthcare Provider, . . ."); see also 73 Fed. Reg. 49603, 49604 (Aug. 22, 2008) ("FDA's comprehensive scientific evaluation is embodied in the labeling for the product which reflects thorough FDA review of the pertinent scientific evidence and communicates to health care practitioners the agency's formal, authoritative

conclusions regarding the conditions under which the product can be used safely and effectively."); *Morlino v. Med. Ctr. of Ocean Cnty.*, 152 N.J. 563, 580, 706 A.2d 721, 729-30 (1998) ("Drug manufacturers write explanations and warnings for doctors, not the general public."); *Martin v. Hacker*, 83 N.Y.2d 1, 9, 628 N.E.2d 1308, 1311 (1993) ("Warnings for prescription drugs are intended for the physician, whose duty it is to balance the risks against the benefits of various drugs and treatments and to prescribe them and supervise their effects."); *Martin*, 83 N.Y.2d at 9, 628 N.E.2d at 1311 ("Manufacturers apprise physicians of dangerous side effects in various ways. The most common are: (1) the inclusion in the Physicians Desk Reference, the annually updated encyclopedia of medications, of a formal description of each manufacturer's drugs; and (2) the manufacturer's formal warning in the package insert of a prescription drug[.]"). What South Carolina prescribers knew or did not know about Risperdal and other antipsychotics and their benefits and risks – the context within which they would have considered the Risperdal package insert and the November 2003 mailing – therefore is undeniably relevant to the question of the materials' "impact on the marketplace" and the "likely to deceive" element of Plaintiff's claim.

3. The Testimony Of The Twenty Randomly-Selected Prescribers, If Needed To Support Dr. Wecker's Opinions, Will Be Admissible And Will Not Be Cumulative.

Dr. Wecker, who is Defendants' designated statistical expert, will testify, in part, to the results of a deposition-based survey of South Carolina Risperdal prescribers. See Expert Report of Dr. William E. Wecker ¶¶ 21-25 ("Report") & Exs. 4, 5 (Ex. 2). In that survey, twenty randomly-selected prescribers were each asked questions about their experiences with Risperdal and other antipsychotics and the benefits and risks of the medicines. Dr. Wecker has analyzed the responses given by the twenty

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prescribers, and has reached certain statistically-valid conclusions about the broader population of South Carolina prescribers. *Id.*² As explained in Section 2, above, such conclusions are relevant to the central issue in this case: whether the November 2003 mailing and the FDA-approved Risperdal package insert were likely to deceive anyone.

As the basis, in part, for his expert testimony, Dr. Wecker will rely on the twenty prescribers' responses to the survey he designed and directed. Assuming that his testimony is admitted, there should be no need to call the prescribers to repeat their responses at the time of the trial (although some might be called for other reasons). The issue of the admissibility of the prescriber testimony only arises to the extent that Plaintiff challenges the reliability of the survey evidence underlying Dr. Wecker's expert opinions. In a separate motion *in limine*, Plaintiff has made such a challenge. In particular, it has moved separately to exclude this part of the Wecker testimony because, Plaintiff says, Dr. Wecker may not base his conclusions on out-of-court testimony. That objection is meritless as Defendants explain in greater detail in the Wecker Opposition. In any event, even if the Court were to sustain Plaintiff's objection, Defendants then would simply be forced to call the twenty prescribers at trial to respond – again – to the survey questions. Under that scenario, Dr. Wecker's opinion would be based only on "in court" testimony, and Plaintiff would have no conceivable objection. Defendants make this point not as a concession that calling all twenty prescribers at trial

² Dr. Wecker's methodology, including the sampling techniques he employed, is addressed in Defendants' Memorandum of Law in Opposition to Plaintiff's Motion to Exclude the Expert Testimony of Dr. William E. Wecker ("Wecker Opposition").

is a necessary or judicially efficient outcome, but only to illustrate the futility of Plaintiff's Motion.

In sum, Plaintiff's challenge here to the testimony of the twenty South Carolina prescribers is both (1) misplaced, because it concerns the separate issue of the admissibility of Dr. Wecker's expert testimony, and (2) premature, because it only arises if Plaintiff is successful in preventing Dr. Wecker from relying on the deposition testimony of the prescribers and forcing Defendants to call the prescribers as live witnesses.

4. The Testimony Of The South Carolina Prescribers Who Responded To The DHHS Alert Letter Is Relevant And Admissible.

Plaintiff may also be asking that the Court preclude the testimony of six South Carolina physicians regarding the DHHS Alert Letter, which the South Carolina DHHS mailed in 2002 and 2003.³ In relevant part, the DHHS Alert Letter informed South Carolina physicians that "[t]he use of clozapine, olanzapine, risperidone [Risperdal] or quetiapine may increase the risk of developing type II diabetes mellitus or impaired glucose tolerance." DHHS Alert Letter at 1 (Ex. 3). It also advised that "[p]atients with a family history of diabetes or with pre-existing diabetes may need to have blood sugar monitored closely or changed to an alternative medication." *Id.*

The testimony of these six South Carolina physicians, all of whom are State employees, is evidence of the long-standing knowledge of South Carolina physicians

³ The six gave deposition testimony. See Dep. of Dr. Robert L. Bank (March 15, 2010); Dep. of Dr. William Anthony King (March 9, 2010); Dep. of Dr. James Perry Mazgaj (March 9, 2010); Dep. of Dr. Karen Sue Stacher (March 16, 2010); Dep. of Dr. B. Broxann Spencer (March 15, 2010); Dep. of Dr. Judith Treadway (March 15, 2010).

and the State itself about the very risks that Plaintiff alleges were inadequately disclosed by Defendants. That, in turn, bears on the likelihood that the Risperdal package insert or the November 2003 mailing would "deceive" anyone, among other things. Thus, contrary to Plaintiff's assertions, Pl.'s Motion at 6, under the applicable evidentiary standards, Defendants clearly have a "legitimate basis for the use of the testimony at trial." Plaintiff's secondary argument that the testimony of all six of these prescribers would be cumulative, Pl.'s Motion at 8-9, is premature; until the testimony of one or more of the six prescribers is offered, the "cumulative testimony" argument cannot fairly be evaluated.

5. Prescriber Testimony Would Not Be Unfairly Prejudicial.

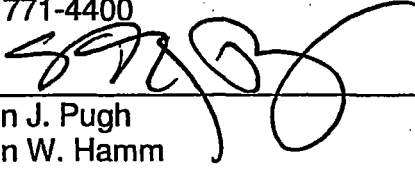
Plaintiff does not explain how the testimony of South Carolina prescribers would "unfairly prejudice" Plaintiff – and it clearly would not. Plaintiff, of course, may not seek preclusion of such testimony simply because it is detrimental to its case. See, *Holmes v. Black River Elec. Coop., Inc.*, 274 S.C. 252, 258, 262 S.E.2d 875, 880 (1980) (affirming trial court's decision to admit evidence despite detriment to opposing party because its probative value greatly outweighed any prejudice).

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III. CONCLUSION

For all the foregoing reasons, Defendants respectfully request that this Court deny Plaintiff's Motion in its entirety.

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EXHIBIT 1

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JANSSEN



PHARMACEUTICA INC.

November 10, 2003

Dear Healthcare Provider,

The Food and Drug Administration (FDA) has requested all manufacturers of atypical antipsychotics to include a warning regarding hyperglycemia and diabetes mellitus in their product labeling. In addition to Janssen, the FDA made this request to the following manufacturers:

AstraZeneca -- Seroquel® (quetiapine)
Bristol-Myers Squibb -- Abilify™ (aripiprazole)
Eli Lilly and Company -- Zyprexa® (olanzapine)
Novartis -- Clozaril® (clozapine)
Pfizer -- Geodon® (ziprasidone)

In an effort to keep you updated with the most current product information available for the management of your patients, enclosed please find updated prescribing information for RISPERDAL® (risperidone).

Hyperglycemia-related adverse events have infrequently been reported in patients receiving RISPERDAL. Although confirmatory research is still needed, a body of evidence from published peer-reviewed epidemiology research^{1a} suggests that RISPERDAL is not associated with an increased risk of diabetes when compared to untreated patients or patients treated with conventional antipsychotics. Evidence also suggests that RISPERDAL is associated with a lower risk of diabetes than some other studied atypical antipsychotics.

For additional information about RISPERDAL or any other Janssen product, please call 1-800-JANSSEN (526-7736) from 9AM to 5PM EST, Monday through Friday.

Sincerely,

Ramy Mahmoud, MD
Vice President CNS Medical Affairs
Janssen Pharmaceutica, Inc.

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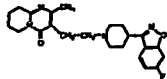
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RISPERDAL® (RISPERIDONE) TABLETS/ORAL SOLUTION

DESCRIPTION

RISPERDAL® (risperidone) is a psychotropic agent belonging to the chemical class of benzisoxazole derivatives. The chemical designation is 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinylethyl]-5,7,8,9-tetramethyl-4H-pyrido[1,2-a]pyrimidin-4-one. Its molecular formula is $C_{26}H_{30}FN_3O_2$ and its molecular weight is 410.49. The structural formula is:



Risperidone is a white to slightly beige powder. It is practically insoluble in water, freely soluble in methylene chloride, and soluble in methanol and 0.1 N HCl.

RISPERDAL® tablets are available in 0.25 mg (dark yellow), 0.5 mg (red-brown), 1 mg (white), 2 mg (orange), 3 mg (yellow), and 4 mg (green) strengths. Inactive ingredients are colloidal silicon dioxide, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, sodium lauryl sulfate, and starch (corn). Tablets of 0.25, 0.5, 2, 3, and 4 mg also contain talc and titanium dioxide. The 0.25 mg tablets contain yellow iron oxide; the 0.5 mg tablets contain red iron oxide; the 2 mg tablets contain FD&C Yellow No. 6 Aluminum Lake; the 3 mg and 4 mg tablets contain D&C Yellow No. 10; the 4 mg tablets contain FD&C Blue No. 2 Aluminum Lake.

RISPERDAL® is also available as a 1 mg/mL oral solution. The inactive ingredients for this solution are tartaric acid, benzoic acid, sodium hydroxide, and purified water.

RISPERDAL® M-TAB™ Orally Disintegrating Tablets are available in 0.5 mg, 1.0 mg, and 2.0 mg strengths and are light coral in color.

RISPERDAL® M-TAB™ Orally Disintegrating Tablets contain the following inactive ingredients: Amberlite® resin, gelatin, mannitol, glycerine, simethicone, carbomer, sodium hydroxide, aspartame, red ferric oxide, and peppermint oil.

CLINICAL PHARMACOLOGY

Pharmacodynamics

The mechanism of action of RISPERDAL® (risperidone), as with other drugs used to treat schizophrenia, is unknown. However, it has been proposed that the drug's therapeutic activity in schizophrenia is mediated through a combination of dopamine Type 2 (D₂) and serotonin Type 2 (5HT₂) receptor antagonism. Antagonism at receptors other than D₂ and 5HT₂ may explain some of the other effects of RISPERDAL®.

RISPERDAL® is a selective monoaminergic antagonist with high affinity (K_i of 0.12 to 7.3 nM) for the serotonin Type 2 (5HT₂), dopamine Type 2 (D₂), α₁ and α₂ adrenergic, and H₁ histaminergic receptors. RISPERDAL® acts as an antagonist at other receptors, but with lower potency. RISPERDAL® has low to moderate affinity (K_i of 47 to 253 nM) for the serotonin 5HT_{1A}, 5HT_{1B}, and 5HT_{1C} receptors, weak affinity (K_i of 620 to 800 nM) for the dopamine D₁ and haloperidol-sensitive sigma sites, and no affinity (when tested at concentrations >10⁻⁶ M) for cholinergic muscarinic or β₁ and β₂ adrenergic receptors.

Pharmacokinetics

Absorption

Risperidone is well absorbed. The absolute oral bioavailability of risperidone is 70% (CV=25%). The relative oral bioavailability of risperidone from a tablet is 94% (CV=10%) when compared to a solution.

Pharmacokinetic studies showed that RISPERDAL® M-TAB™ Orally Disintegrating Tablets are bioequivalent to RISPERDAL® Tablets.

Plasma concentrations of risperidone, its major metabolite, 9-hydroxyrisperidone, and risperidone plus 9-hydroxyrisperidone are dose proportional over the dosing range of 1 to 16 mg daily (0.5 to 8 mg BID). Following oral administration of solution or tablet, mean peak plasma concentrations of risperidone occurred at about 1 hour. Peak concentrations of 9-hydroxyrisperidone occurred at about 3 hours in extensive metabolizers, and 17 hours in poor metabolizers. Steady-state concentrations of risperidone are reached in 1 day in extensive metabolizers and would be expected to reach steady state in about 5 days in poor metabolizers. Steady-state concentrations of 9-hydroxyrisperidone are reached in 5-6 days (measured in extensive metabolizers).

Food Effect

Food does not affect either the rate or extent of absorption of risperidone. Thus, risperidone can be given with or without meals.

Distribution

Risperidone is rapidly distributed. The volume of distribution is 1-2 L/kg. In plasma, risperidone is bound to albumin and α₁-acid glycoprotein. The plasma protein binding of risperidone is 90%, and that of its major metabolite, 9-hydroxyrisperidone, is 77%. Neither risperidone nor 9-hydroxyrisperidone displaces each other from plasma binding sites. High therapeutic concentrations of sulfamethoxazole (100 mg/mL), warfarin (10 μg/mL), and carbamazepine (10 μg/mL) caused only a slight increase in the free fraction of risperidone at 10 ng/mL and 9-hydroxyrisperidone at 50 ng/mL, changes of unknown clinical significance.

Metabolism

Risperidone is extensively metabolized in the liver. The main metabolic pathway is through hydroxylation of risperidone to 9-hydroxyrisperidone by the enzyme, CYP 2D6. A minor metabolic pathway is through N-dealkylation. The main metabolite, 9-hydroxyrisperidone, has similar pharmacological activity as risperidone. Consequently, the clinical effect of the drug (i.e., the active moiety) results from the combined concentrations of risperidone plus 9-hydroxyrisperidone.

CYP 2D6, also called debrisoquine hydroxylase, is the enzyme responsible for metabolism of many neuroleptics, antidepressants, antiarrhythmics, and other drugs. CYP 2D6 is subject to genetic polymorphism (about 6%-8% of Caucasians, and a very low percentage of Asians, have little or no activity and are "poor metabolizers" and to inhibition by a variety of substrates and some non-substrates, notably quinidine. Extensive CYP 2D6 metabolizers convert risperidone rapidly into 9-hydroxyrisperidone, whereas poor CYP 2D6 metabolizers convert it much more slowly. Although extensive metabolizers have lower risperidone and higher 9-hydroxyrisperidone concentrations than poor metabolizers, the pharmacokinetics of the active moiety, after single and multiple doses, are similar in extensive and poor metabolizers.

Risperidone could be subject to two kinds of drug-drug interactions (see Drug Interactions under PRECAUTIONS). First, inhibitors of CYP 2D6 interfere with conversion of risperidone to 9-hydroxyrisperidone. This occurs with quinidine, giving essentially all recipients a risperidone pharmacokinetic profile typical of poor metabolizers. The therapeutic benefits and adverse effects of risperidone in patients receiving quinidine have not been evaluated, but observations in a modest number (n=70) of poor metabolizers given risperidone do not suggest important differences between poor and extensive metabolizers. Second, co-administration of known enzyme inducers (e.g., phenytoin, rifampin, and phenobarbital) with risperidone may cause a decrease in the combined plasma concentrations of risperidone and 9-hydroxyrisperidone. It would also be possible for risperidone to interfere with metabolism of other drugs metabolized by CYP 2D6. Relatively weak binding of risperidone to the enzyme suggests this is unlikely.

Excretion

Risperidone and its metabolites are eliminated via the urine and, to a much lesser extent, via the feces. As illustrated by a mass balance study of a single 1 mg oral dose of ¹⁴C-risperidone administered as solution to three healthy male volunteers, total recovery of radioactivity at 1 week was 84%, including 70% in the urine and 14% in the feces.

The apparent half-life of risperidone was 3 hours (CV=30%) in extensive metabolizers and 20 hours (CV=40%) in poor metabolizers. The apparent half-life of 9-hydroxyrisperidone was about 21 hours (CV=20%) in extensive metabolizers and 30 hours (CV=25%) in poor metabolizers. The pharmacokinetics of the active moiety, after single and multiple doses, were similar in extensive and poor metabolizers, with an overall mean elimination half-life of about 20 hours.

Special Populations

Renal Impairment

In patients with moderate to severe renal disease, clearance of the sum of risperidone and its active metabolite decreased by 50% compared to young healthy subjects. RISPERDAL® doses should be reduced in patients with renal disease (see PRECAUTIONS and DOSAGE AND ADMINISTRATION).

Hepatic Impairment

While the pharmacokinetics of risperidone in subjects with liver disease were comparable to those in young healthy subjects, the mean free fraction of risperidone in plasma was increased by about 35% because of the diminished concentration of both albumin and α₁-acid glycoprotein. RISPERDAL® doses should be reduced in patients with liver disease (see PRECAUTIONS and DOSAGE AND ADMINISTRATION).

RISPERDAL® M-TAB™ (RISPERIDONE) ORALLY DISINTEGRATING TABLETS

Elderly

In healthy elderly subjects renal clearance of both risperidone and 9-hydroxyrisperidone was decreased, and elimination half-lives were prolonged compared to young healthy subjects. Dosing should be modified accordingly in the elderly patients (see DOSAGE AND ADMINISTRATION).

Race and Gender Effects

No specific pharmacokinetic study was conducted to investigate race and gender effects, but a population pharmacokinetic analysis did not identify important differences in the disposition of risperidone due to gender (whether corrected for body weight or not) or race.

Clinical Trials

Short-Term Efficacy

The efficacy of RISPERDAL® in the treatment of schizophrenia was established in four short-term (4 to 8-week) controlled trials of psychotic inpatients who met DSM-III-R criteria for schizophrenia.

Several instruments were used for assessing psychiatric signs and symptoms in these studies, among them the Brief Psychiatric Rating Scale (BPRS), a multi-item inventory of general psychopathology traditionally used to evaluate the effects of drug treatment in schizophrenia. The BPRS psychosis cluster (conceptual disorganization, hallucinatory behavior, suspiciousness, and unusual thought content) is considered a particularly useful subset for assessing actively psychotic schizophrenic patients. A second traditional assessment, the Clinical Global Impression (CGI), reflects the impression of a skilled observer, fully familiar with the manifestations of schizophrenia, about the overall clinical state of the patient. In addition, two more recently developed, but less well evaluated scales, were employed; these included the Positive and Negative Syndrome Scale (PANSS) and the Scale for Assessing Negative Symptoms (SANS).

The results of the trials follow:

(1) In a 6-week, placebo-controlled trial (n=160) involving titration of RISPERDAL® in doses up to 10 mg/day (BID schedule), RISPERDAL® was generally superior to placebo on the BPRS total score, on the BPRS psychosis cluster, and marginally superior to placebo on the SANS.

(2) In an 8-week, placebo-controlled trial (n=513) involving 4 fixed doses of RISPERDAL® (2, 6, 10, and 16 mg/day, on a BID schedule), all 4 RISPERDAL® groups were generally superior to placebo on the BPRS total score, BPRS psychosis cluster, and CGI severity score; the 3 highest RISPERDAL® dose groups were generally superior to placebo on the PANSS negative subscale. The most consistently positive responses on all measures were seen for the 8 mg dose group, and there was no suggestion of increased benefit from larger doses.

(3) In an 8-week, dose comparison trial (n=1356) involving 5 fixed doses of RISPERDAL® (1, 4, 8, 12, and 16 mg/day, on a BID schedule), the four highest RISPERDAL® dose groups were generally superior to the 1 mg RISPERDAL® dose group on BPRS total score, BPRS psychosis cluster, and CGI severity score. None of the dose groups were superior to the 1 mg group on the PANSS negative subscale. The most consistently positive responses were seen for the 4 mg dose group.

(4) In a 4-week, placebo-controlled dose comparison trial (n=246) involving 2 fixed doses of RISPERDAL® (4 and 8 mg/day on a QD schedule), both RISPERDAL® dose groups were generally superior to placebo on several PANSS measures, including a response measure (>20% reduction in PANSS total score), PANSS total score, and the BPRS psychosis cluster (derived from PANSS). The results were generally stronger for the 8 mg than for the 4 mg dose group.

Long-Term Efficacy

In a longer-term trial, 365 adult outpatients predominantly meeting DSM-IV criteria for schizophrenia and who had been clinically stable for at least 4 weeks on an antipsychotic medication were randomized to RISPERDAL® (2-8 mg/day) or to an active comparator, for 1 to 2 years of observation for relapse. Patients receiving RISPERDAL® experienced a significantly longer time to relapse over this time period compared to those receiving the active comparator.

INDICATIONS AND USAGE

RISPERDAL® (risperidone) is indicated for the treatment of schizophrenia.

The efficacy of RISPERDAL® in schizophrenia was established in short-term (6 to 8 weeks) controlled trials of schizophrenic inpatients (see CLINICAL PHARMACOLOGY).

The efficacy of RISPERDAL® in delaying relapse was demonstrated in schizophrenic patients who had been clinically stable for at least 4 weeks before initiation of treatment with RISPERDAL® or an active comparator and who were then observed for relapse during a period of 1 to 2 years (see Clinical Trials, under CLINICAL PHARMACOLOGY). Nevertheless, the physician who elects to use RISPERDAL® for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient (see DOSAGE AND ADMINISTRATION).

CONTRAINDICATIONS

RISPERDAL® (risperidone) is contraindicated in patients with a known hypersensitivity to the product.

WARNINGS

Neuroleptic Malignant Syndrome (NMS)

A potentially fatal, syndrome sometimes referred to as Neuroleptic Malignant Syndrome (NMS), has been reported in association with antipsychotic drugs. Clinical manifestations of NMS include hyperreflexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse, blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases in which the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system pathology.

The management of NMS should include: (1) immediate discontinuation of antipsychotic drug and other agents not essential to concurrent therapy; (2) intensive symptomatic treatment and medical monitoring; and (3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reprecipitation of drug therapy should be carefully considered. The patient should be carefully monitored, since re-emergence of NMS has been reported.

Tardive Dyskinesia

A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

The risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

Given these considerations, RISPERDAL® (risperidone) should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that (1) is known to respond to antipsychotic drugs, and (2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient treated on RISPERDAL®, drug discontinuation should be considered. However, some patients may require treatment with RISPERDAL® despite the presence of the syndrome.

Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients With Dementia

Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, were reported in patients (mean age 85 years; range 73-97) in trials of risperidone in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of cerebrovascular adverse events in patients treated with risperidone compared to patients treated with placebo. RISPERDAL® is not approved for the treatment of patients with dementia-related psychosis.

Hyperglycemia and Diabetes Mellitus

Hyperglycemia, in some cases extreme and associated with ketoadidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including RISPERDAL®. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of

an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

PRECAUTIONS

General

Orthostatic Hypotension

RISPERDAL® (risperidone) may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, especially during the initial dose-titration period, probably reflecting its alpha-adrenergic antagonistic properties. Syncope was reported in 0.2% (3/2007) of RISPERDAL®-treated patients in Phase 3 studies. The risk of orthostatic hypotension and syncope may be minimized by limiting the initial dose to 2 mg total (either QD or 1 mg BID) in normal adults and 0.5 mg BID in the elderly and patients with renal or hepatic impairment (see DOSAGE AND ADMINISTRATION). Monitoring of orthostatic vital signs should be considered in patients for whom this is of concern. A dose reduction should be considered if hypotension occurs. RISPERDAL® should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemia, heart failure, or conduction abnormalities), cerebrovascular disease, and conditions which would predispose patients to hypotension, e.g., dehydration and hypovolemia. Clinically significant hypotension has been observed with concomitant use of RISPERDAL® and antihypertensive medication.

Seizures

During premarketing testing, seizures occurred in 0.3% (9/2607) of RISPERDAL®-treated patients, two in association with hypotension. RISPERDAL® should be used cautiously in patients with a history of seizures.

Dysphagia

Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in patients with advanced Alzheimer's dementia. RISPERDAL® and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

Hyperprolactinemia

As with other drugs that antagonize dopamine D₂ receptors, risperidone elevates prolactin levels and the elevation persists during chronic therapy. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported with prolactin-elevating compounds, the clinical significance of elevated serum prolactin levels is unknown for most patients. As is common with compounds which increase prolactin release, an increase in pituitary gland, mammary gland, and pancreatic islet cell hyperplasia and/or neoplasia has been observed in the risperidone carcinogenicity studies conducted in mice and rats (see CARCINOGENESIS). However, neither clinical studies nor epidemiologic studies conducted to date have shown an association between chronic administration of this class of drugs and tumorigenesis in humans; the available evidence is considered too limited to be conclusive at this time.

Potential for Cognitive and Motor Impairment

Somnolence was a commonly reported adverse event associated with RISPERDAL® treatment, especially when ascertained by direct questioning of patients. This adverse event is dose-related, and in a study utilizing a checklist to detect adverse events, 41% of the high dose patients (RISPERDAL® 16 mg/day) reported somnolence compared to 16% of placebo patients. Direct questioning is more sensitive for detecting adverse events than spontaneous reporting, by which 8% of RISPERDAL® 16 mg/day patients and 1% of placebo patients reported somnolence as an adverse event. Since RISPERDAL® has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that RISPERDAL® therapy does not affect them adversely.

Priapism

Rare cases of priapism have been reported. While the relationship of the events to RISPERDAL® use has not been established, other drugs with alpha-adrenergic blocking effects have been reported to induce priapism, and it is possible that RISPERDAL® may share this capacity. Severe priapism may require surgical intervention.

Thrombotic Thrombocytopenic Purpura (TTP)

A single case of TTP was reported in a 22-year-old female patient receiving RISPERDAL® in a large, open premarketing experience (approximately 1300 patients). She experienced jaundice, fever, and bruising, but eventually recovered after receiving plasmapheresis. The relationship to RISPERDAL® therapy is unknown.

Antiemetic Effect

Risperidone has an antiemetic effect in animals; this effect may also occur in humans, and may mask signs and symptoms of overdose with certain drugs or of conditions such as intestinal obstruction, Reye's syndrome, and brain tumor.

Body Temperature Regulation

Disruption of body temperature regulation has been attributed to antipsychotic agents. Both hyperthermia and hypothermia have been reported in association with oral RISPERDAL® use. Caution is advised when prescribing for patients who will be exposed to temperature extremes.

Suicide

The possibility of a suicide attempt is inherent in schizophrenia, and close supervision of high-risk patients should accompany drug therapy. Prescriptions for RISPERDAL® should be written for the smallest quantity of tablets, consistent with good patient management, in order to reduce the risk of overdose.

Use in Patients With Concomitant Illness

Clinical experience with RISPERDAL® in patients with certain concomitant systemic illnesses is limited. Caution is advisable in using RISPERDAL® in patients with diseases or conditions that could affect metabolism or hemodynamic responses.

RISPERDAL® has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were excluded from clinical studies during the product's premarketing testing.

Increased plasma concentrations of risperidone and 9-hydroxyrisperidone occur in patients with severe renal impairment (creatinine clearance <30 mL/min/1.73 m²), and an increase in the free fraction of risperidone is seen in patients with severe hepatic impairment. A lower starting dose should be used in such patients (see DOSAGE AND ADMINISTRATION).

Information for Patients

Physicians are advised to discuss the following issues with patients for whom they prescribe RISPERDAL®:

Orthostatic Hypotension

Patients should be advised of the risk of orthostatic hypotension, especially during the period of initial dose titration.

Interference With Cognitive and Motor Performance

Since RISPERDAL® has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that RISPERDAL® therapy does not affect them adversely.

Pregnancy

Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy.

Nursing

Patients should be advised not to breast-feed an infant if they are taking RISPERDAL®.

Concomitant Medication

Patients should be advised to inform their physicians if they are taking, or plan to take, any prescription or over-the-counter drugs, since there is a potential for interactions.

Alcohol

Patients should be advised to avoid alcohol while taking RISPERDAL®.

Phenylethanolamines

Phenylethanolamine is a component of aspartame. Each 2 mg RISPERDAL® M-TAB™ Orally Disintegrating Tablet contains 0.58 mg phenylethanolamine; each 1 mg RISPERDAL® M-TAB™ Orally Disintegrating Tablet contains

0.28 mg phenylethanolamine; and each 0.5 mg RISPERDAL® M-TAB™ Orally Disintegrating Tablet contains 0.14 mg phenylethanolamine.

Laboratory Tests

No specific laboratory tests are recommended.

Drug Interactions

The interactions of RISPERDAL® and other drugs have not been systematically evaluated. Given the primary CNS effects of risperidone, caution should be used when RISPERDAL® is taken in combination with other centrally acting drugs and alcohol. Because of its potential for inducing hypotension, RISPERDAL® may enhance the hypotensive effects of other therapeutic agents with this potential.

RISPERDAL® may antagonize the effects of levodopa and dopamine agonists.

Chronic administration of clozapine with risperidone may decrease the clearance of risperidone.

Carbamazepine and Other Enzyme Inducers

In a drug interaction study in schizophrenic patients, 11 subjects received risperidone (titrated to 6 mg/day for 3 weeks), followed by concurrent administration of carbamazepine for an additional 3 weeks. During co-administration, the plasma concentrations of risperidone and its pharmacologically active metabolite, 9-hydroxyrisperidone, were decreased by about 50%. Plasma concentrations of carbamazepine did not appear to be affected. The dose of risperidone may need to be titrated accordingly for patients receiving carbamazepine, particularly during initiation or discontinuation of carbamazepine therapy. Co-administration of other known enzyme inducers (e.g., phenytoin, rifampin, and phenobarbital) with risperidone may cause similar decreases in the combined plasma concentrations of risperidone and 9-hydroxyrisperidone, which could lead to decreased efficacy of risperidone treatment.

Fluoxetine

Fluoxetine (20 mg QD) has been shown to increase the plasma concentration of risperidone 2.5-2.8 fold, while the plasma concentration of 9-hydroxyrisperidone was not affected. When concomitant fluoxetine is initiated or discontinued, the physician should re-evaluate the dosing of RISPERDAL®. The effects of discontinuation of concomitant fluoxetine therapy on the pharmacokinetics of risperidone and 9-hydroxyrisperidone have not been studied.

Lithium

Repeated oral doses of risperidone (3 mg BID) did not affect the exposure (AUC) or peak plasma concentrations (C_{max}) of lithium (n=13).

Valproate

Repeated oral doses of risperidone (4 mg QD) did not affect the pre-dose or average plasma concentrations (AUC) of valproate (1000 mg/day in three divided doses) compared to placebo (n=21). However, there was a 20% increase in valproate peak plasma concentration (C_{max}) after concomitant administration of risperidone.

Drugs That Inhibit CYP 2D6 and Other CYP Isozymes

Risperidone is metabolized to 9-hydroxyrisperidone by CYP 2D6, an enzyme that is polymorphic in the population and that can be inhibited by a variety of psychotropic and other drugs (see CLINICAL PHARMACOLOGY, Drug Interactions) that reduce the metabolism of risperidone to 9-hydroxyrisperidone would increase the plasma concentrations of risperidone and lower the concentrations of 9-hydroxyrisperidone. Analysis of clinical studies involving a modest number of poor metabolizers (n=70) does not suggest that poor and extensive metabolizers have different rates of adverse effects. No comparison of effectiveness in the two groups has been made.

In vitro studies showed that drugs metabolized by other CYP isozymes, including 1A1, 1A2, 2C8, MP, and 3A4, are only weak inhibitors of risperidone metabolism.

Drugs Metabolized by CYP 2D6

In vitro studies indicate that risperidone is a relatively weak inhibitor of CYP 2D6. Therefore, RISPERDAL® is not expected to substantially inhibit the clearance of drugs that are metabolized by this enzymatic pathway. However, clinical data to confirm this expectation are not available.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis
Carcinogenicity studies were conducted in Swiss albino mice and Wistar rats. Risperidone was administered in the diet at doses of 0.63, 2.5, and 10 mg/kg for 18 months to mice and for 25 months to rats. These doses are equivalent to 0.4, 0.4, and 37.5 times the maximum recommended human dose (MRHD) (16 mg/day) on a mg/kg basis or 0.2, 0.75, and 3 times the MRHD (mice) or 0.4, 1.5, and 6 times the MRHD (rats) on a mg/m² basis. A maximum tolerated dose was not achieved in male mice. There were statistically significant increases in pituitary gland adenomas, endocrine pancreas adenomas, and mammary gland adenocarcinomas. The following table summarizes the multiples of the human dose on a mg/m² (mg/kg) basis at which these tumors occurred.

Tumor Type	Species	Sex	Multiples of Maximum Human Dose on a mg/m ² (mg/kg) Basis	
			Lowest Effect Level	Significant No. Effect Level
Pituitary adenomas	mouse	female	0.75 (9.4)	0.2 (2.4)
Endocrine pancreas adenomas	rat	male	1.5 (9.4)	0.4 (2.4)
Mammary gland adenocarcinomas	mouse	female	0.2 (2.4)	0.2 (2.4)
	rat	female	0.4 (2.4)	0.4 (2.4)
	rat	male	6 (37.5)	1.5 (9.4)
Mammary gland neoplasms, Total	rat	male	1.5 (9.4)	1.5 (9.4)

Antipsychotic drugs have been shown to chronically elevate prolactin levels in rodents. Serum prolactin levels were not measured during the risperidone carcinogenicity studies; however, assessments during subsequent toxicity studies showed that risperidone elevated serum prolactin levels 5 to 6 fold in mice and rats at the same doses used in the carcinogenicity studies. An increase in mammary, pituitary, and endocrine pancreas neoplasms has been found in rodents after chronic administration of other antipsychotic drugs and is considered to be prolactin-mediated. The relevance for human risk of the findings of prolactin-mediated endocrine tumors in rodents is unknown (see Hyperprolactinemia under PRECAUTIONS, GENERAL).

Mutagenesis

No evidence of mutagenic potential for risperidone was found in the Ames reverse mutation test, mouse lymphoma assay, *in vitro* rat hepatocyte DNA-repair assay, *in vivo* micronucleus test in mice, the sex-linked recessive lethal test in *Drosophila*, or the chromosomal aberration test in human lymphocytes or Chinese hamster cells.

Impairment of Fertility

Risperidone (0.18 to 5 mg/kg) was shown to impair mating, but not fertility, in Wistar rats in three reproductive studies (two Segment I and a multigenerational study) at doses 0.1 to 3 times the maximum recommended human dose (MRHD) on a mg/m² basis. The effect appeared to be in females, since impaired mating behavior was not noted in the Segment I study in which males only were treated. In a subchronic study in Beagle dogs in which risperidone was administered at doses of 0.31 to 6 mg/kg, sperm motility and concentration were decreased at doses 0.6 to 10 times the MRHD on a mg/m² basis. Dose-related decreases were also noted in serum testosterone at the same doses. Serum testosterone and sperm parameters partially recovered, but remained decreased after treatment was discontinued. No no-effect doses were noted in either rat or dog.

Pregnancy

Pregnancy Category C

The teratogenic potential of risperidone was studied in three Segment II studies in Sprague-Dawley and Wistar rats (0.63-10 mg/kg or 0.4 to 6 times the maximum recommended human dose (MRHD) on a mg/m² basis) and in one Segment II study in New Zealand rabbits (0.31-5 mg/kg or 0.4 to 6 times the MRHD on a mg/m² basis). The incidence of malformations was not increased compared to control in offspring of rats or rabbits given 0.4 to 6 times the MRHD on a mg/m² basis. In three reproductive studies in rats (two Segment III and a multigenerational study), there was an increase in pup deaths during the first 4 days of lactation at doses of 0.18-5 mg/kg or 0.1 to 3 times the MRHD on a mg/m² basis. It is not known whether these deaths were due to a direct effect on the fetuses or pups or to effects on the dams.

There was no no-effect dose for increased rat pup mortality. In one Segment III study, there was an increase in stillborn rat pups at a dose of 2.5 mg/kg or 1.5 times the MRHD on a mg/m² basis. In a cross-fostering study in Wistar rats, toxic effects on the fetus or pups, as evidenced by a decrease in the number of live pups and an increase in the number of dead pups at birth (Day 0), and a decrease in birth weight in pups of drug-treated dams were observed. In addition, there was an increase in deaths by Day 1 among pups of drug-treated dams.

regardless of whether or not the pups were cross-fostered. Risperidone also appeared to impair maternal behavior in that pup body weight gain and survival from Day 1 to 4 of lactation were reduced in pups born to control but reared by drug-treated dams. These effects were all noted at the one dose of risperidone tested, i.e., 5 mg/kg or 3 times the MARD on a mg/kg basis.

Placental transfer of risperidone occurs in all pups. There are no adequate and well-controlled studies in pregnant women. However, there was one report of a case of arrest of the corpus callosum in an infant exposed to risperidone in utero. The causal relationship to RISPERDAL® therapy is unknown.

RISPERDAL® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery
The effect of RISPERDAL® on labor and delivery in humans is unknown.

Nursing Mothers

In animal studies, risperidone and 9-hydroxyrisperidone are excreted in milk. Risperidone and 9-hydroxyrisperidone are also excreted in human breast milk. Therefore, women receiving risperidone should not breast-feed.

Pediatric Use

Safety and effectiveness in children have not been established.

Geriatric Use

Clinical studies of RISPERDAL® did not include sufficient numbers of patients aged 65 and over to determine whether or not they respond differently than younger patients. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, a lower starting dose is recommended for an elderly patient, reflecting a decreased pharmacokinetic clearance in the elderly, as well as a greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy (see CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION). While elderly patients exhibit a greater tendency to orthostatic hypotension, its risk in the elderly may be minimized by limiting the initial dose to 0.5 mg BID followed by careful titration (see PRECAUTIONS). Monitoring of orthostatic vital signs should be considered in patients for whom this is of concern.

This drug is substantially excreted by the kidneys, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see DOSAGE AND ADMINISTRATION).

ADVERSE REACTIONS

Associated With Discontinuation of Treatment

Approximately 9% (244/2607) of RISPERDAL® (risperidone)-treated patients in Phase 2-3 studies discontinued treatment due to an adverse event, compared with about 7% on placebo and 10% on active control drugs. The more common events (≥ 0.3%) associated with discontinuation and considered to be possibly or probably drug-related included:

Adverse Event	RISPERDAL®	Placebo
Extrapyramidal symptoms	2.1%	0%
Dizziness	0.7%	0%
Hyperkinesia	0.6%	0%
Somnolence	0.5%	0%
Nausea	0.3%	0%

Suicide attempt was associated with discontinuation in 1.2% of RISPERDAL®-treated patients compared to 0.8% of placebo patients, but, given the almost 40-fold greater exposure time in RISPERDAL® compared to placebo patients, it is unlikely that suicide attempt is a RISPERDAL®-related adverse event (see PRECAUTIONS). Discontinuation for extrapyramidal symptoms was 0% in placebo patients, but 3.5% in active-control patients in the Phase 2-3 trials.

Incidence in Controlled Trials

Commonly Observed Adverse Events in Controlled Clinical Trials

In two 6 to 8-week placebo-controlled trials, spontaneously-reported, treatment-emergent adverse events with an incidence of 5% or greater in at least one of the RISPERDAL® groups and at least twice that of placebo were: anxiety, somnolence, extrapyramidal symptoms, dizziness, constipation, nausea, dyspepsia, rhinitis, rash, and tachycardia.

Adverse events were also elicited in one of these two trials (i.e., in the fixed-dose trial comparing RISPERDAL® at doses of 2, 6, 10, and 16 mg/day with placebo) utilizing a checklist for detecting adverse events, a method that is more sensitive than spontaneous reporting. By this method, the following additional common and drug-related adverse events occurred at an incidence of at least 5% and twice the rate of placebo: increased dream activity, increased duration of sleep, accommodation disturbances, reduced salivation, micturition disturbances, diarrhea, weight gain, menorrhagia, diminished sexual desire, erectile dysfunction, ejaculatory dysfunction, and organic dysfunction.

Adverse Events Occurring at an Incidence of 1% or More Among RISPERDAL®-Treated Patients

The table that follows enumerates adverse events that occurred at an incidence of 1% or more, and were at least as frequent among RISPERDAL®-treated patients treated at doses of ≤ 10 mg/day than among placebo-treated patients in the pooled results of two 6 to 8-week controlled trials. Patients received RISPERDAL® doses of 2, 6, 10, or 16 mg/day in the dose comparison trial, or up to a maximum dose of 10 mg/day in the titration study. This table shows the percentage of patients in each dose group (≤ 10 mg/day or 16 mg/day) who spontaneously reported at least one episode of an event at some time during their treatment. Patients given doses of 2, 6, or 10 mg did not differ materially in these rates. Reported adverse events were classified using the World Health Organization preferred terms.

The prescriber should be aware that these figures cannot be used to predict the incidence of side effects in the course of usual medical practice where patient characteristics and other factors differ from those which prevailed in the clinical trial. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses and investigators. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and non-drug factors to the side effect incidence rate in the population studied.

Table 1
Incidence of Treatment-Emergent Adverse Events
in 6 to 8-Week Controlled Clinical Trials¹

Body System/ Preferred Term	RISPERDAL®		Placebo (N=142)
	≤10 mg/day (N=324)	16 mg/day (N=77)	
Psychiatric			
Insomnia	26%	23%	19%
Agitation	22%	26%	20%
Anxiety	12%	20%	9%
Somnolence	3%	8%	1%
Aggressive reaction	1%	3%	1%
Central & peripheral nervous system			
Extrapyramidal symptoms ²	17%	34%	16%
Dizziness	14%	12%	12%
Drowsiness	4%	7%	1%
Gastrointestinal			
Constipation	7%	13%	3%
Nausea	6%	4%	3%
Dyspepsia	5%	10%	4%
Vomiting	5%	7%	4%
Abdominal pain	4%	1%	0%
Saliva increased	2%	0%	1%
Toothache	2%	0%	0%
Respiratory system			
Rhinitis	10%	8%	4%
Coughing	3%	3%	1%
Strusitis	2%	1%	1%
Pharyngitis	2%	3%	0%
Dyspnea	1%	0%	0%
Body as a whole - general			
Back pain	2%	0%	1%
Chest pain	2%	3%	1%
Fever	2%	3%	0%
Dermatological			
Rash	2%	5%	1%
Dry skin	2%	4%	0%
Seborrhea	1%	0%	0%

Table 1 (continued)
Incidence of Treatment-Emergent Adverse Events
in 6 to 8-Week Controlled Clinical Trials¹

Body System/ Preferred Term	RISPERDAL®		Placebo (N=142)
	≤10 mg/day (N=324)	16 mg/day (N=77)	
Infections			
Upper respiratory	3%	3%	1%
Visual			
Abnormal vision	2%	1%	1%
Musculo-Skeletal			
Arthralgia	2%	3%	0%
Cardiovascular			
Tachycardia	3%	5%	0%

¹ Events reported by at least 1% of patients treated with RISPERDAL® ≤ 10 mg/day are included, and are rounded to the nearest %. Comparative rates for RISPERDAL® 16 mg/day and placebo are provided as well. Events for which the RISPERDAL® incidence (in both dose groups) was equal to or less than placebo are not listed in the table, but included the following: nervousness, injury, and fungal infection.

² Includes tremor, dystonia, hypokinesia, hyperkinesia, oculogyric crisis, ataxia, abnormal gait, involuntary muscle contractions, hyporeflexia, akathisia, and extrapyramidal disorders. Although the incidence of extrapyramidal symptoms does not appear to differ for the 10 mg/day group and placebo, the data for individual dose groups in fixed dose trials do suggest a dose-response relationship (see DOSE DEPENDENCY OF ADVERSE EVENTS).

Dose Dependency of Adverse Events

Extrapyramidal Symptoms

Data from two fixed-dose trials provided evidence of dose-relatedness for extrapyramidal symptoms associated with risperidone treatment.

Two methods were used to measure extrapyramidal symptoms (EPS) in an 8-week trial comparing 4 fixed doses of risperidone (2, 6, 10, and 16 mg/day), including (1) a parkinsonism score (mean change from baseline) from the Extrapyramidal Symptom Rating Scale, and (2) incidence of spontaneous complaints of EPS:

Dose Groups	Placebo	Ris 2	Ris 6	Ris 10	Ris 16
Parkinsonism	1.2	0.9	1.8	2.4	2.6
EPS incidence	13%	13%	16%	20%	31%

Similar methods were used to measure extrapyramidal symptoms (EPS) in an 8-week trial comparing 5 fixed doses of risperidone (1, 4, 8, 12, and 16 mg/day):

Dose Groups	Ris 1	Ris 4	Ris 8	Ris 12	Ris 16
Parkinsonism	0.6	1.7	2.4	2.9	4.1
EPS incidence	7%	12%	18%	18%	21%

Other Adverse Events

Adverse event data elicited by a checklist for side effects from a large study comparing 5 fixed doses of RISPERDAL® (1, 4, 8, 12, and 16 mg/day) were explored for dose-relatedness of adverse events. A Cochran-Armitage Test for trend in these data revealed a positive trend (p<0.05) for the following adverse events: sleepiness, increased duration of sleep, accommodation disturbances, orthostatic dizziness, palpitations, weight gain, erectile dysfunction, ejaculatory dysfunction, organic dysfunction, asthenia/fatigue/increased fatigue, and increased pigmentation.

Vital Sign Changes

RISPERDAL® is associated with orthostatic hypotension and tachycardia (see PRECAUTIONS).

Weight Changes

The proportions of RISPERDAL® and placebo-treated patients meeting a weight gain criterion of ≥ 7% of body weight were compared in a pool of 6 to 8-week, placebo-controlled trials, revealing a statistically significant greater incidence of weight gain for RISPERDAL® (18%) compared to placebo (9%).

Laboratory Changes

A between-group comparison for 6 to 8-week placebo-controlled trials revealed no statistically significant RISPERDAL®/placebo differences in the proportions of patients experiencing potentially important changes in routine serum chemistry, hematology, or urinalysis parameters. Similarly, there were no RISPERDAL®/placebo differences in the incidence of discontinuations for changes in serum chemistry, hematology, or urinalysis. However, RISPERDAL® administration was associated with increases in serum prolactin (see PRECAUTIONS).

ECG Changes

Between-group comparisons for pooled placebo-controlled trials revealed no statistically significant differences between risperidone and placebo in mean changes from baseline in ECG parameters, including QT, QTc, and PR intervals, and heart rate. When all RISPERDAL® doses were pooled from randomized controlled trials (locality), there was a mean increase in heart rate of 1 beat per minute compared to no change for placebo patients. In short-term schizophrenia trials, higher doses of risperidone (8-16 mg/day) were associated with a higher mean increase in heart rate compared to placebo (4-6 beats per minute).

Other Events Observed During the Premarketing Evaluation of RISPERDAL®

During its premarketing assessment, multiple doses of RISPERDAL® (risperidone) were administered to 2607 patients in Phase 2 and 3 studies. The conditions and duration of exposure to RISPERDAL® varied greatly and included (in overlapping categories) open-label and double-blind studies, uncontrolled (open-label) studies, inpatient and outpatient studies, fixed-dose and titration studies, and short-term or long-term exposure. In most studies, untoward events associated with this exposure were obtained by spontaneous report and recorded by clinical investigators using terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of untoward events into a smaller number of standardized event categories. In two large studies, adverse events were also elicited utilizing the UGJ (direct questioning) side effect rating scale, and these events were not further categorized using standard terminology. (Note: These events are marked with an asterisk in the listings that follow.)

In the listings that follow, spontaneously reported adverse events were classified using World Health Organization (WHO) preferred terms. The frequencies presented, therefore, represent the proportion of the 2607 patients exposed to multiple doses of RISPERDAL® who experienced an event of the type cited on at least one occasion while receiving RISPERDAL®. All reported events are included, except those already listed in Table 1, those events for which a drug cause was remote, and those event terms which were so general as to be uninformative. It is important to emphasize that, although the events reported occurred during treatment with RISPERDAL®, they were not necessarily caused by it.

Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring in at least 1/100 patients (only those not already listed in the tabulated results from placebo-controlled trials appear in this listing); infrequent adverse events are those occurring in 1/100 to 1/1000 patients; rare events are those occurring in fewer than 1/1000 patients.

Psychiatric Disorders

Frequent: increased dream activity*, diminished sexual desire*, nervousness. **Infrequent:** impaired concentration, depression, apathy, catatonic reaction, euphoria, increased libido, amnesia. **Rare:** emotional lability, nightmares, delirium, withdrawal syndrome, yawning.

Central and Peripheral Nervous System Disorders

Frequent: increased sleep duration*. **Infrequent:** dysarthria, vertigo, stupor, paresthesia, confusion. **Rare:** aphasia, choreiform syndrome, hyposthesia, tongue paralysis, leg cramps, torticollis, hypotonia, coma, migraine, hyperreflexia, choreoathetosis.

Gastrointestinal Disorders

Frequent: anorexia, reduced salivation*. **Infrequent:** flatulence, diarrhea, increased appetite, stomatitis, melena, dysphagia, hemorrhoids, gastritis. **Rare:** fecal incontinence, eructation, gastroesophageal reflux, gastroenteritis, esophagitis, tongue discoloration, cholelithiasis, tongue edema, diverticulitis, gingivitis, discolored feces, GI hemorrhage, hematemesis.

Body as a Whole/General Disorders

Frequent: fatigue. **Infrequent:** edema, rigors, malaise, influenza-like symptoms. **Rare:** pallor, enlarged abdomen, anergic reaction, asthenia, sarcoidosis, flushing.

Respiratory System Disorders

Infrequent: hyperventilation, bronchospasm, pneumonia, stridor. **Rare:** asthma, increased sputum, aspiration.

Skin and Appendage Disorders

Frequent: increased pigmentation*, photosensitivity*, infrequent: increased sweating, acne, decreased sweating, alopecia, hyperkeratosis, pruritus, skin exfoliation. *Rare:* bullous eruption, skin ulceration, aggravated psoriasis, furunculosis, verruca, dermatitis herpetiformis, hypertrichosis, genital pruritus, urticaria.

Cardiovascular Disorders

Infrequent: palpitation, hypertension, hypotension, AV block, myocardial infarction. *Rare:* ventricular tachycardia, angina pectoris, premature aortic contractions, T wave inversions, ventricular extrasystoles, ST depression, myocarditis.

Vision Disorders

Infrequent: abnormal accommodation, xerophthalmia. *Rare:* diplopia, eye pain, blepharitis, photopsia, photophobia, abnormal lacrimation.

Metabolic and Nutritional Disorders

Infrequent: hypotension, weight increase, creatine phosphokinase increase, thirst, weight decrease, diabetes mellitus. *Rare:* decreased serum iron, cachexia, dehydration, hypokalemia, hypoproteinemia, hyperphosphatemia, hyperglycemia, hyperuricemia, hypoglycemia.

Urinary System Disorders

Frequent: polyuria/polydipsia*. Infrequent: urinary incontinence, hematuria, dysuria. *Rare:* urinary retention, cystitis, renal insufficiency.

Musculo-Skeletal System Disorders

Infrequent: myalgia. *Rare:* arthralgia, synostosis, bursitis, arthritis, skeletal pain.

Reproductive Disorders, Female

Frequent: menorrhagia*, orgasmic dysfunction*, dry vagina*. Infrequent: nonpuerperal lactation, amenorrhea, female breast pain, leukorrhea, mastitis, dysmenorrhea, female genital pain, intermenstrual bleeding, vaginal hemorrhage.

Liver and Biliary System Disorders

Infrequent: increased SGOT, increased SGPT. *Rare:* hepatic failure, cholestatic hepatitis, cholecystitis, cholelithiasis, hepatitis, hepatocellular damage.

Platelet, Bleeding, and Clotting Disorders

Infrequent: epistaxis, purpura. *Rare:* hemorrhage, superficial phlebitis, thrombophlebitis, thrombocytopenia.

Hearing and Vestibular Disorders

Rare: tinnitus, hyperacusis, decreased hearing.

Red Blood Cell Disorders

Infrequent: anemia, hypochromic anemia. *Rare:* normocytic anemia.

Reproductive Disorders, Male

Frequent: erectile dysfunction*. Infrequent: ejaculation failure.

White Cell and Resistance Disorders

Rare: leukocytosis, lymphadenopathy, leukopenia, Pelger-Huet anomaly.

Endocrine Disorders

Rare: gynecomastia, male breast pain, antidiuretic hormone disorder.

Special Senses

Rare: bitter taste.

* Incidence based on elicited reports.

Postintroduction Reports

Adverse events reported since market introduction which were temporally (but not necessarily causally) related to RISPERDAL* therapy, include the following: anaphylactic reaction, angioedema, apnea, atrial fibrillation, cerebrovascular disorder, including cerebrovascular accident, hyperglycemia, diabetes mellitus aggravated, including diabetic ketoacidosis, intestinal obstruction, jaundice, mania, pancreatitis, Parkinson's disease aggravated, pulmonary embolism. There have been rare reports of sudden death and/or cardiopulmonary arrest in patients receiving RISPERDAL*. A causal relationship with RISPERDAL* has not been established. It is important to note that sudden and unexpected death may occur in psychotic patients whether they remain untreated or whether they are treated with other antipsychotic drugs.

DRUG ABUSE AND DEPENDENCE

Controlled Substance Class

RISPERDAL* (risperidone) is not a controlled substance.

Physical and Psychologic Dependence

RISPERDAL* has not been systematically studied in animals or humans for its potential for abuse, tolerance, or physical dependence. While the clinical trials did not reveal any tendency for drug-seeking behavior, these observations were not systematic and it is not possible to predict on the basis of this limited experience the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed. Consequently, patients should be evaluated carefully for a history of drug abuse, and such patients should be observed closely for signs of RISPERDAL* misuse or abuse (e.g., development of tolerance, increases in dose, drug-seeking behavior).

OVERDOSAGE

Human Experience

Premarketing experience included eight reports of acute RISPERDAL* (risperidone) overdosage with estimated doses ranging from 20 to 300 mg and no fatalities. In general, reported signs and symptoms were those resulting from an exaggeration of the drug's known pharmacological effects, i.e., drowsiness and sedation, tachycardia and hypotension, and extrapyramidal symptoms. One case, involving an estimated overdose of 240 mg, was associated with hyponatremia, hypokalemia, prolonged QT, and widened QRS. Another case, involving an estimated overdose of 36 mg, was associated with a seizure.

Postmarketing experience includes reports of acute RISPERDAL* overdosage, with estimated doses of up to 360 mg. In general, the most frequently reported signs and symptoms are those resulting from an exaggeration of the drug's known pharmacological effects, i.e., drowsiness, sedation, tachycardia, hypotension, and extrapyramidal symptoms. Other adverse events reported since market introduction which were temporally (but not necessarily causally) related to RISPERDAL* overdosage, include torsade de pointes, prolonged QT interval, convulsions, cardiopulmonary arrest, and rare fatality associated with multiple drug overdosage.

Management of Overdosage

In case of acute overdosage, establish and maintain an airway and ensure adequate oxygenation and ventilation. Gastric lavage (after intubation, if patient is unconscious) and administration of activated charcoal together with a laxative should be considered. Because of the rapid deconjugation of risperidone orally disintegrating tablets, pill fragments may not appear in gastric contents obtained with lavage.

The possibility of obtundation, seizures, or dystonic reaction of the head and neck following overdosage may create a risk of aspiration with induced emesis. Cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias. If antiarrhythmic therapy is administered, disopyramide, procainamide, and quinidine carry a theoretical hazard of QT-prolonging effects that might be additive to those of risperidone. Similarly, it is reasonable to expect that the alpha-blocking properties of buprenorphine might be additive to those of risperidone, resulting in problematic hypotension.

There is no specific antidote to RISPERDAL*. Therefore, appropriate supportive measures should be instituted. The possibility of multiple drug involvement should be considered. Hypotension and circulatory collapse should be treated with appropriate measures, such as intravenous fluids and/or sympathomimetic agents (epinephrine and dopamine should not be used, since beta stimulation may worsen hypotension in the setting of risperidone-induced alpha blockade). In cases of severe extrapyramidal symptoms, anticholinergic medication should be administered. Close medical supervision and monitoring should continue until the patient recovers.

DOSEAGE AND ADMINISTRATION

Usual Initial Dose

RISPERDAL* (risperidone) can be administered on either a BID or a QD schedule. In early clinical trials, RISPERDAL* was generally administered at 1 mg BID initially, with increases in increments of 1 mg BID on the second and third day, as tolerated, to a target dose of 3 mg BID by the third day. Subsequent controlled trials have indicated that total daily risperidone doses of up to 8 mg on a QD regimen are also safe and effective. However, regardless of which regimen is employed, in some patients a slower titration may be medically appropriate. Further dosage adjustments, if indicated, should generally occur at intervals of not less than 1 week, since steady state for the active metabolite would not be achieved for approximately 1 week in the typical patient. When dosage adjustments are necessary, small dose increments/decrements of 1-2 mg are recommended.

Efficacy in schizophrenia was demonstrated in a dose range of 4 to 16 mg/day in the clinical trials supporting effectiveness of RISPERDAL*. However, maximal effect was generally seen in a range of 4 to 8 mg/day. Doses above 8 mg/day for BID dosing were not demonstrated to be more efficacious than lower doses, were associated with more extrapyramidal symptoms and other adverse effects, and are not generally recommended. In a single study supporting QD dosing, the efficacy results were generally stronger for 8 mg than for 4 mg. The safety of doses above 16 mg/day has not been evaluated in clinical trials.

Pediatric Use

Safety and effectiveness of RISPERDAL* in pediatric patients have not been established.

Dosage in Special Populations

The recommended initial dose is 0.5 mg BID in patients who are elderly or debilitated, patients with severe renal or hepatic impairment, and patients either predisposed to hypotension or for whom hypotension would pose a risk. Dosage increases in these patients should be in increments of no more than 0.5 mg BID. Increases to dosages above 1.5 mg BID should generally occur at intervals of at least 1 week. In some patients, slower titration may be medically appropriate.

Elderly or debilitated patients, and patients with renal impairment, may have less ability to eliminate RISPERDAL* than normal adults. Patients with impaired hepatic function may have increases in the free fraction of risperidone, possibly resulting in an enhanced effect (see CLINICAL PHARMACOLOGY). Patients with a predisposition to hypotensive reactions or for whom such reactions would pose a particular risk likewise need to be titrated cautiously and carefully monitored (see PRECAUTIONS). If a once-a-day dosing regimen in the elderly or debilitated patient is being considered, it is recommended that the patient be titrated on a twice-a-day regimen for 2-3 days at the target dose. Subsequent switches to a once-a-day dosing regimen can be done thereafter.

Directions for Use of RISPERDAL* M-TAB™ Orally Disintegrating Tablets

RISPERDAL* M-TAB™ Orally Disintegrating Tablets are supplied in blister packs of 4 tablet units each.

Tablet Accessing

Do not open the blister until ready to administer. For single tablet removal, separate one of the four blister units by tearing apart at the perforations. Bend the corner where indicated. Peel back foil to expose the tablet. DO NOT push the tablet through the foil because this could damage the tablet.

Tablet Administration

Using dry hands, remove the tablet from the blister unit and immediately place the entire RISPERDAL* M-TAB™ Orally Disintegrating Tablet on the tongue. The RISPERDAL* M-TAB™ Orally Disintegrating Tablet should be consumed immediately, as the tablet cannot be stored once removed from the blister unit. RISPERDAL* M-TAB™ Orally Disintegrating Tablets disintegrate in the mouth within seconds and can be swallowed subsequently with or without liquid. Patients should not attempt to spit or to chew the tablet.

Maintenance Therapy

While there is no body of evidence available to answer the question of how long the schizophrenic patient treated with RISPERDAL* should remain on it, the effectiveness of RISPERDAL* 2 mg/day to 4 mg/day at delaying relapse was demonstrated in a controlled trial in patients who had been clinically stable for at least 4 weeks and were then followed for a period of 1 to 2 years. In this trial, RISPERDAL* was administered on a QD schedule, at 1 mg QD initially, with increases to 2 mg QD on the second day, and to a target dose of 4 mg QD on the third day (see Clinical Trials, under CLINICAL PHARMACOLOGY). Nevertheless, patients should be periodically reassessed to determine the need for maintenance treatment with an appropriate dose.

Reinitiation of Treatment in Patients Previously Discontinued

Although there are no data to specifically address reinitiation of treatment, it is recommended that when restarting patients who have had an interval off RISPERDAL*, the initial titration schedule should be followed.

Switching From Other Antipsychotics

There are no systematically collected data to specifically address switching schizophrenic patients from other antipsychotics to RISPERDAL*, or concerning concomitant administration with other antipsychotics. While immediate discontinuation of the previous antipsychotic treatment may be acceptable for some schizophrenic patients, more gradual discontinuation may be most appropriate for others. In all cases, the period of overlapping antipsychotic administration should be minimized. When switching schizophrenic patients from depot antipsychotics, it is medically appropriate to initiate RISPERDAL* therapy in place of the next scheduled injection. The need for continuing existing EPS medication should be re-evaluated periodically.

HOW SUPPLIED

RISPERDAL* (risperidone) tablets are imprinted "JANSSEN", and either "Ris" and the strength "0.25", "0.5", "1", or "2" and the strength "1", "2", "3", or "4".

0.25 mg dark yellow tablet bottles of 60 NDC 50458-301-04, bottles of 500 NDC 50458-301-50.

0.5 mg red-brown tablet bottles of 60 NDC 50458-302-06, bottles of 500 NDC 50458-302-50.

1 mg white tablet bottles of 60 NDC 50458-300-06, blister pack of 100 NDC 50458-300-01, bottles of 500 NDC 50458-300-50.

2 mg orange tablet bottles of 60 NDC 50458-320-06, blister pack of 100 NDC 50458-320-01, bottles of 500 NDC 50458-320-50.

3 mg yellow tablet bottles of 60 NDC 50458-330-06, blister pack of 100 NDC 50458-330-01, bottles of 500 NDC 50458-330-50.

4 mg green tablet bottles of 60 NDC 50458-350-06, blister pack of 100 NDC 50458-350-01.

RISPERDAL* (risperidone) 1 mg/mL oral solution (NDC 50458-305-03) is supplied in 30 mL bottles with a calibrated (in milligrams and milliliters) pipette. The minimum calibrated volume is 0.25 mL, while the maximum calibrated volume is 3 mL.

Tests indicate that RISPERDAL* (risperidone) oral solution is compatible in the following beverages: water, coffee, orange juice, and low-fat milk. It is NOT compatible with either cola or tea, however.

RISPERDAL* M-TAB™ (risperidone) Orally Disintegrating Tablets are etched on one side with "RIS", "R2", respectively, and are packaged in blister packs of 4 (2 X 2) tablets.

0.5 mg light coral, round, biconvex tablets: 7 blister packages per box, NDC 50458-305-24, blings 300 of 30 tablets NDC 50458-305-30.

1 mg light coral, square, biconvex tablets: 7 blister packages per box, NDC 50458-315-24, blings 300 of 30 tablets NDC 50458-315-30.

2 mg light coral, round, biconvex tablets: 7 blister packages per box, NDC 50458-325-24, blings 300 of 30 tablets NDC 50458-325-30.

3 mg yellow tablet bottles of 60 NDC 50458-330-06, blister pack of 100 NDC 50458-330-01, bottles of 500 NDC 50458-330-50.

4 mg green tablet bottles of 60 NDC 50458-350-06, blister pack of 100 NDC 50458-350-01.

RISPERDAL* tablets should be stored at controlled room temperature 15°-25°C (59°-77°F) (see USP Controlled Room Temperature).

RISPERDAL* tablets should be stored at controlled room temperature 15°-25°C (59°-77°F) (see USP Controlled Room Temperature).

Keep out of reach of children.

RISPERDAL* 1 mg/mL oral solution should be stored at controlled room temperature 15°-25°C (59°-77°F) (see USP Controlled Room Temperature).

Protect from light and freezing.

Keep out of reach of children.

RISPERDAL* M-TAB™ Orally Disintegrating Tablets should be stored at controlled room temperature 15°-25°C (59°-77°F) (see USP Controlled Room Temperature).

Keep out of reach of children.

7503225

US Patent 4,804,663

Revised October 2003

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RISPERDAL* tablets are manufactured by:

JOLLC, Gurneo, Puerto Rico or

Janssen-Cilag, SpA, Latina, Italy

RISPERDAL* oral solution is manufactured by:

Janssen Pharmaceutica N.V.,

Beerse, Belgium

RISPERDAL* M-TAB™ Orally Disintegrating Tablets are manufactured by:

JOLLC, Gurneo, Puerto Rico

RISPERDAL* tablets, RISPERDAL* M-TAB™ Orally Disintegrating Tablets,

and oral solution are distributed by:

Janssen Pharmaceutica Products, L.P.,

Titusville, NJ 08560

JANSSEN
PHARMACEUTICA
PRODUCTS, L.P.

EXHIBIT 2

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IN THE COURT OF COMMON PLEAS

FOR THE SEVENTH JUDICIAL CIRCUIT

Case No.: 2007-CP-42-1438

VERSUS

DEFENDANTS.

DECEMBER 3, 2010

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- Exhibit 5: Population Estimates from Responses to Deposition Questions
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- Exhibit 7: Antipsychotic Drugs and Alleged Side Effects (Data as of Nov. 10, 2003)
- Exhibit 8: Antipsychotic Drugs and Time to Discontinuation
- Exhibit 9: Antipsychotic Prescriptions by Month
Percent Risperdal Prescriptions by Month

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1. My name is William E. Wecker. I am a statistician and applied mathematician. I received the Bachelor of Science degree (Basic Sciences) from the United States Air Force Academy in 1963. I received both the Master of Science degree (Operations Research, 1970) and Doctor of Philosophy degree (Statistics and Management Science, 1972) from the University of Michigan. I have served on the faculties of the University of Chicago, the University of California, Davis, and Stanford University where I taught statistics and applied mathematics at the graduate level. I have performed research in statistical theory, statistical methods, and applied mathematics since 1972. I am currently President of William E. Wecker Associates, Inc., an applied mathematics consulting firm located in Novato, California. I am a member of the American Statistical Association, the Institute of Mathematical Statistics, and the Society for Risk Analysis. I have served as associate editor of the *Journal of the American Statistical Association* for four years and of the *Journal of Business and Economic Statistics* for eighteen years. These qualifications and a list of my professional publications are shown in my curriculum vitae, which is appended to this report as Exhibit 1.

2. A list of all cases in which I have testified as an expert at trial or by deposition since January 1, 2006, is appended to this report as Exhibit 2. The billing rate for my time working on this matter is \$650 per hour.

3. My report consists of three primary sections that follow this introduction. First, in Section I, I identify and cite some of the primary allegations made by plaintiff of purportedly unlawful conduct by Janssen. Also in Section I, I identify the central questions that plaintiff's allegations raise for my expert analysis in this case and the data sources that are available for statistical analysis and evaluation of plaintiff's allegations. The available data include statistical surveys of South Carolina doctors, patient claims data produced by the

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plaintiff, and peer-reviewed epidemiological and experimental studies. The results of my statistical survey of South Carolina doctors and analysis of patient claims data are presented in Section II. In Section III, I review and analyze the eight peer-reviewed epidemiological studies existing as of November 2003 that compared the risk of diabetes in patients treated with Risperdal to the risk in untreated schizophrenia patients, patients treated with conventional antipsychotics, or patients treated with other second generation antipsychotics. Also in Section III, I discuss the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study.

4. In forming my opinions, I have considered the documents listed on Exhibit 3 and the data and electronic files provided to the plaintiff in conjunction with this report. It is my understanding that plaintiff has thus far provided reports from only two of the three experts it intends to present at trial in this case: Dr. Laura Plunkett and Dr. William Wirshing. I reserve the right to conduct further analysis of plaintiff's allegations and the work of plaintiff's experts, and further reserve the right to review and offer opinions on additional material as it becomes available.

5. I am providing electronic files that document my work and are a part of this report.

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**I. Plaintiff's Allegations and Available Data Sources
for Analysis of Plaintiff's Allegations**

6. In plaintiff's Second Amended Complaint ("2d Am. Compl."), plaintiff alleges that Janssen made misrepresentations about Risperdal's safety and effectiveness and marketed Risperdal for off-label uses. In particular, plaintiff alleges:

a. Defendants made "false and misleading misrepresentations of fact regarding Risperdal's risk profile, including but not limited to misrepresenting the likelihood and severity of the side effects associated with Risperdal, including diabetes, stroke, high blood pressure, weight gain, and other serious and potentially life-threatening conditions." (2d Am. Compl. ¶ 57(a).)

b. Defendants "misrepresent[ed] that Risperdal is safer and more effective than less expensive first generation 'typical' antipsychotics." (2d Am. Compl. ¶ 57(c).)

c. Defendants "heavily marketed Risperdal for multiple non-approved purposes." (2d Am. Compl. ¶ 23.)

d. A November 10, 2003 mailing from defendant Janssen to health care providers misled doctors concerning the risk of diabetes with Risperdal. (2d Am. Compl. ¶ 46.)

e. "[T]he CATIE study proved what Defendants knew since launching Risperdal: (1) that Risperdal is no more effective in treating schizophrenia; (2) that Risperdal is no safer; and (3) that Risperdal has intolerable side effects making it no more desirable than the less expensive atypical antipsychotics." (2d Am. Compl. ¶ 52.)

7. Plaintiff's allegations raise several questions for my analysis. At a broad level, the question for analysis is whether the allegations of wrongful conduct by Janssen are valid. On a more specific level, plaintiff's allegations raise the questions of how Risperdal's safety and efficacy compare to first generation antipsychotics and other second generation antipsychotics, how Janssen marketed Risperdal to doctors in South Carolina, and how South Carolina patients responded when treated with Risperdal, as compared to alternative medications. Plaintiff's allegations concerning Janssen's November 10, 2003 mailing to health

care providers raise the question of whether data and literature—in the form of South Carolina patient claims data and the eight peer-reviewed epidemiological studies cited by Janssen—support the statements Janssen made in the cover letter that accompanied the revised Risperdal package insert that Janssen sent to South Carolina doctors. Finally, plaintiff's allegations regarding the CATIE study raise the question of whether the conclusions reached by the study or those that plaintiff attempts to draw from it are valid.

8. I have identified three primary, available data sources that provide information related to the fundamental questions raised by plaintiff's allegations:

a. Documented South Carolina physician experience, such as may be found from South Carolina doctors who treat patients with Risperdal, including the doctors' experience with Risperdal's efficacy, experience with the potential side effects of antipsychotic medications, the circumstances in which off-label use is regarded by the physician as appropriate, and Janssen promotional practices.

b. Observational data, such as the claims data produced by plaintiff from the State Fee-for-Service ("FFS") and State Health Plan ("SHP") benefits programs.

c. Published experimental and epidemiological studies.

9. My analysis of physician experience and observational data is explained in Section II, below. I address published experimental and epidemiological studies in Section II. The explanations provided here are supplemented by the presentation of results in the tables and charts at the end of this report and in the electronic files that are being produced with this report and are a part of my expert work in this case.

II. Statistical Analysis of Plaintiff's Allegations

A. Documented Physician Experience

10. Given the size of the relevant prescriber population, it would be prohibitively time-consuming and expensive to interview each prescriber of Risperdal in South

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Carolina concerning his or her experience with Risperdal and other antipsychotic medications. However, a properly representative sample of South Carolina doctors provides an economically feasible, reasonably accurate approximation of the same information. It is generally accepted among professional statisticians as well as scientists and scholars in related fields that statistical sampling is the only generally applicable, scientifically valid method for creating a representative sample from a universe that is too large to process exhaustively. By means of statistical sampling it is possible to produce unbiased, reasonably accurate approximations, having a known degree of potential error, to questions whose exact answers would be impracticably expensive or burdensome to obtain. I therefore obtained information about the experience of South Carolina doctors from legal depositions of randomly identified doctors who treated FFS and SHP beneficiaries in the State.

11. The theory and practice of statistical sampling, including sample survey of human subjects, has been a fundamental topic within the science of statistics at least since early twentieth century. During the decades of my education and career as a professional statistician in academia and consulting, I have acquired extensive experience with numerous aspects of sampling theory, sample and survey design, sample and survey implementation, and the analysis of sample and survey data.

12. Richard Johnson and Gouri Bhattacharyya recognized the importance of statistical sampling in their text *Statistics Principles and Methods*: "The subject of statistics provides the methodology to make inferences about the population from the collection and

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analysis of sample data. These methods enable one to derive plausible generalizations and then assess the extent of uncertainty underlying these generalizations.”¹

13. Leading statistician William Cochran has also recognized the importance of statistical sampling for decision-makers in his book *Sampling Techniques*.²

14. Johnson and Bhattacharyya emphasize that “[s]tatistical concepts are also essential during the planning stage of an investigation when decisions must be made as to the mode and extent of the sampling process,” thus the “design of the sampling process is an important step” and “[a] good design for the process of data collection permits efficient inferences, often with a straightforward analysis.”³

15. In this case, the population sampled consists of doctors who prescribed antipsychotic drugs for South Carolina patients in the Fee-for-Service (FFS) or State Health Plan (SHP) claims databases.

16. Generally speaking, physicians who prescribed antipsychotic drugs to greater numbers of patients can be expected to have more experience regarding the efficacy of Risperdal and more experience regarding marketing and promotional activities of Janssen than physicians with fewer such patients. Because the Court limited Janssen to surveying 20 doctors through deposition, my survey sample was randomly identified from the 101 doctors who prescribed antipsychotics most frequently.⁴

¹ Richard Johnson and Gouri Bhattacharyya, *Statistics Principles and Methods*, John Wiley & Sons, 3rd edition, 1996, 14.

² Cochran, William G., *Sampling Techniques*, John Wiley & Sons, New York, 1977.

³ Johnson and Bhattacharyya, *op. cit.*, 14.

⁴ The population to be sampled was the top 100 prescribers. Two doctors tied for 100th place, so the sample was drawn from a population of 101 prescribers.

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17. From the 101 most frequent prescribers, I selected, at random, with equal probability of selection, a sample of 20.⁵ I used a random process—a sequence of random numbers generated by a computer—to identify the final sample members from a list of all doctors eligible for selection.⁶ This random selection procedure guarantees a statistically representative sample because it rules out any purposive or inadvertent selection bias that could skew the composition of the sample towards any favored subgroup of doctors. Random sampling of this kind is a standard procedure in scientific survey research.

18. Counsel for Janssen endeavored to contact the selected doctors in the deposition sample to arrange for and conduct their depositions. Certain of the selected doctors were not available for deposition.⁷ In each of those instances, the next member in the random selection sequence was designated as a replacement.

19. The specific questions posed to the 20 doctors who were deposed are set forth in Exhibit 4 together with the doctors' responses. Exhibit 4 also shows the percentage of doctor-deponents answering "yes" or "probably yes" to each question.

20. The questions to doctors in deposition asked doctors about their experience with Risperdal and other antipsychotic medications and their specific exposure to Janssen promotional activity and communications. I sought fact-based answers from doctors in response to questions about whether Janssen had marketed Risperdal to them for off-label uses,

⁵ "Equal probability samples" are also called "simple random samples."

⁶ I employed the following standard procedure for selecting the sample. Let N denote the population size, and n the designated sample size. I used the SAS statistical software package to assign independently to each of the N population members a decimal-fraction random number between zero and one, equally likely to fall within either of any given pair of subintervals of equal length within the overall interval from zero to one. I then sorted the list of N population members in order of these assigned random numbers, and selected the first n members of the sorted list as the sample.

⁷ One doctor was unavailable due to terminal illness; one had moved to California; one refused to be deposed; and three could not be located. See Wecker electronic file "sample list.xls".

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whether they had received specific correspondence from Janssen, and how their patients fared while taking Risperdal and other antipsychotics.

21. As noted, the methodology I employed is a well-established one that allows statisticians to reach conclusions about a population from the collection and analysis of sample data. Exhibit 5 shows the conclusions that can be derived from the responses of 20 doctor-deponents about the entire population of the 101 most frequent prescribers. In aggregate, those 101 doctors wrote 33 percent of the antipsychotic prescriptions paid for through the FFS and SHP programs.⁸

22. The depositions regarding the actual experience of South Carolina doctors prescribing Risperdal and other antipsychotics yield results that contradict the plaintiff's allegations. For example, the great majority of physicians affirmed the following statements based on their experience: Risperdal is generally effective for treating the positive symptoms of schizophrenia; Risperdal is generally effective for treating the negative symptoms of schizophrenia; Risperdal typically has a more moderate side effect profile than first generation antipsychotics; both efficacy and tolerability increase the likelihood that a patient will take antipsychotic medication consistently; and patients who consistently take their antipsychotic medications are less likely to require costly follow-up treatment, such as in-patient psychiatric care, than patients who do not consistently take their medications.

23. Plaintiff's allegations are also contradicted by the result that no doctors affirmed that: any Janssen sales representative ever promoted to them any off-label use of Risperdal in children or geriatric patients; or that any Janssen sales representative ever promoted to them any off-label use of Risperdal at all. No Janssen sales representative ever represented

⁸ See Wecker electronic file "ffs_top_101.apd_pct.lst".

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anything inconsistent with the warnings about Risperdal that are provided on the FDA-approved package insert, and no Janssen sales representative ever misrepresented information about the potential side effects associated with Risperdal use to a deposed doctor.

24. Only a small number of physicians recall seeing Janssen's November 10, 2003 mailing to health care professionals. Of those, almost none changed their choice of antipsychotic medication based on the mailing. These responses are consistent with the history of the frequency with which doctors prescribed Risperdal, discussed below, which showed almost no change in Risperdal sales as a percentage of overall antipsychotic prescriptions after the mailing was sent to South Carolina doctors.

25. The commonly-used and accepted statistical tools that allow me to draw conclusions about the entire population of frequent South Carolina prescribers to FFS and SHP patients based on the answers provided in the survey show that the experience of South Carolina doctors contradicts plaintiff's allegations. The sample size of 20 allows me to reach reliable population estimates for the 101 most frequent prescribers, as shown in Exhibit 5.

B. Observational Data

26. Claims data produced by the plaintiff from South Carolina State databases is also useful for analyzing plaintiff's allegations.⁹ I performed three different analyses. First, I was able to utilize claims data produced by the State to compare the incidence of side effects alleged by plaintiff to be risks from Risperdal use to the incidence of the same side effects in untreated patients suffering from psychotic disorders; patients treated with first generation (conventional) antipsychotics; and patients treated with other second generation (atypical)

⁹ For my analyses of plaintiff's claims data, I combined HMO claims data with the FFS claims data. The two programs use a common patient identification code and some patients had claims records in both data bases.

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antipsychotics. Second, I was able to utilize claims data to compare time to discontinuation—the primary measure of efficacy of the CATIE study—in Risperdal patients to patients using first generation antipsychotics. Third, I was able to determine Risperdal use as a percentage of all antipsychotic use by patients in the FFS or SHP programs over time.

B.1. Incidence of Alleged Side Effects

27. I analyzed the claims data to calculate the incidence of side effects that plaintiff alleges are caused by Risperdal, and to compare the incidence of those side effects in patients receiving Risperdal to the incidence of those side effects in untreated patients suffering from psychotic disorders; patients treated with first generation (conventional) antipsychotics; and patients treated with other second generation (atypical) antipsychotics.

28. In order to perform this analysis, I first identified patients who, based on their FFS or SHP claims, were receiving only Risperdal, only first generation antipsychotics, or only other second generation antipsychotics. I then examined all claims in the 36 months after their first antipsychotic drug prescription for diagnoses indicating an alleged side effect. To attempt to ensure that the first antipsychotic drug prescription recorded in the State claims data was a patient's first use of the drug, I required a minimum of 12 months of uninterrupted eligibility prior to the first antipsychotic drug prescription. To attempt to ensure that I was comparing patients with similar histories with respect to each side effect, I required that there be no diagnosis indicating the side effect prior to the first antipsychotic drug prescription. To analyze untreated patients, I separately identified patients with uninterrupted eligibility for a period of at least 36 months prior to their first antipsychotic drug prescription and no diagnosis indicating the side effect prior to the 36 month period. I then examined all claims in that 36 month period for diagnoses indicating an alleged side effect. I analyzed two time periods: the

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full claims data base, providing data for 1994–2007 and the period limited to claims on or before November 10, 2003.¹⁰

29. The results of a direct comparison of the side effects reported in the claims database, for patients treated with different antipsychotic drugs, is shown in Exhibits 6 and 7. The percents of South Carolina patients with first alleged side effect diagnosis during the 36 months after their first antipsychotic drug prescription (treated patients) or before their first antipsychotic drug prescription reflect elevated side effect rates compared to Risperdal. Statistically significant differences from Risperdal are indicated by asterisks.

30. My analysis shows that:

a. Diabetes. Patients treated with conventional antipsychotics, patients treated with other atypical antipsychotics, and untreated patients had a statistically significantly elevated risk of diabetes compared to patients treated with Risperdal, whether measured based on analysis of all data or data existing as of November 10, 2003.

b. Metabolic adverse events.¹¹ Patients treated with conventional antipsychotics, patients treated with other atypical antipsychotics, and untreated patients had a statistically significantly elevated risk of metabolic adverse events compared to patients treated with Risperdal based on analysis of all data. Patients treated with other atypical antipsychotics had a statistically significantly elevated risk of metabolic adverse events compared to patients treated with Risperdal based on analysis of data existing as of November 10, 2003.

c. Increased prolactin secretion. Patients treated with conventional antipsychotics, patients treated with other atypical antipsychotics, and

¹⁰ I do not believe it is proper to limit analysis to data existing as of November 10, 2003 when seeking to determine whether the South Carolina claims data supports statements made by Janssen about Risperdal in the November 10, 2003 mailing. Instead, statisticians and other scientists should look at all available evidence, regardless of when it became available, to evaluate whether Janssen's statements were true or false. I have nevertheless included analysis of data as of November 10, 2003, in case plaintiff or any of its experts take the position that the truth or falsity of Janssen's communications should be evaluated without reference to anything that occurred after Janssen sent the November 10, 2003 mailing.

¹¹ Includes diabetes mellitus, secondary diabetes mellitus, abnormal glucose, abnormal weight gain, obesity, and other hyperalimentation.

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untreated patients had a statistically significantly elevated risk of increased prolactin secretion compared to patients treated with Risperdal based on analysis of all data.¹²

31. The data for South Carolina patients contradicts the opinion of plaintiff's expert Dr. William Wirshing that "risperidone elevates prolactin more than any marketed antipsychotic except the more recently marketed Janssen product paliperidone, a metabolite of risperidone." (Wirshing Report, p. 7). Dr. Wirshing's criticism of Janssen for "believ[ing] that the FDA mandated class labeling change and to a slightly lesser extent the consensus guidelines painted all of the medications with the same toxic brush" (Wirshing Report, p. 8) is similarly contradicted by the experience of South Carolina patients, because patient experience demonstrates differences in risk for Risperdal compared to other antipsychotics.

B.2. Time to Discontinuation

32. Plaintiff alleges in its Petition that the authors of the CATIE study "concluded that Risperdal is no more effective than the first generation, 'typical' antipsychotic perphenazine, in treating schizophrenia. In addition, the time to discontinuation because of intolerable side effects, including movement disorders, were similar among all groups." (2d Compl., ¶ 52.)

33. The CATIE study used "all-cause discontinuation" as the primary outcome measure of efficacy, meaning that the "failure" of a drug was attributed to the patient's discontinuation of the drug for any reason. The longer a patient took a drug in the CATIE trial, the more effective it was deemed to be by the study authors. I will return to the question of what the CATIE study shows, or does not show, about "all-cause discontinuation" times. But first, I

¹² The November 10, 2003 mailing did not discuss increased prolactin secretion.

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will describe my analysis of all-cause discontinuation times in the South Carolina population of State beneficiaries.

34. I have performed a statistical analysis of claims contained in the FFS and SHP data to determine all-cause discontinuation times in the South Carolina population of State beneficiaries. Using the claims data, I analyzed the comparative time to discontinuation for South Carolina patients treated with different antipsychotics. In order to be confident that I was measuring the first use of a drug, or first use after a substantial period of time in which the patient had not taken the drug for which I was measuring time to discontinuation, I identified those claims that were preceded by a minimum of 12 months of uninterrupted eligibility with no claims for the drug in question.

35. I then measured time to discontinuation following the first prescription by tracking patient claims histories for 18 months, as the CATIE study does. To determine discontinuation, I looked for periods of time without refills that followed the expiration of a patient's last prescription for the drug using three different, alternative time periods without refills to define discontinuation: 15 days, 30 days and 60 days. For example, if a patient received a prescription for a 30-day supply of Risperdal on April 1, but did not obtain another prescription until May 28, the patient would be deemed to have discontinued Risperdal use under the 15 days period, but not the 30 day or 60 day periods, because there was a 28 day period without a Risperdal refill prescription following the expiration of the 30 days supply prescribed on April 1. There is support in the medical literature for each of the time periods I use to define discontinuation: 15 days,¹³ 30 days,¹⁴ and 60 days.¹⁵

¹³ Mullins, C. Daniel, *et al.*, *Risk of discontinuation of atypical antipsychotic agents in the treatment of schizophrenia*, Schizophrenia Research, Vol. 98 (2008), § 2.3.1.1 p. 9; Ren, X. S., *et al.*, *An alternative approach to*

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36. My results show that Risperdal has a longer time to discontinuation compared to first generation antipsychotics in the FFS and SHP population under each of the three definitions of time to discontinuation. The complete results are set out in Exhibit 8. My analysis shows that:

a. Defining discontinuation as a 60-day period. Average time to discontinuation was 211 days for Risperdal, 133 days for perphenazine, 130 days for Haldol, and 58 days for all other first generation antipsychotics considered as a group.

b. Defining discontinuation as a 30-day period. Average time to discontinuation was 166 days for Risperdal, 107 days for perphenazine, 99 days for Haldol, and 44 days for all other first generation antipsychotics considered as a group.

c. Defining discontinuation as a 15-day period. Average time to discontinuation was 126 days for Risperdal, 83 days for perphenazine, 78 days for Haldol, and 35 days for all other first generation antipsychotics considered as a group.

B.3. Risperdal Use Over Time

37. Using the claims data, I was also able to analyze Risperdal prescriptions a percentage of all antipsychotic prescriptions paid for by the State through the FFS or SHP benefits programs and determine whether the comparative frequency of Risperdal prescriptions changed following events that plaintiff cites in its Complaint: the November 10, 2003 and July 21, 2004 mailings from Janssen to health care providers; the April 2005 FDA advisory and

measuring treatment persistence with antipsychotic agents among patients with schizophrenia in the Veterans Health Administration, Neuropsychiatric Disease and Treatment, Vol. 3, No. 2 (2007), p. 279; Ren, X. S., et al., Treatment persistence: a comparison among patients with schizophrenia who were initiated on atypical antipsychotic agents, J. Clin. Pharm. and Therap., Vol. 31 (2006), p. 59.

¹⁴ Ren, X. S., et al., *An alternative approach to measuring treatment persistence with antipsychotic agents among patients with schizophrenia in the Veterans Health Administration, Neuropsychiatric Disease and Treatment, Vol. 3, No. 2 (2007), p. 279.*

¹⁵ Kilzieh, Nael, et al., *Time to Discontinuation and Self-Discontinuation of Olanzapine and Risperidone in Patients With Schizophrenia in a Naturalistic Outpatient Setting, J. Clin. Psychopharmacol., Vol 28, No. 1 (Feb. 2008), p. 75; Zhu, Baojin, et al., Time to Discontinuation of Depot and Oral First-Generation Antipsychotics in the Usual Care of Schizophrenia, Psychiatric Services, Vol. 59, No. 3 (Mar. 2008), p. 316.*

subsequent black box warning for geriatric use; or the publication of the CATIE trial results in September 2005.

38. In order to determine the percentage of all antipsychotic prescriptions that Risperdal accounts for, I first eliminated claims that were reversed and duplicate claims within the database, so that each prescription for an antipsychotic medication would be counted only once. I then counted Risperdal prescriptions for each month from January 2003–December 2005. I separately counted all antipsychotic prescriptions in the same months. It was then straightforward to determine the number of Risperdal prescriptions as a percentage of all antipsychotic prescriptions paid for by the State through the FFS and SHP programs.

39. The results of my analysis are presented numerically and graphically in Exhibit 9. As the graph in Exhibit 9 shows, I was able to specifically analyze whether the events cited in the Complaint were followed by any change in the frequency with which South Carolina doctors prescribed Risperdal to patients in the FFS or SHP programs, as compared to all antipsychotic prescriptions.

40. In particular, I found no change in Risperdal prescribing frequency following Janssen's November 10, 2003 mailing to health care providers. If, as plaintiff contends, Janssen misled doctors about Risperdal's safety compared to other antipsychotics, I would expect to see an increase in the frequency with which doctors prescribed Risperdal compared to other antipsychotics. There was no such increase.

41. There was likewise no change in Risperdal prescribing frequency following July 2004, when Janssen sent its "correction" letter to South Carolina doctors at the request of the DDMAC division of FDA. The data also demonstrates that Risperdal use did not decline after the FDA issued its April 2005 advisory and subsequently required a black box

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warning for risk of death in geriatric patients or in the time period following the publication of the CATIE study results in September 2005. If, as plaintiff contends, these events mark times when doctors were exposed to information previously withheld or when “the public perception of Risperdal created by Defendants was dealt a crushing blow” (2d Am. Compl. ¶ 50), I would expect to see a decline in the frequency with which doctors prescribed Risperdal compared to other antipsychotics. That did not occur.

III. Analysis of Peer-Reviewed Literature

A. The Eight Studies Cited by Janssen in Its November 10, 2003 Mailing

42. Plaintiff alleges that a November 10, 2003 mailing from Janssen to doctors in South Carolina contained misleading information about the risk of diabetes in patients taking Risperdal. As shown in Exhibits 4–7 and addressed above, the experience of South Carolina doctors and South Carolina patients supports the statements that Janssen made in the mailing:

Although confirmatory research is still needed, a body of evidence from published peer-reviewed epidemiological research¹⁻⁸ suggests that RISPERDAL is not associated with an increased risk of diabetes when compared to untreated patients or patients treated with conventional antipsychotics. Evidence also suggests that RISPERDAL is associated with a lower risk of diabetes than some other studies atypical antipsychotics.

Janssen’s statements are also supported by the eight then-existing peer-reviewed epidemiological studies addressing the risk of diabetes in patients taking Risperdal compared to untreated patients, patients taking conventional antipsychotics and patients taking other atypical antipsychotics.

43. The eight studies cited by Janssen, which collectively analyze data from 6 million patients,¹⁶ are:

¹⁶ See Wecker electronic file “eight studies patient counts.xls”.

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a. Buse JB, Cavazonni P, Hornbuckle K et al. A retrospective cohort study of diabetes mellitus and antipsychotic treatment in the United States. *J Clin Epidemiology* 2003; 56: 164-170.

b. Caro JJ, Ward A, Levinton C and Robinson K. The risk of diabetes during olanzapine use compared with risperidone use: a retrospective database analysis. *J Clin Psychiatry* 2002; 63:1135-1139.

c. Fuller MA, Shermock KM, Secic M and Grogg AL. Comparative study of the development of diabetes mellitus in patients taking risperidone and olanzapine. *Pharmacotherapy* 2003; 23(8): 1037-1043.

d. Gianfrancesco F, White R, Wang RH and Nasrallah HA. Antipsychotic-induced type 2 diabetes: evidence from a large health plan database. *J Clin Psychopharmacol* 2003; 23(4): 328-335 ("Gianfrancesco 1").

e. Gianfrancesco F, Grogg AL, Mahmoud RA et al. Differential effects of antipsychotic agents on the risk of development of type 2 diabetes mellitus in patients with mood disorders. *Clin Therapeutics* 2003; 25(4): 1150-1171 ("Gianfrancesco 2").

f. Gianfrancesco F, Grogg AL, Mahmoud RA et al. Differential effect of risperidone, olanzapine, clozapine and conventional antipsychotics on type II diabetes: Findings from a large health plan database. *J Clin Psychiatry* 2002; 63: 920-930 ("Gianfrancesco 3").

g. Koro CE, Fedder DO, L'Italien GJ et al. Assessment of independent effect of olanzapine and risperidone on risk of diabetes among patients with schizophrenia: population based nested case-control study. *BMJ* 2002; 325: 243-245.

h. Sernyak MJ, Leslie DL, Alarcon RD et al. Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia. *Am J Psychiatry* 2002; 159: 561-566.

44. I have reviewed and analyzed the statistical conclusions presented in the eight studies. Four of the eight studies contain results comparing patients treated with Risperdal to untreated patients: Gianfrancesco 1, Gianfrancesco 2, Gianfrancesco 3 and Koro. All four of these studies find "that RISPERDAL is not associated with an increased risk of diabetes when compared to untreated patients"

45. Six of the eight studies contain results comparing patients treated with Risperdal to patients treated with conventional antipsychotics: Buse, Gianfrancesco 1, Gianfrancesco 2, Gianfrancesco 3, Koro and Sernyak. All six of these studies find “that RISPERDAL is not associated with an increased risk of diabetes when compared to ... patients treated with conventional antipsychotics.”

46. Buse warrants additional attention. Buse found overall that the incidence of diabetes mellitus for patients treated with Risperdal was lower than for patients treated with conventional antipsychotics. The hazard ratio for Risperdal was also lower than the hazard ratio for conventional antipsychotics.¹⁷ Buse separately reported results for a subgroup analysis that compared each of the four atypical antipsychotics, including Risperdal, to the haloperidol cohort.¹⁸ As a part of his subgroup analysis, Buse calculated that Risperdal’s hazard ratio compared to haloperidol was 1.23, with a 95% confidence interval of 1.01–1.50 and a p-value of 0.040. A p-value of 0.040 would indicate a statistically significant result for a primary endpoint of a study, but it does not indicate a statistically significant result for a secondary, subgroup analysis. Subgroup p-values need to be interpreted based on the number of comparisons made in subgroups that are analyzed—at least four in this case.¹⁹ Properly interpreted, the p-value of 0.040, which is part of the haloperidol subgroup analysis is not a statistically significant result.²⁰

¹⁷ Buse at 168, Table 3.

¹⁸ Buse at 168, Table 4.

¹⁹ Walsh, Bruce. *Multiple Comparisons: Bonferroni Corrections and False Discovery Rates*, Lecture notes for EEB 581, 2004.

²⁰ There are several formulaic ways to assess statistical significance for a subgroup analysis. The most common and easiest method to apply is the method of Bonferroni. (See Walsh, *op. cit.*) In the case of the haloperidol subgroup analysis and the p-value of 0.040, which is a part of that analysis, the Bonferroni p-value is 0.16 (= 4 x 0.040) which is not a statistically significant result.

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47. All eight studies contain results comparing patients treated with Risperdal to patients treated with another atypical antipsychotic, and four of those eight found statistically significant results: Ward, Fuller, Gianfrancesco 2, and Gianfrancesco 3. All four of these studies find "that RISPERDAL is associated with a [statistically significantly] lower risk of diabetes than some other studied atypical antipsychotics."

48. Taken together, the results of the eight studies, like the experience of South Carolina doctors and patients, contradict the contention of plaintiff's expert Laura Plunkett, that "the language of the November 2003 'Dear Health Care Provider' letter was not an accurate reflection of the risks posed by Risperdal." (Plunkett Report, ¶ 50.) Contrary to Dr. Plunkett's opinion, Janssen's statement in the mailing was an accurate reflection of the risks posed by Risperdal, whether judged by the then-existing body of published peer-reviewed epidemiological literature or the data from South Carolina doctors and patients.

B. The CATIE Study

49. As described above, the experience of South Carolina doctors with Risperdal and other antipsychotic medications contradicts plaintiff's interpretation of the CATIE study:

[T]he CATIE study proved what Defendants knew since launching Risperdal: (1) that Risperdal is no more effective in treating schizophrenia; (2) that Risperdal is no safer; and (3) that Risperdal has intolerable side effects making it no more desirable than the less expensive atypical antipsychotics. (2d Am. Compl. ¶ 52.)

In the experience of South Carolina doctors, Risperdal is more effective; has a more moderate side effect profile; and is better tolerated than first generation antipsychotics.

50. The experience of South Carolina patients also contradicts plaintiff's interpretation of the CATIE study. Time to discontinuation of Risperdal, for South Carolina

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patients, is longer than time to discontinuation of perphenazine, Haldol, or other first generation antipsychotics.

51. It takes no deep statistical analysis to show that the CATIE study itself demonstrates that Risperdal is more effective than and safer than perphenazine, the first generation drug included in the CATIE study. The study protocol states that perphenazine is "contraindicated" for patients with a prior history of tardive dyskinesia.²¹ This contraindication alone is sufficient to show that Risperdal is more effective than and safer than perphenazine for at least this large segment of the patient population.

52. Any direct comparisons of results from the perphenazine group to other treatment groups in the CATIE study will produce only ambiguous results, because the perphenazine group excluded patients with tardive dyskinesia while the other groups did not. Thus, the perphenazine group differs from the other groups in two ways: a difference in treatment and a difference in the patients treated. Because the perphenazine group differs from the other groups in more than one way, it is not valid to claim that any difference in outcomes between the perphenazine group versus any of the other treatment groups is due to the difference in treatment alone.

53. In an apparent attempt to cure the problem caused by the difference in patients treated with perphenazine compared to patients who received other treatments, the CATIE study chose to ignore results from patients with a prior history of tardive dyskinesia when making certain comparisons between treatment groups. But ignoring patients with a prior history of tardive dyskinesia is not a cure, because perphenazine, which is contraindicated for such patients, can be expected to have a differential and less satisfactory outcome for such

²¹ Protocol, Comparative Effectiveness of Antipsychotic Medications in Patients with Schizophrenia, 26-27.

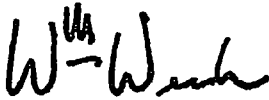
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patients. Ignoring outcomes for patients for whom perphenazine is expected to be ineffective or harmful amounts to ignoring an important difference in treatment results that will occur in the general population, which makes such comparisons inapplicable to the general population.

IV. Conclusion

54. In summary, for the reasons I have explained, statistical analysis of the primary data sources that provide information related to the central questions at issue refutes plaintiff's allegations.

December 3, 2010



William E. Wecker

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EDUCATION

B.S. Basic Science, U.S. Air Force Academy (1963)
M.S. Operations Research, University of Michigan (1970)
Ph.D. Statistics and Management Science, University of Michigan (1972)

EMPLOYMENT

1963-1967 Fighter pilot, U.S. Air Force
1968-1969 Chief of Protocol, U.S. Air Force, Berlin, Germany
1970-1972 Graduate Student, University of Michigan
1973-1976 Assistant Professor, Graduate School of Business, University of Chicago
1977-1983 Associate Professor, Graduate School of Business, University of Chicago
1984-1985 Associate Professor, Graduate School of Management, University of California, Davis
1985-1989 Professor, Graduate School of Management, University of California, Davis
1994-1998 Consulting Professor of Law, School of Law, Stanford University
1990- President, William E. Wecker Associates, Inc.

ACTIVITIES

1977-1981 Associate Editor (Theory and Methods), Journal of the American Statistical Association
1981-1999 Associate Editor, Journal of Business and Economic Statistics
1990-1992 Management Committee, Journal of Business and Economic Statistics
1976-1994 Seminar Leader, NSF/NBER Seminar on Time Series Analysis
1993-1994 National Advisory Council on Environmental Policy and Technology
(Lead Subcommittee)

Member of: American Association for the Advancement of Science
American Statistical Association
Institute of Mathematical Statistics
Society for Risk Analysis

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PUBLICATIONS

- "A Nonparametric Approach to the Construction of Prediction Intervals for Time Series Forecasts" (with W. A. Spivey), Proceedings of the Business and Economic Statistics Section--American Statistical Association, 1972.
- "Regional Economic Forecasting: Concepts and Methodology" (with W. A. Spivey), The Regional Science Association Papers, Vol. 28, 1972, pp. 257-276.
- "On the Weighted Average Cost of Capital" (with R. R. Reilly), Journal of Financial and Quantitative Analysis, January 1973, Vol. VIII, pp. 123-126.
- "On Random Walks with Absorbing Barriers" (with Thomas E. Morton), Proceedings of the Business and Economic Statistics Section-- American Statistical Association, 1973.
- "Prediction Methods for Censored Time Series," Proceedings of the Business and Economic Statistics Section--American Statistical Association, 1974.
- "More on the Weighted Average Cost of Capital: Reply" (with R. R. Reilly), Journal of Financial and Quantitative Method, June 1975.
- "Predicting Mail Order Demand for Style Goods," Proceedings of the Business and Economic Statistics Section--American Statistical Association, 1975.
- "The Prediction of Turning Points," Proceedings of the Business and Economic Statistics Section--American Statistical Association, 1976.
- "Bounds on Absorption Probabilities for the m-Dimensional Random Walk" (with T. Morton), Journal of the American Statistical Association, March 1977.
- "Discounting, Ergodicity and Convergence of Markov Decision Processes" (with T. Morton), Management Science, April 1977.
- "Comments on 'Forecasting with Econometric Methods: Folklore versus Fact'," Journal of Business, 1978, pp. 585-586.
- "Comment on 'Seasonal Adjustment When Both Deterministic and Stochastic Seasonality Are Present'," Proceedings of the NBER-CENSUS Conference on "Seasonal Analysis of Economic Time Series", U.S. Government Printing Office, Washington, D.C., 1978, pp. 274-280.
- "Predicting Demand from Sales Data in the Presence of Stockouts," Management Science, 1978, Vol. 34, No. 10, pp. 1043-1054.
- "The Time Series Which Is the Product of Two Stationary Time Series," Stochastic Processes and Their Application, 1978, pp. 153-157.
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"A New Approach to Seasonal Adjustment," Proceedings of the Business and Economic Statistics Section--American Statistical Association, 1979.

"Linear and Nonlinear Regression Viewed as a Signal Extraction Problem" (with C. Ansley), Proceedings of the Business and Economic Statistics Section-- American Statistical Association, 1980.

"Asymmetric Time Series," Journal of the American Statistical Association, March 1981.

"Predicting a Multitude of Time Series" (with R. A. Thisted), Journal of the American Statistical Association, September 1981.

"Applications of the Signal Extraction Approach to Regression" (with C. Ansley), Proceedings of the Business and Economic Statistics Section--American Statistical Association, 1981.

"Nonparametric Multiple Regression by Projection Iteration" (with C. Ansley), Proceedings of the Business and Economic Statistics Section--American Statistical Association, 1982.

"The Signal Extraction Approach to Nonlinear Regression and Spline Smoothing" (with C. Ansley), Journal of the American Statistical Association, March 1983.

"Extensions and Examples of the Signal Extraction Approach to Regression" (with C. Ansley), Applied Time Series Analysis of Economic Data, A. Zellner (ed.), Washington, D.C.: Bureau of the Census/ASA, 1983.

"The Signal Extraction Approach to Estimating Income and Price Elasticities: A Data Example" (with C. Ansley), Proceedings of the Business and Economic Statistics Section--American Statistical Association, 1983.

"A Nonparametric Bayesian Approach to the Calibration Problem," (with C. Ansley), Proceedings of the Business and Economic Statistics Section--American Statistical Association, 1984.

"On Dips in the Spectrum of a Seasonally Adjusted Time Series" (with C. Ansley), Journal of Business and Economic Statistics, October 1984.

"Estimating Damages in a Class Action Litigation" (with E. George), Journal of Business and Economic Statistics, April 1985.

"Statistics in Accounting, Marketing, Finance and Production" (with R. Hamada, J. Patell, R. Staelin), Proceedings of the Business and Economic Statistics Section--American Statistical Association, 1986.

"The Role of Statistics in Accounting, Marketing, Finance and Production" (with R. Hamada, J. Patell, R. Staelin), Journal of Business and Economic Statistics, 1988.

"Assessing the Accuracy of Time Series Model Forecasts of Count Observations," Journal of Business and Economic Statistics, October 1989.

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"Impact of the Soviet Grain Embargo; A Comparison of Methods" (with A. Webb, et al), Journal of Policy Modeling, pp. 361-389, 1989.

"Modeling Daily Milk Yield in Holstein Cows Using Time Series Analysis" (with H. Deluyker, et al.), Journal of Dairy Science, pp. 539 - 548, 1990.

"Controlling Emissions from Motor Vehicles: A Benefit-Cost Analysis of Vehicle Emission Control Alternatives" (with L. Lave, et al.), Environmental Science & Technology, August 1990.

"Statistical Estimation of Incremental Cost from Accounting Data" (with R. Weil), Handbook of Litigation Services for Accountants and Lawyers, John Wiley & Sons, 1990.

"Correcting for Omitted-Variables and Measurement-Error Bias in Regression with an Application to the Effect of Lead on IQ" (with M. L. Marais), Journal of the American Statistical Association, June 1998.

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Exhibit 2

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Deposition and Trial Testimony
January 1, 2006 – December 3, 2010

1. Carla P. Cox v. Ford Motor Company and Mullinax Ford South, Inc. Circuit Court, Broward County, Florida, No. 02012391.
2. Cook, et al., v. Rockwell International Corp., et al. USDC, Denver, Colorado, No. 90-K-181.
3. Misty Arias, et al. v. Award Homes, Inc., et al. Superior Court, Monterey County, California, No. M54183.
4. Marjorie Rosenthal, et al. v. Ford Motor Company, et al. USDC, Connecticut, No. 3:05-cv-478(JCH).
5. Karen Jean Hubbard, et al. v. Ford Motor Company, et al. Superior Court, Macon County, Georgia, No. 2003CV-283-P.
6. Ronene J. Bracken, et al. v. Ford Motor Company, et al. USDC, Nevada, No. CV-05-1543-RLH(RJJ).
7. Thelma Byrd, et al. v. Ford Motor Company, et al. Circuit Court, Copiah County, Mississippi, No. 2002-0446.
8. Yolanda Adams v. Ford Motor Company. District Court of the Virgin Islands, Division of St. Croix.
9. Ford Explorer Cases, Coordination Proceeding (Gray; Tompkins; Katz; Montoya and McLachlan v. Ford Motor Company). Superior Court, Sacramento County, California, JCCP Nos. 4226 and 4270.
10. State of California ex rel. Barakat Consulting Incorporated and Samir F. Barakat v. Los Angeles Department of Water and Power. Superior Court, San Bernardino County, California, No. SCVSS 100293.
11. Hohnbaum, et al. v. Brinker Restaurant Corporation, et al. Superior Court, San Diego County, California, No. GIC834348.
12. Leslie J. Whiteley and Leonard Whiteley v. Raybestos-Manhattan, Inc., et al. Superior Court, San Francisco, California, No. 303184.

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13. Dallas R. Maxwell and Angela J. Maxwell v. U-Haul International, Inc., Ford Motor Company, et al. Circuit Court, Jackson County, Missouri, No. 04CV226516.
14. Lindsay Rae Burnett, et al. v. Pirelli North America, Inc., Ford Motor Company, et al. District Court, Clark County, Nevada, No. A476187.
15. Rodrigo Ibarra, et al. v. Goodyear Tire and Rubber Company, Ford Motor Company, et al. District Court, Clark County, Nevada, No. A485304.
16. National Economic Research Associates, Inc. and Marsh & McLennan Companies, Inc. v. David S. Evans, LECG Corporation and LECG, LLC. Superior Court Department of the Trial Court, Suffolk, Massachusetts, No. 04-2618.
17. Michael Gutzler, et al. vs. General Motors Corporation. Circuit Court, Jackson County, Missouri, No. 03CV208786.
18. Self-Insurers' Security Fund v. Gallagher Bassett Services, Inc. USDC, Northern District of California, San Francisco Division, No. C 06-02828 JSW/JCS.
19. Autry Petroleum Company and McDonald Oil Company v. BP Products North America, Inc. USDC, Middle District of Georgia, Columbus Division, No. 4:05-CV-113 (CDL).
20. Wyeth v. Impax Laboratories, Inc. USDC, Delaware, No. C.A. 06-222 (JJF).
21. Discover Financial Services, DFS Services LLC, and Discover Bank v. Visa, U.S.A. Inc., Visa International Services Association, Mastercard Incorporated and Mastercard International Incorporated. USDC, Southern District of New York, No. 04-CV-844 (BSJ).
22. In re: New Motor Vehicles Canadian Export Antitrust Litigation. USDC, Maine, MD No. 03-md-1532.
23. Lyle Verry and Carla Verry v. General Motors Corporation. USDC, Eastern District of California, No. 2:06-CV-01566-LKK-PAN.
24. Equal Employment Opportunity Commission v. University of Phoenix, Inc. and Apollo Group, Inc. USDC, Arizona, No. CV06-2303-PHX-MHM.
25. Charles Foti, Attorney General *ex rel*, State of Louisiana v. Janssen Pharmaceutica, Inc. et al. Judicial District Court, Parish of St. Landry, Louisiana, No. 04-C-3967-D.
26. Sabrina Black Manuel v. Ford Motor Company, et al. Beverly Barber-Crouse v. Ford Motor Company, et al. Eugene Manuel, Jr. v. Ford Motor Company, et al. USDC, North District of Illinois, Eastern District, Nos. 07C5320, 07C5324, 07C5325.

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27. i4i Limited Partnership v. Microsoft Corporation. USDC, Eastern District of Texas, Tyler Division, No. 6:07-CV-113-LED.
28. Wyeth v. Apotex Inc. and Apotex, Corp. USDC, Southern District of Florida, No. 1:2008cv22308.
29. Steven Wirsz v. Nissan North America, Inc., et al. Superior Court, Los Angeles County, California, No. BC 377417.
30. L-3 Communications Integrated Systems, LP v. Lockheed Martin Corporation. USDC, Northern District of Texas, Dallas Division, No. 3-07CV0341-B.
31. Zurn PEX Plumbing Products Liability Litigation. USDC Minnesota, MDL 08-MD-1958.
32. Network-1 Security Solutions, Inc. v. Cisco Systems, Inc. USDC, Eastern Division of Texas, Tyler Division, No. 6:08cv030-LED.
33. In Re Payment Card Interchange Fee and Merchant Discount Antitrust Litigation. USDC, Eastern District of New York, No. 1:05-MD-1720 (JG)(JO).
34. In Re: Tobacco Litigation (Individual Personal Injury Cases). Circuit Court, Ohio County, West Virginia, No. 00-C-5000.
35. City of St. Louis, et al. v. American Tobacco Company, et al. Circuit Court, City of St. Louis, Missouri, No. 982-9652.

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Exhibit 3

List of Materials Considered

Datasets and Electronic Files:

South Carolina Fee For Service, State Health Plan, and HMO claims data produced by plaintiff (including eligibility data).

Cover letters, data dictionaries, correspondence between plaintiff and defense counsel regarding data production.

Depositions:

Millard Clinton Trott
Delfin Valite
Eugene F. Smith
Andrew W. Hedgepath
Balbir Coshal
William H. Bragdon
Rosen J. Lawsin
Glenn Hooker
Anil Juneja
James Frank Riddle
Lori W. Barwick
Laurel A. Weston
Sallie Amanda Carter
Kathy Marie Waggett
Kenneth G. Kassebaum
Ricardo J. Fermo
Evan L. Vogel
Michael J. Wood
Paul P. Lowe
James L. Elmore

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Books, Articles and Papers:

Richard Johnson and Gouri Bhattacharyya, *Statistics Principles and Methods*, John Wiley & Sons, 3rd edition, 1996.

Cochran, William G., *Sampling Techniques*, John Wiley & Sons, New York, 1977.

Mullins, C. Daniel, *et al.*, *Risk of discontinuation of atypical antipsychotic agents in the treatment of schizophrenia*, Schizophrenia Research, Vol. 98 (2008).

Ren, X. S., *et al.*, *An alternative approach to measuring treatment persistence with antipsychotic agents among patients with schizophrenia in the Veterans Health Administration*, Neuropsychiatric Disease and Treatment, Vol. 3, No. 2 (2007).

Ren, X. S., *et al.*, *Treatment persistence: a comparison among patients with schizophrenia who were initiated on atypical antipsychotic agents*, J. Clin. Pharm. and Therap., Vol. 31 (2006).

Kilzieh, Nael, *et al.*, *Time to Discontinuation and Self-Discontinuation of Olanzapine and Risperidone in Patients With Schizophrenia in a Naturalistic Outpatient Setting*, J. Clin. Psychopharmacol., Vol 28, No. 1 (Feb. 2008).

Zhu, Baojin, *et al.*, *Time to Discontinuation of Depot and Oral First-Generation Antipsychotics in the Usual Care of Schizophrenia*, Psychiatric Services, Vol. 59, No. 3 (Mar. 2008).

Buse JB, Cavazonni P, Hornbuckle K, *et al.*, *A retrospective cohort study of diabetes mellitus and antipsychotic treatment in the United States*, J. Clin. Epidemiology 2003, 56:164-170.

Caro JJ, Ward A, Levinton C and Robinson K, *The risk of diabetes during olanzapine use compared with risperidone use: a retrospective database analysis*, J. Clin. Psychiatry 2002, 63:1135-1139.

Fuller MA, Shermock KM, Secic M and Grogg AL, *Comparative study of the development of diabetes mellitus in patients taking risperidone and olanzapine*, Pharmacotherapy 2003, 23(8):1037-1043.

Gianfrancesco F, White R, Wang RH and Nasrallah HA, *Antipsychotic-induced type diabetes: evidence from a large health plan database*, J. Clin. Psychopharmacol 2003, 23(4):328-335.

Gianfrancesco F, Grogg AL, Mahmoud RA *et al.*, *Differential effects of antipsychotic agents on the risk of development of type 2 diabetes mellitus in patients with mood disorders*, Clin. Therapeutics 2003, 25(4):1150-1171.

Gianfrancesco F, Grogg AL, Mahmoud RA *et al.*, *Differential effect of risperidone, olanzapine, clozapine and conventional antipsychotics on type II diabetes: Findings from a large health plan database*, J. Clin. Psychiatry 2002, 63:920-930.

Koro CE, Fedder DO, L'Italien GJ *et al.*, *Assessment of independent effect of olanzapine and risperidone on risk of diabetes among patients with schizophrenia: population based nested case-control study*, BMJ 2002, 325:243-245.

Sernyak MJ, Leslie DL, Alarcon RD et al. *Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia*, Am. J. Psychiatry 2002, 159:561-566.

Lieberman, J., et al., *Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia (CATIE)*, New Eng. J. Med., 353(12) (Sept. 2005).

Rosenheck, R., et al., *Cost Effectiveness of Second-Generation Antipsychotics and Perphenazine in a Randomized Trial of Treatment for Chronic Schizophrenia*, Am. J. of Psych., 163(12) (2006).

Rosenheck RA, et al. (2006), Supplemental table A, Patient characteristics at the time of random assignment by initial treatment, available at <http://ajp.psychiatryonline.org/>.

Walsh, Bruce, *Multiple Comparisons: Bonferroni Corrections and False Discovery Rates*, Lecture notes for EEB 581, 2004.

Pleadings, Court Filings and Discovery:

Second Amended Complaint.

July 1, 2009 Order (a ruling on Janssen's request to take doctor depositions).

Expert Reports of William E. Wirshing, M.D., July 10, 2009.

Expert Report of Laura M. Plunkett, Ph.D., DABT, July 7, 2009.

Declaration of Lon S. Schneider, M.D., July 10, 2009,

Expert Report of John Abramson, M.D., July 10, 2009.

Supplemental Expert Report of Laura M. Plunkett, Ph.D., DABT; August 4, 2010.

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Other documents:

Janssen November 10, 2003 mailing to health care providers.

Risperdal package inserts and drug labels.

Protocol, Comparative Effectiveness of Antipsychotic Medications in Patients with Schizophrenia (Rev. Oct. 15, 2001).

Exhibit 4

Deposition Questions and Responses of 20 Doctors

Question	Yes	Probably Yes	No	Probably No	Refills Only	Dont Recall	Dont Know	It Depends	First Generation Antipsychotic	Second Generation Antipsychotic	More Effective	Safer	Other Answers	Not Asked	Total	Percent Responding "Yes" or "Probably Yes"
Have you ever treated pediatric patients, meaning patients 0 through 12 years old?	19		1												20	95%
Have you ever treated adolescent patients, meaning patients 13 through 17 years old?	20														20	100%
Have you ever treated non-geriatric adult patients, meaning patients 18 through 64 years old.	20														20	100%
Have you ever treated geriatric patients, meaning patients 65 or older?	19		1												20	95%
Have you ever prescribed Risperdal® for any of your patients?	20														20	100%
Have you ever prescribed Risperdal® for a pediatric patient?	14		2		1	3									20	70%
For an adolescent patient?	14		2			4									20	70%
For a non-geriatric adult patient?	20														20	100%
For a geriatric patient?	16	1	2			1									20	85%
For a South Carolina Medicaid patient?	20														20	100%
For a South Carolina State Health Plan patient?	8	3	2			2	5								20	55%
Have you ever prescribed antipsychotic medications other than Risperdal® for any of your patients?	20														20	100%
Have you ever prescribed antipsychotic medications other than Risperdal® for a pediatric patient?	14	2	2		1	1									20	80%
For an adolescent patient?	17	1	1			1									20	90%
For a non-geriatric adult patient?	20														20	100%
For a geriatric patient?	17	2	1												20	95%
Have you ever prescribed first generation antipsychotics for any of your patients?	20														20	100%
Have you ever prescribed second generation antipsychotics other than Risperdal® for any of your patients?	19													1	20	95%
In your experience, is Risperdal® generally effective for treating the positive symptoms of schizophrenia?	20														20	100%
In your experience, is Risperdal® generally effective for treating the negative symptoms of schizophrenia?	14						2						3		20	70%

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Exhibit 4

Deposition Questions and Responses of 20 Doctors

Question	Yes	Probably Yes	No	Probably No	Refills Only	Dont Recall	Dont Know	It Depends	First Generation Antipsychotic	Second Generation Antipsychotic	More Effective	Safer	Other Answers	Not Asked	Total	Percent Responding "Yes" or "Probably Yes"
In your experience, do patients who take Risperdal® have better overall outcomes more frequently than patients who take a first generation antipsychotic?	12	1	3				1	2					1		20	65%
In your practice, for patients requiring antipsychotic medications, do you generally prefer to use first generation antipsychotics, or, second generation antipsychotics? [Percent shown is for "second generation".]								1	1	14			4		20	70%
In your experience, are patients who take first generation antipsychotics, such as Haldol and Thorazine, more likely to experience extrapyramidal and anticholinergic side effects than patients who take second	20														20	100%
In your experience, are patients who take first generation antipsychotics, such as Haldol and Thorazine, more likely to experience Tardive Dyskinesia than patients who take second generation antipsychotics?	18						2								20	90%
In your experience, does Risperdal® typically have a more moderate side effect profile than first generation antipsychotics?	14						1	4					1		20	70%
In your experience, is Risperdal® typically better tolerated than first generation antipsychotics?	17							1					2		20	85%
In your experience with antipsychotic medications, are both efficacy and tolerability important considerations in the choice of which antipsychotic to prescribe?	19												1		20	95%
In your experience, do both efficacy and tolerability increase the likelihood that a patient will take an antipsychotic medication consistently?	19													1	20	95%
In your experience, are patients who consistently take their antipsychotic medications less likely to require costly follow-up treatment, such as in-patient psychiatric care, than patients who do not	19						1								20	95%
In your experience, are patients who consistently take their antipsychotic medications less likely, to require costly follow-up treatment, such as emergency room care, than patients who do not	17						1							2	20	85%
In your experience, does increased patient compliance with antipsychotic prescriptions result in overall conservation, as opposed to consumption, of healthcare resources?	17		1				2								20	85%
In your experience, does the use of Risperdal® typically conserve healthcare resources as compared to first generation antipsychotics?	9		1				4	2					4		20	45%
In your experience, does increased patient compliance with antipsychotic prescriptions typically decrease the human consequences of psychiatric illnesses?	20														20	100%
In your experience, does compliance taking antipsychotic medications typically make patients less likely to experience recurrence of	20														20	100%
Less likely to be violent?	17						2								20	90%

R. 8154

Exhibit 4

Deposition Questions and Responses of 20 Doctors

Question	Yes	Probably Yes	No	Probably No	Refills Only	Dont Recall	Dont Know	It Depends	First Generation Antipsychotic	Second Generation Antipsychotic	More Effective	Safer	Other Answers	Not Asked	Total	Percent Responding "Yes" or "Probably Yes"
Less likely to be an extreme burden on family members?	20														20	100%
Less likely to experience worsening of their conditions?	19						1								20	95%
Overall, in your experience, is Risperdal® a reasonably safe and effective medication for treating schizophrenia and other psychotic disorders?	19												1		20	95%
Overall, in your experience, is Risperdal® a safer and more effective medication for treating schizophrenia and other psychotic disorders than the first generation medications?	11		1				3	2			1	2			20	55%
In your experience, are there circumstances when the off-label use of medications is appropriate?	20														20	100%
In your experience, is it fair to say that off-label use of medications is not an uncommon practice?	18												2		20	90%
In your experience, are there circumstances when the off-label use of antipsychotic medications is appropriate?	18			1									1		20	90%
In your experience, is it fair to say that off-label use of antipsychotic medications is not an uncommon practice?	18						1						1		20	90%
Have you ever prescribed a medication for off-label use?	19					1									20	95%
In those circumstances, did you expect your patients to benefit from the off-label use of the medication?	19													1	20	95%
Have you ever prescribed an antipsychotic medication for off-label use?	18		1			1									20	90%
Have you ever prescribed Risperdal® for off-label use?	16	2	1			1									20	90%
Did you expect your patients to benefit from the off-label use of Risperdal®?	18													2	20	90%
Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® in children?			19			1									20	0%
Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® in geriatric patients?			19										1		20	0%
Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® at all?			19										1		20	0%
Have you ever received or seen any communication from Janssen promoting the off-label use of Risperdal®?			20												20	0%
Based on your training and experience, is it common for medications to have both benefits and risks?	20														20	100%

R. 8155

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Exhibit 4

Deposition Questions and Responses of 20 Doctors

Question	Yes	Probably Yes	No	Probably No	Refills Only	Dont Recall	Dont Know	It Depends	First Generation Antipsychotic	Second Generation Antipsychotic	More Effective	Safer	Other Answers	Not Asked	Total	Percent Responding "Yes" or "Probably Yes"
Based on your training and experience, is it your understanding that all antipsychotic medications -- both first generation and second generation -- have potential side effects?	20														20	100%
Are you aware of an association between antipsychotic medications and weight gain?	20														20	100%
Are you aware of an association between antipsychotic medications and risk of diabetes?	19													1	20	95%
When you prescribe antipsychotic medications, including Risperdal®, do you monitor your patients for weight gain?	20														20	100%
If you see or learn of rapid weight gain in a patient after the patient begins taking antipsychotics, do you typically consider changing the dosage and medication?	12		2					6							20	60%
If you see or learn of a change in blood glucose level in a patient after the patient begins taking antipsychotics, do you typically consider changing the dosage and medication?	12		2					6							20	60%
Would you agree that the 1993 package insert for Risperdal® advised of an association between Risperdal® and weight gain?	20														20	100%
Would you agree that the 1993 package insert for Risperdal® advised of an association between Risperdal® and diabetes?	20														20	100%
Would you agree that the 2004 package insert for Risperdal® incorporated a class warning of hyperglycemia and diabetes?	20														20	100%
Were you aware of an association between second generation antipsychotics, and weight gain or a risk of diabetes, prior to the 2004 revision to the package insert for Risperdal®?	16					2	2								20	80%
Did the change to the package insert for Risperdal® in 2004 cause you to change the circumstances in which you prescribe Risperdal® for patients?	2	1	15				1						1		20	15%
Has any Janssen sales representative ever represented to you anything inconsistent with the warnings about Risperdal® that are provided on the package insert?			19			1									20	0%
Has any Janssen sales representative ever represented to you that there is no association between Risperdal® and increased mortality in the elderly?			20												20	0%
Has any Janssen sales representative ever misrepresented to you information about the potential side effects associated with Risperdal® use?			19											1	20	0%
Have you ever seen this letter before? [November 10, 2003]	1	3	2			10	4								20	20%
Did this letter cause you to change the circumstances in which you prescribe antipsychotics to your patients?	1					1	1							13	20	5%

R. 8156

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Exhibit 4

Deposition Questions and Responses of 20 Doctors

Question	Yes	Probably Yes	No	Probably No	Refills Only	Dont Recall	Dont Know	It Depends	First Generation Antipsychotic	Second Generation Antipsychotic	More Effective	Safer	Other Answers	Not Asked	Total	Percent Responding "Yes" or "Probably Yes"
Did it cause you to change your choice of which antipsychotic to prescribe?		1	4										1	14	20	5%
Did it cause you to change your methods for monitoring for side effects in your patients on antipsychotic medications?	1		4			1								14	20	5%
Prior to the deposition today, have you had any communications with any of the attorneys for the Plaintiff in this case?	3		15											2	20	15%

See Wecker electronic file summary.deps.xls.

R. 8157

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Exhibit 5

Population Estimates from Responses to Deposition Questions

Question	Estimated Percent Responding "Yes" or "Probably Yes"	95% Confidence Limits
Have you ever treated pediatric patients, meaning patients 0 through 12 years old?	95.0%	(77.2% , 99.0%)
Have you ever treated adolescent patients, meaning patients 13 through 17 years old?	100.0%	(85.1% , 100.0%)
Have you ever treated non-geriatric adult patients, meaning patients 18 through 64 years old.	100.0%	(85.1% , 100.0%)
Have you ever treated geriatric patients, meaning patients 65 or older?	95.0%	(77.2% , 99.0%)
Have you ever prescribed Risperdal® for any of your patients?	100.0%	(85.1% , 100.0%)
Have you ever prescribed Risperdal® for a pediatric patient?	70.0%	(48.5% , 86.1%)
For an adolescent patient?	70.0%	(48.5% , 86.1%)
For a non-geriatric adult patient?	100.0%	(85.1% , 100.0%)
For a geriatric patient?	85.0%	(64.4% , 95.0%)
For a South Carolina Medicaid patient?	100.0%	(85.1% , 100.0%)
For a South Carolina State Health Plan patient?	55.0%	(33.7% , 74.3%)
Have you ever prescribed antipsychotic medications other than Risperdal® for any of your patients?	100.0%	(85.1% , 100.0%)
Have you ever prescribed antipsychotic medications other than Risperdal® for a pediatric patient?	80.0%	(59.4% , 93.1%)
For an adolescent patient?	90.0%	(71.3% , 98.0%)
For a non-geriatric adult patient?	100.0%	(85.1% , 100.0%)
For a geriatric patient?	95.0%	(77.2% , 99.0%)
Have you ever prescribed first generation antipsychotics for any of your patients?	100.0%	(85.1% , 100.0%)
Have you ever prescribed second generation antipsychotics other than Risperdal® for any of your patients?	95.0%	(77.2% , 99.0%)

R. 8158

M. HOPE BLACKLEY

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Page 1 of 5

Exhibit 5

Population Estimates from Responses to Deposition Questions

Question	Estimated Percent Responding "Yes" or "Probably Yes"	95% Confidence Limits
In your experience, is Risperdal® generally effective for treating the positive symptoms of schizophrenia?	100.0%	(85.1% , 100.0%)
In your experience, is Risperdal® generally effective for treating the negative symptoms of schizophrenia?	70.0%	(48.5% , 86.1%)
In your experience, do patients who take Risperdal® have better overall outcomes more frequently than patients who take a first generation antipsychotic?	65.0%	(43.6% , 82.2%)
In your practice, for patients requiring antipsychotic medications, do you generally prefer to use first generation antipsychotics, or, second generation antipsychotics? [Percent shown is for "second generation".]	70.0%	(48.5% , 86.1%)
In your experience, are patients who take first generation antipsychotics, such as Haldol and Thorazine, more likely to experience extrapyramidal and anticholinergic side effects than patients who take second generation antipsychotics?	100.0%	(85.1% , 100.0%)
In your experience, are patients who take first generation antipsychotics, such as Haldol and Thorazine, more likely to experience Tardive Dyskinesia than patients who take second generation antipsychotics?	90.0%	(71.3% , 98.0%)
In your experience, does Risperdal® typically have a more moderate side effect profile than first generation antipsychotics?	70.0%	(48.5% , 86.1%)
In your experience, is Risperdal® typically better tolerated than first generation antipsychotics?	85.0%	(64.4% , 95.0%)
In your experience with antipsychotic medications, are both efficacy and tolerability important considerations in the choice of which antipsychotic to prescribe?	95.0%	(77.2% , 99.0%)
In your experience, do both efficacy and tolerability increase the likelihood that a patient will take an antipsychotic medication consistently?	95.0%	(77.2% , 99.0%)
In your experience, are patients who consistently take their antipsychotic medications less likely to require costly follow-up treatment, such as in-patient psychiatric care, than patients who do not consistently take their medications?	95.0%	(77.2% , 99.0%)
In your experience, are patients who consistently take their antipsychotic medications less likely, to require costly follow-up treatment, such as emergency room care, than patients who do not consistently take their medications?	85.0%	(64.4% , 95.0%)
In your experience, does increased patient compliance with antipsychotic prescriptions result in overall conservation, as opposed to consumption, of healthcare resources?	85.0%	(64.4% , 95.0%)
In your experience, does the use of Risperdal® typically conserve healthcare resources as compared to first generation antipsychotics?	45.0%	(25.7% , 66.3%)

R. 8159

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Exhibit 5

Population Estimates from Responses to Deposition Questions

Question	Estimated Percent Responding "Yes" or "Probably Yes"	95% Confidence Limits
In your experience, does increased patient compliance with antipsychotic prescriptions typically decrease the human consequences of psychiatric illnesses?	100.0%	(85.1% , 100.0%)
In your experience, does compliance taking antipsychotic medications typically make patients less likely to experience recurrence of psychosis?	100.0%	(85.1% , 100.0%)
Less likely to be violent?	90.0%	(71.3% , 98.0%)
Less likely to be an extreme burden on family members?	100.0%	(85.1% , 100.0%)
Less likely to experience worsening of their conditions?	95.0%	(77.2% , 99.0%)
Overall, in your experience, is Risperdal® a reasonably safe and effective medication for treating schizophrenia and other psychotic disorders?	95.0%	(77.2% , 99.0%)
Overall, in your experience, is Risperdal® a safer and more effective medication for treating schizophrenia and other psychotic disorders than the first generation medications?	55.0%	(33.7% , 74.3%)
In your experience, are there circumstances when the off-label use of medications is appropriate?	100.0%	(85.1% , 100.0%)
In your experience, is it fair to say that off-label use of medications is not an uncommon practice?	90.0%	(71.3% , 98.0%)
In your experience, are there circumstances when the off-label use of antipsychotic medications is appropriate?	90.0%	(71.3% , 98.0%)
In your experience, is it fair to say that off-label use of antipsychotic medications is not an uncommon practice?	90.0%	(71.3% , 98.0%)
Have you ever prescribed a medication for off-label use?	95.0%	(77.2% , 99.0%)
In those circumstances, did you expect your patients to benefit from the off-label use of the medication?	95.0%	(77.2% , 99.0%)
Have you ever prescribed an antipsychotic medication for off-label use?	90.0%	(71.3% , 98.0%)
Have you ever prescribed Risperdal® for off-label use?	90.0%	(71.3% , 98.0%)
Did you expect your patients to benefit from the off-label use of Risperdal®?	90.0%	(71.3% , 98.0%)

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Exhibit 5

Population Estimates from Responses to Deposition Questions

Question	Estimated Percent Responding "Yes" or "Probably Yes"	95% Confidence Limits
Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® in children?	0.0%	(0.0% , 11.9%)
Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® in geriatric patients?	0.0%	(0.0% , 11.9%)
Has any Janssen sales representative ever promoted to you any off-label use of Risperdal® at all?	0.0%	(0.0% , 11.9%)
Have you ever received or seen any communication from Janssen promoting the off-label use of Risperdal®?	0.0%	(0.0% , 11.9%)
Based on your training and experience, is it common for medications to have both benefits and risks?	100.0%	(85.1% , 100.0%)
Based on your training and experience, is it your understanding that all antipsychotic medications – both first generation and second generation – have potential side effects?	100.0%	(85.1% , 100.0%)
Are you aware of an association between antipsychotic medications and weight gain?	100.0%	(85.1% , 100.0%)
Are you aware of an association between antipsychotic medications and risk of diabetes?	95.0%	(77.2% , 99.0%)
When you prescribe antipsychotic medications, including Risperdal®, do you monitor your patients for weight gain?	100.0%	(85.1% , 100.0%)
If you see or learn of rapid weight gain in a patient after the patient begins taking antipsychotics, do you typically consider changing the dosage and medication?	60.0%	(38.6% , 78.2%)
If you see or learn of a change in blood glucose level in a patient after the patient begins taking antipsychotics, do you typically consider changing the dosage and medication?	60.0%	(38.6% , 78.2%)
Would you agree that the 1993 package insert for Risperdal® advised of an association between Risperdal® and weight gain?	100.0%	(85.1% , 100.0%)
Would you agree that the 1993 package insert for Risperdal® advised of an association between Risperdal® and diabetes?	100.0%	(85.1% , 100.0%)
Would you agree that the 2004 package insert for Risperdal® incorporated a class warning of hyperglycemia and diabetes?	100.0%	(85.1% , 100.0%)
Were you aware of an association between second generation antipsychotics, and weight gain or a risk of diabetes, prior to the 2004 revision to the package insert for Risperdal®?	80.0%	(59.4% , 93.1%)
Did the change to the package insert for Risperdal® in 2004 cause you to change the circumstances in which you prescribe Risperdal® for patients?	15.0%	(5.0% , 35.6%)

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Exhibit 5

Population Estimates from Responses to Deposition Questions

Question	Estimated Percent Responding "Yes" or "Probably Yes"	95% Confidence Limits
Has any Janssen sales representative ever represented to you anything inconsistent with the warnings about Risperdal® that are provided on the package insert?	0.0%	(0.0% , 11.9%)
Has any Janssen sales representative ever represented to you that there is no association between Risperdal® and increased mortality in the elderly?	0.0%	(0.0% , 11.9%)
Has any Janssen sales representative ever misrepresented to you information about the potential side effects associated with Risperdal® use?	0.0%	(0.0% , 11.9%)
Have you ever seen this letter before? [November 10, 2003]	20.0%	(6.9% , 40.6%)
Did this letter cause you to change the circumstances in which you prescribe antipsychotics to your patients?	5.0%	(1.0% , 22.8%)
Did it cause you to change your choice of which antipsychotic to prescribe?	5.0%	(1.0% , 22.8%)
Did it cause you to change your methods for monitoring for side effects in your patients on antipsychotic medications?	5.0%	(1.0% , 22.8%)
Prior to the deposition today, have you had any communications with any of the attorneys for the Plaintiff in this case?	15.0%	(5.0% , 35.6%)

See Wecker electronic file, confidence_limits.nb.

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Exhibit 6

Analysis of South Carolina Fee for Service, State Health Plan, and HMO Claims
Antipsychotic Drugs and Alleged Side Effects

Excess Side Effect Risk
Relative to Risperdal

		Alleged Side Effect		
		Diabetes	Metabolic Adverse Events	Increased Prolactin Secretion
Antipsychotic Drug Prescribed:	1st Generation	1.62% (*)	1.46% (*)	3.64% (*)
	Other 2nd Generation	2.33% (*)	4.47% (*)	1.82% (*)
	Untreated	1.29% (*)	0.99% (*)	2.22% (*)

Notes: 1. Percent of Patients with First Alleged Side Effect Diagnosis within 36 Months from First Antipsychotic Drug Prescription.

2. Treated patients excluded if prescribed more than one type of antipsychotic drug; if less than 12 months of uninterrupted eligibility prior to their first antipsychotic drug prescription; if diagnosis of alleged side effect occurs prior to their first antipsychotic drug prescription; or if less than 36 months of uninterrupted eligibility following their first antipsychotic drug prescription.

3. Untreated patients excluded if less than 48 months of uninterrupted eligibility prior to their first antipsychotic drug prescription; or if diagnosis of alleged side effect occurs prior to 36 months before their first antipsychotic drug prescription.

4. Asterisk (*) indicates value is statistically significantly different from Risperdal value at 95% confidence level.

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See Wecker electronic files side.effect.diab.lst, side.effect.metab.lst, and side.effect.prlc.lst.

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Exhibit 7

Analysis of South Carolina Fee for Service, State Health Plan, and HMO Claims
Antipsychotic Drugs and Alleged Side Effects
Data as of November 10, 2003

Excess Side Effect Risk
Relative to Risperdal

		Alleged Side Effect	
		Diabetes	Metabolic Adverse Events
Antipsychotic Drug Prescribed:	1st Generation	1.17% (*)	0.65%
	Other 2nd Generation	1.84% (*)	3.02% (*)
	Untreated	1.32% (*)	0.78%

Notes: 1. Percent of Patients with First Alleged Side Effect Diagnosis within 36 Months from First Antipsychotic Drug Prescription.

2. Treated patients excluded if prescribed more than one type of antipsychotic drug; if less than 12 months of uninterrupted eligibility prior to their first antipsychotic drug prescription; if diagnosis of alleged side effect occurs prior to their first antipsychotic drug prescription; or if less than 36 months of uninterrupted eligibility following their first antipsychotic drug prescription.

3. Untreated patients excluded if less than 48 months of uninterrupted eligibility prior to their first antipsychotic drug prescription; or if diagnosis of alleged side effect occurs prior to 36 months before their first antipsychotic drug prescription.

4. Asterisk (*) indicates value is statistically significantly different from Risperdal value at 95% confidence level.

5. The November 10, 2003 mailing did not include increased prolactin secretion.

See Wecker electronic files side.effect.diab.lst, side.effect.mae.lst, and side.effect.prlc.lst.

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Exhibit 8

Analysis of South Carolina Fee for Service, State Health Plan, and HMO Claims
Antipsychotic Drugs and Time to Discontinuation

Average Days to Discontinuation

Antipsychotic Drug Prescribed:	Patient Count	"Treatment Discontinuation" Defined as X or More Days without Drug Supply		
		X=15 Days	X=30 Days	X=60 Days
Risperdal	27,197	125.59	166.00	211.23
Perphenazine	976	82.70 (*)	106.50 (*)	132.84 (*)
Haldol	7,071	77.86 (*)	98.96 (*)	130.43 (*)
Other 1st Generation	18,531	34.81 (*)	44.40 (*)	58.14 (*)

(*) Value is statistically significantly different from Risperdal value at 95% confidence level.

Notes: Patients are followed up for 18 months.

Patients excluded if less than 12 months of uninterrupted eligibility prior to start of treatment, or less than 18 months of uninterrupted eligibility after start of treatment.

See Wecker electronic file time_to_discontinuation.lst.

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Exhibit 9

South Carolina Fee for Service, State Health Plan, and HMO Claims Data
Antipsychotic Prescriptions by Month

Month and Year	Risperdal	First Generation Antipsychotics	Other Second Generation Antipsychotics	Total	Percent Risperdal
Jan 2003	6,945	3,798	13,034	23,777	29.21%
Feb 2003	6,518	3,503	12,415	22,436	29.05%
Mar 2003	7,068	3,606	13,569	24,243	29.15%
Apr 2003	7,254	3,696	13,742	24,692	29.38%
May 2003	7,199	3,601	14,082	24,882	28.93%
Jun 2003	6,906	3,464	13,916	24,286	28.44%
Jul 2003	7,179	3,669	14,593	25,441	28.22%
Aug 2003	7,111	3,564	14,341	25,016	28.43%
Sep 2003	7,131	3,490	14,820	25,441	28.03%
Oct 2003	7,603	3,558	15,278	26,439	28.76%
Nov 2003	6,809	3,230	14,067	24,106	28.25%
Dec 2003	7,648	3,644	15,918	27,210	28.11%
Jan 2004	7,073	3,272	14,546	24,891	28.42%
Feb 2004	6,954	3,107	14,254	24,315	28.60%
Mar 2004	7,811	3,505	16,540	27,856	28.04%
Apr 2004	7,653	3,336	15,607	26,596	28.78%
May 2004	7,429	3,177	15,276	25,882	28.70%
Jun 2004	7,884	3,345	16,177	27,406	28.77%
Jul 2004	7,721	3,266	15,901	26,888	28.72%
Aug 2004	7,886	3,273	16,447	27,606	28.57%
Sep 2004	7,764	3,234	16,312	27,310	28.43%
Oct 2004	7,809	3,233	16,184	27,226	28.68%
Nov 2004	8,047	3,314	16,852	28,213	28.52%
Dec 2004	8,090	3,373	17,011	28,474	28.41%
Jan 2005	7,460	3,094	16,041	26,595	28.05%
Feb 2005	7,199	2,947	15,516	25,662	28.05%
Mar 2005	7,975	3,266	17,410	28,651	27.83%
Apr 2005	7,748	3,152	16,995	27,895	27.78%
May 2005	7,970	3,175	17,483	28,628	27.84%
Jun 2005	7,918	3,300	17,641	28,859	27.44%
Jul 2005	7,549	2,970	16,632	27,151	27.80%
Aug 2005	8,625	3,296	18,350	30,271	28.49%
Sep 2005	8,204	3,294	17,616	29,114	28.18%
Oct 2005	8,336	3,246	17,614	29,196	28.55%
Nov 2005	8,471	3,221	18,037	29,729	28.49%
Dec 2005	8,227	3,108	17,102	28,437	28.93%

Notes: 1. Percent=Risperdal/Total x 100

2. Claims counts are net of reversals.

See Wecker electronic file risp.percent.lst.

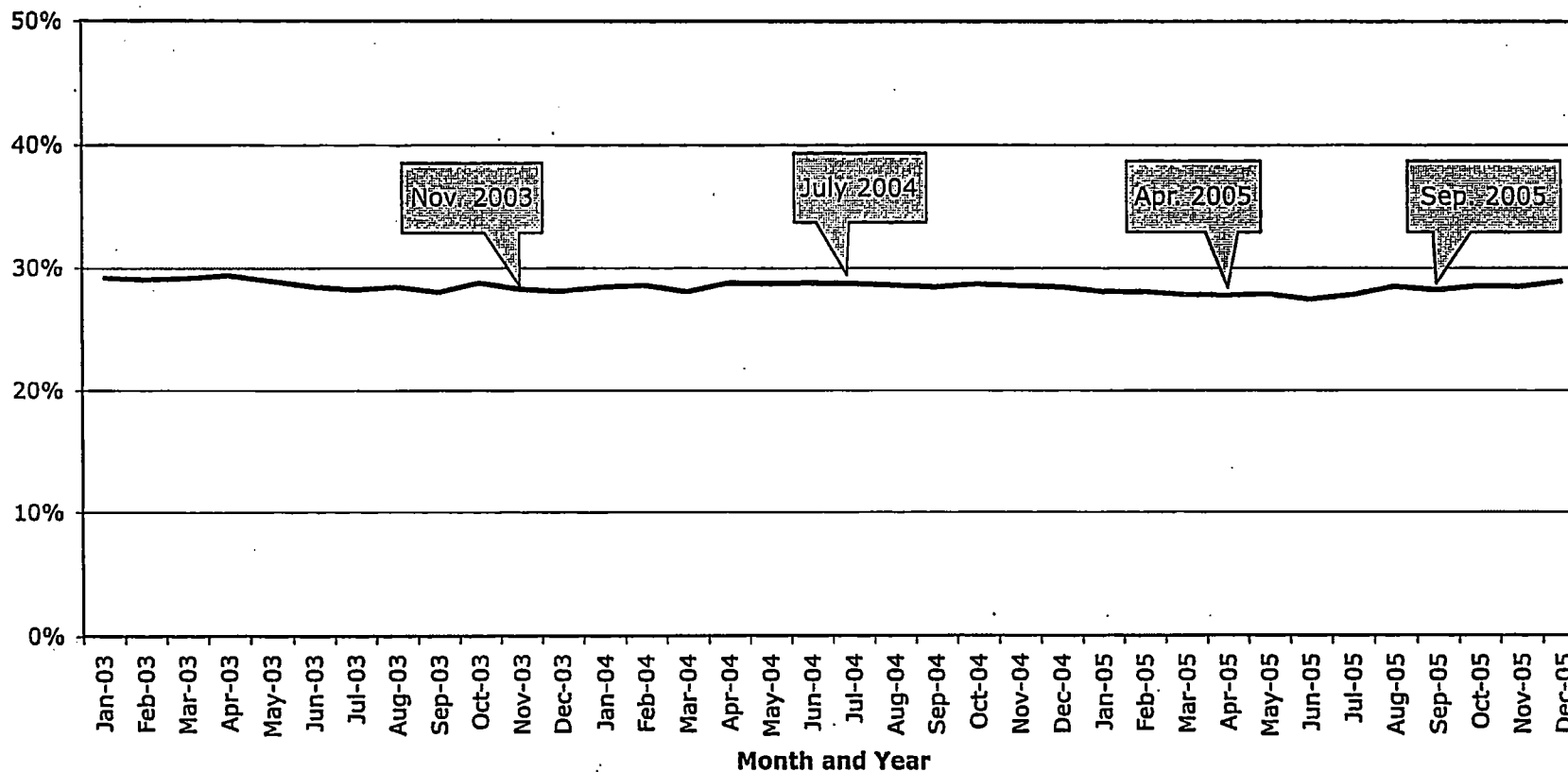
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Exhibit 9 (cont.)

**South Carolina Fee for Service, State Health Plan, and HMO Claims Data
Percent Risperdal Prescriptions by Month**



Notes: Percent=Risperdal/(Antipsychotic Prescriptions Total) x 100

November 2003: Janssen's November 10, 2003 mailing to health care providers.

July 2004: Janssen's "correction" letter.

April 2005: FDA advisory.

September 2005: publication of the CATIE trial results in N Engl J Med.

See Wecker electronic file risp.percent.lst.

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H. HOPKINS BLANCHARD

EXHIBIT 3

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M. HOPE BLACKLEY



SOUTH CAROLINA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
DRUG UTILIZATION REVIEW PROGRAM

September 19, 2002

ENGLES, TODD H
105 BELFAIR RD
IRMO, SC 29063

DEAR PRESCRIBER ENGLES:

In compliance with the OBRA '90 federal legislation, state Medicaid agencies are mandated to institute Retrospective Drug Utilization Review Programs (retroDUR). The program's goal is to ensure that Medicaid patients receive optimal drug therapy at the lowest reasonable cost. One way to achieve this goal is to identify potential drug therapy problems that may place patients at risk, particularly if multiple providers are identified. This retroDUR program is informational in nature and allows you to incorporate the information provided into your continuing assessment of the patient's drug therapy requirements.

During a recent review of the enclosed drug history profile, it was noted that your patient, [REDACTED] is receiving SEROQUEL. The use of clozapine, olanzapine, risperidone or quetiapine may increase the risk of developing type II diabetes mellitus or impaired glucose tolerance. Patients with a family history of diabetes or with pre-existing diabetes may need to have blood sugar monitored closely or changed to an alternative medication. In presenting this information to you, we recognize that the management of each patient's drug therapy depends upon an assessment of the patient's entire clinical situation about which we are not fully aware.

The success of the DUR program is enhanced by effective two-way exchange of information. Therefore, at your convenience, we would appreciate learning of your assessment of this information and of any action taken in response to this notice. Although your participation in this program is voluntary, we find your feedback helpful in adjusting our program to address clinically important problems. Please use the enclosed response to note your comments and return it in the enclosed envelope or fax it to the number below.

At the bottom of this letter are the specific prescriptions attributed to you by the dispensing pharmacy. In addition, if multiple prescribers are involved in the therapy identified above, each will receive this information. Thank you for your professional consideration.

RX #(s): 6646748

Sincerely,

W. Murray Yarbrough, M.D.

W. Murray Yarbrough, M.D.
Medical Director
Health Information Designs, Inc.

Case#: 259
Enclosures

Administered by Health Information Designs, Inc.
1550 Pumphrey Ave.
Auburn, AL 36832-9956
(800)225-6998 x 37 Fax(800)748-0016HID-SC 232

M. HOPE BLACKLEY

2011 JAN 20 PM 4:40

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SPARTANBURG COUNTY



**SOUTH CAROLINA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
DRUG UTILIZATION REVIEW PROGRAM**

PRESCRIBER RESPONSE

All information used to generate the enclosed letter, including Prescriber Identification, was obtained from Pharmacy Claims Data. If there appears to be an error in the information provided, please note the discrepancy. Thank you for your cooperation.

1. This patient is under my care:

- ☐ I have reviewed the information and will continue without change.
☐ however, I did not prescribe the following medication(s) _____
☐ and has an appointment to discuss drug therapy.
☐ however, has not seen me recently.
☐ however, I was not aware of other prescribers.
☐ I have reviewed the information and modified drug therapy.
☐ I have not modified drug therapy because benefits outweigh the risks.
☐ I have tried to modify therapy, however the patient refuses to change.
☐ I have tried to modify therapy, however symptoms reoccurred.

2. This patient is not under my care:

- ☐ however, I did prescribe medication while covering for other MD or in the ER.
☐ but has previously been a patient of mine.
☐ because the patient recently expired.
☐ and has never been under my care.

3. I have reviewed the enclosed information and found it:

☐ very useful ☐ useful ☐ neutral ☐ somewhat useful ☐ not useful.

4. Please check here if you wish to receive reference information on the identified problem (Please provide a fax number if available _____)

Comments: _____

ENGLES, TODD H Case# 259

Letter Type 500

The use of clozapine, olanzapine, risperidone or quetiapine may increase the risk of developing type II diabetes mellitus or impaired glucose tolerance. Patients with a family history of diabetes or with pre-existing diabetes may need to have blood sugar monitored closely or changed to an alternative medication.
586

Administered by Health Information Designs, Inc.

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Auburn, AL 36832-9956

(800)225-6998 x 37 Fax (800)748-0016 HID-SC 233

FILED
CLERK OF COURT
SPARTANBURG COUNTY
2011 JAN 20 PM 4:40
M. HOPE BLACKLEY

STATE OF SOUTH CAROLINA	)	IN THE COURT OF COMMON PLEAS
	)	
COUNTY OF SPARTANBURG	)	FOR THE SEVENTH JUDICIAL CIRCUIT
	)	
STATE OF SOUTH CAROLINA	)	
ex. rel. Henry McMaster, in his capacity	)	Civil Action No.: 2007-CP-42-1438
as Attorney General of the State of	)	
South Carolina,	)	
	)	
PLAINTIFF,	)	
	)	
v.	)	PLAINTIFF THE STATE OF SOUTH
	)	CAROLINA'S RESPONSE IN
	)	OPPOSITION TO DEFENDANTS'
ORTHO-MCNEIL-JANSSEN	)	MOTION FOR SUMMARY JUDGMENT
PHARMACEUTICALS, INC., f/k/a	)	AS TO PLAINTIFF'S UNFAIR TRADE
JANSSEN PHARMACEUTICA, INC.,	)	PRACTICES CLAIM BASED ON THE
and/or JANSSEN, L.P., AND	)	NOVEMBER 10, 2003 MAILING
JOHNSON & JOHNSON, INC.	)	
	)	
DEFENDANTS.	)	
	)	

TO: STEVEN J. PUGH AND KENNETH A. MURPHY, ATTORNEYS FOR DEFENDANTS

Plaintiff, the State of South Carolina, *ex rel.* Alan Wilson,¹ in his capacity as Attorney General of the State of South Carolina (hereinafter, "the State"), by and through the undersigned counsel, hereby submits its Response in Opposition to the Motion for Summary Judgment as to Plaintiff's Unfair Trade Practices Claim Based on the November 10, 2003 Mailing ("Motion") filed by Defendant Ortho-McNeil-Janssen Pharmaceuticals, Inc. f/k/a Janssen Pharmaceutica, Inc., and/or Janssen, L.P., and Johnson & Johnson, Inc. (collectively, "Janssen" or "Defendant"), and would respectfully show the Court as follows:

¹ Pursuant to South Carolina Rule of Civil Procedure 25(d)(1), the Honorable Alan Wilson has been substituted for the Honorable Henry McMaster as Attorney General for the State of South Carolina.

I.
SUMMARY OF THE ARGUMENT

By its Motion, Janssen presents two untenable arguments in avoidance of liability under the South Carolina Unfair Trade Practices Act (“SCUTPA”). To start, Janssen misapprehends the State’s claims and the appurtenant trigger that commences the running of the statute of limitations period. In attempts to divert this Court’s attention from the State’s actual or constructive knowledge of Janssen’s wrongful conduct in South Carolina, which would start the limitations period, Janssen remarkably contends that the very publication for which the State seeks civil penalties under SCUTPA for being “false” and “misleading”—the November 2003 “Dear Doctor” letter—commenced the running of the limitations period under SCUTPA, thus barring the State’s claims. Janssen bases its unsuccessful argument on the premise that “any of the physicians and other prescribers to whom the letter was addressed—and the State—had the ability to review the publically-available published studies to which Janssen pointed them and to ‘discover’ any alleged deception in the opinion Janssen offered about them.”² Janssen’s argument is unsound and belied by the fact that the publically-available published studies to which Janssen cited were admittedly flawed, company-sponsored, or otherwise unreliable.

Moreover, this issue has already been decided authoritatively by this Court. In the *Lilly* case, the Court opined that “[k]nowledge by the State that” a prescription drug “may have contributed to weight gain, diabetes, or related diseases . . . does not place the State on notice that [the defendant] is involved in any of the enumerated wrongful acts.”³ Janssen’s conclusory

² Def.’s Mem. at 9.

³ *State of South Carolina v. Eli Lilly & Co.*, No. 2007-CP-42-1855, slip op. at 10 (S.C.Com.Pl. Sept. 22, 2009) (denying pharmaceutical manufacturer’s Motion for Summary Judgment on Statute of Limitations Grounds) (attached as Exhibit A).

assertion that by virtue of the November 2003 “Dear Doctor” letter, the State was on notice, or should have been on notice, at that time, of Janssen’s wrongdoing with respect to its labeling of Risperdal, is entirely incommensurate with the Court’s prior rulings in this regard and should be rejected.

For a variety of other implausible reasons, Janssen claims that the November 2003 “Dear Doctor” letter is not actionable under SCUTPA, because it did not have a “tendency to deceive” or was not “likely to deceive” South Carolina physicians. Of course, South Carolina law and applicable federal law do not require the State to prove deceptiveness, but, rather, that the alleged *unfair* act or practice had the mere *potential* for repetition *or* was offensive to public policy, immoral, unethical, or oppressive—all of which the State has demonstrated for summary judgment purposes. But, this Court has also recognized that the “alleged systematic misrepresentation of the usefulness of a drug, its side effects on the using public as well as the agencies that paid for the drug, and for the consequences of the side effects”—all allegations that are specific to the November 2003 “Dear Doctor” letter—“are consumer protection issues which *are precisely the issues concerning which the South Carolina Legislature enacted SCUTPA.*”⁴

Like the November 2003 “Dear Doctor” letter, the April 19, 2004 Warning Letter falls within SCUTPA’s “wide net” of enforcement.⁵ Indeed, “[o]nce a deceptive or unfair act in the commerce of [this] State is identified as affecting the public interest as a whole,” such as the November 2003 “Dear Doctor” letter, “then it would seem that the legislature [must] seek[] broad enforcement of the Act” relative to the violation.⁶

⁴ *Id.* at 25 (emphasis added).

⁵ *Id.* at 27.

⁶ *Id.*

For the reasons outlined herein, Janssen's Motion must be denied in its entirety.

II. PROCEDURAL HISTORY & FACTUAL BACKGROUND

A. Statement of the Case.

On April 23, 2007, the State initiated this action against Janssen, manufacturer of the atypical antipsychotic drug Risperdal, to recover, *inter alia*, civil penalties pursuant to S.C. Code Ann. § 39-5-110(a) for Janssen's willful, deceptive and unfair course of conduct in its product labeling. On March 19, 2010, the State filed its Second Amended Civil Action Complaint, (hereinafter, "Amended Complaint"), petitioning the Court to assess against Janssen such penalties in an amount up to five thousand dollars for each "method, act or practice declared unlawful by § 39-5-20" and the willful use thereof. S.C. Code Ann. § 39-5-110(a). The State's Amended Complaint alleges, in brief, that Janssen: (1) "willfully engaged in a protracted, deceptive and unfair course of conduct in violation of SCUTPA" through its "labeling of Risperdal, which willfully, deceptively, and unfairly minimized, misrepresented, and/or concealed the drug's dangerous side effects"; (2) "had actual knowledge that Risperdal causes weight gain" and "other severe adverse effects" upon product launch, but "failed to include a warning of the potential for weight gain and the possible development of diabetes as a result of the use of Risperdal in its U.S. labeling for many years," and "failed to warn adequately of these adverse effects," in all subsequent label changes; (3) was "chastised by the FDA for being brazenly 'false' and 'misleading'" in its Dear Doctor Letters by "[f]ailing to disclose the addition of information relating to hyperglycemia and diabetes mellitus to the labeling; [m]inimizing the risks of potentially fatal hyperglycemia-related adverse events; [f]ailing to recommend regular glucose control monitoring to identify diabetes mellitus as soon as possible; and [m]isleadingly

claiming that Risperdal is safer than other atypical antipsychotics”; and, (4) “made, and continue[s] to make, orally and in writing, false, misleading or deceptive representations,” and “continue[s] to disseminate false, misleading, or deceptive information to the public . . . regarding the health risks and benefits associated with using Risperdal.” (Pl.’s Second Am. Compl. ¶¶ 8, 13, 24, 26, 45, 46, 57, 58.)

B. The November 2003 “Dear Doctor” Letter.

On September 11, 2003, the federal Food & Drug Administration (“FDA”) informed all manufacturers of atypical antipsychotic drugs, including Janssen that, due to an increasing prevalence of diabetes-related illnesses associated with this class of drugs, all labeling must bear the following language in the Warnings section:

Hyperglycemia and Diabetes Mellitus

Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiologic studies suggest an increased risk of treatment emergent hyperglycemia-related adverse events in patients treated with atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical

antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.⁷

Despite the FDA's directive that Janssen immediately warn of the above-described dangers and inform prescribers of the mandated diabetes warning label change applicable to all atypical antipsychotics, Janssen waited months, until November 10, 2003, to send South Carolina prescribing physicians a "Dear Doctor" letter purportedly advising of the new warnings.⁸ However, through the November 2003 "Dear Doctor" letter, Janssen sought to distance Risperdal from the mandated class-wide labeling change by representing to prescribers "that RISPERDAL is not associated with an increased risk of diabetes"⁹

Accordingly, on April 19, 2004, the FDA's Division of Drug Marketing, Advertising and Communications ("DDMAC") issued a Warning Letter (the "April 2004 Warning Letter") reprimanding Janssen for its brazenly "false," "misleading," and illegal representations made to more than 7,000 South Carolina physicians¹⁰ in the November 2003 "Dear Doctor" letter, and requiring immediate corrective action.¹¹ More specifically, according to the FDA, Janssen's letter unequivocally misled its recipients by:

⁷ Def.'s Summ. J. Ex. 1.

⁸ See Def.'s Summ. J. Ex. 7.

⁹ *Id.* (emphasis added).

¹⁰ See Def.'s Resp. to State's Fifth Set of Interrog. ("Based on the available distribution list, Janssen understands that 7,194 copies of the attached ["Dear Doctor"] letter dated November 10, 2003 were sent to addresses in the State of South Carolina.") (attached as Exhibit B).

¹¹ Def.'s Summ. J. Ex. 9 at 1, 4-5.

- “fail[ing] to disclose the addition of information relating to hyperglycemia and diabetes mellitus to the approved product labeling”¹²;
- “minimiz[ing] the risk of hyperglycemia-related adverse events, which . . . is associated with serious adverse events including ketoacidosis, hypersmolar coma, and death”¹³;
- “fail[ing] to recommend regular glucose control monitoring to identify diabetes mellitus as soon as possible”¹⁴; and,
- “misleadingly claim[ing] that Risperdal is safer than other atypical antipsychotics.”¹⁵

The FDA concluded that the November 2003 “Dear Doctor” letter was violative of sections 502(a) and 201(n) of the Federal Food, Drug, and Cosmetic Act (Act) (21 U.S.C. 352(a) and 321(n)) and demanded that Janssen “immediately cease the dissemination of promotional materials for Risperdal that contain claims the same as or similar to those described above and provide a plan of action to disseminate accurate and complete information to the audience(s) that received the violative promotional materials.”¹⁶ The FDA further cautioned that the violations detailed above did not constitute an exhaustive list, and that it was “continuing to evaluate other aspects of [Janssen’s] promotional campaign for Risperdal, and may determine that additional measures will be necessary to fully correct the false or misleading messages resulting from [Janssen’s] violative conduct.”¹⁷ Finally, the FDA warned Janssen that its “[f]ailure to correct

¹² *Id.* at 1.

¹³ *Id.*

¹⁴ *Id.*

¹⁵ *Id.*

¹⁶ *Id.* at 4.

¹⁷ *Id.* at 6.

the violations . . . may result in FDA regulatory action, including seizure or injunction, without further notice.”¹⁸

More than three months later, on July 21, 2004, Janssen finally sent a corrective “Dear Doctor” letter that contained the new warnings.¹⁹ This was more than ten months after the FDA initially instructed Janssen to adequately warn physicians.

III. ARGUMENT & AUTHORITIES

A. Standard.

“Summary judgment is a drastic remedy, which should be cautiously invoked so that no person will be improperly deprived of a trial of the disputed factual issues.” *Thomas Sand Co. v. Colonial Pipeline Co.*, 563 S.E.2d 109, 112 (S.C. Ct. App. 2002) (quoting *Doe ex rel. Doe v. Batson*, 548 S.E.2d 854, 857 (S.C. 2001)). It “is proper *only* when it is *clear* that ‘there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law.’” *Koester v. Carolina Rental Center, Inc.*, 443 S.E.2d 392, 394 (S.C. 1994) (citing S.C. R. Civ. P. 56(c)) (emphasis added). “In determining whether any triable issues of fact exist, the evidence and all inferences which can be reasonably drawn from the evidence must be viewed in the light most favorable to the non-moving party.” *Id.* (citing *Hamilton v. Miller*, 389 S.E.2d 652, 653 (S.C. 1990)). “[E]ven where there is no dispute as to the evidentiary facts, but only as to the conclusions or inferences to be drawn therefrom, summary judgment should not be granted.” *Jamison v. Howard*, 247 S.E.2d 450, 451 (S.C. 1978). Thus, “[i]t is the duty of the court, on a motion for summary judgment, not to try issues of fact, but only determine whether there are genuine issues of fact to be tried; and, once having found that triable issues exist, must

¹⁸ *Id.* at 5.

¹⁹ See Def.’s Summ. J. Ex. 11.

leave those issues for determination at a trial.” *Thomas Sand Co.*, 563 S.E.2d at 112; *see also Hammond v. Scott*, 232 S.E.2d 336, 339 (S.C. 1977) (“A court should never attempt to determine contested material factual issues on a motion for summary judgment.”).

The State’s SCUTPA claims are adequate as a matter of law, and, accordingly, by its Response, the State submits several genuine issues of material fact sufficient to withstand summary judgment. As evidenced by its Motion, Janssen, alternatively, has no legal support for judgment in its favor, and, therefore, the Court should properly deny Janssen’s Motion and submit the issue of Defendant’s willfully deceptive and unfair course of conduct in its labeling of Risperdal to a jury.

B. This Court Has Made Clear That The Information Relied Upon By Janssen Is Wholly Insufficient To Trigger The Running Of The Applicable Statute Of Limitations.

Janssen’s argument is premised on the fallacy that the November 2003 “Dear Doctor” letter—which the State contends misrepresented Risperdal’s safety and efficacy profile to South Carolina healthcare providers—was not “a provably false factual representation that could ‘deceive’ the persons to whom it was made,” or otherwise actionable under SCUTPA. (Def.’s Mem. at 14.) Correspondingly, Janssen claims that upon its dissemination, “any of the physicians and other prescribers to whom the letter was addressed—and the State—had the ability to review the publically-available published studies to which Janssen pointed them and to ‘discover’ any alleged deception in the opinion Janssen offered about them.” (Def.’s Mem. at 9.)

In making that argument, Janssen boldly ignores this Court’s prior Order on defendant’s Motion for Summary Judgment on Statute of Limitations Grounds in *Lilly*:

The information cited by Lilly stating that the Plaintiff should have been on notice that it had a claim or potentially had a claim is *separate and distinct from the wrongs alleged by the State*.

Knowledge by the State that Zyprexa may have contributed to weight gain, diabetes or related diseases . . . does not place the State on notice that Lilly is involved in any of the enumerated wrongful acts above[.]

which include

deceptive promotions, misrepresentations and concealment of information about the safety and efficacy of Zyprexa.

Further, *the anecdotal information . . . does not rise to the level of putting the State on notice* that Lilly was involved in any of the above specified wrongs.

Lilly, slip op. at 10-11 (emphases added).

Denying defendant's motion, Your Honor concluded that

[i]n this case at the very least there is a substantial conflict of evidence as to the date upon which the statute of limitations would have begun to run. In such cases, "*where there is conflicting testimony regarding the time of discovery, it becomes an issue for the jury to decide.*" *Arrant v. Kressler*, 489 S.E.2d 206 (S.C. 1997).

Id. at 11 (emphasis added).

The Court should, therefore, have no difficulty in deciding that the recycled arguments presented by Janssen's Motion are frivolous and remain unpersuasive. Janssen offered no new legal authority or facts to support its claims; rather, it largely relied upon speculation and anecdotal information, which this Court carefully distinguished in *Lilly*.

More specifically, in *Lilly*, this Court detailed the applicable statute of limitations, attendant to the "discovery rule," which runs from the date the injured party either knows or should have known by the exercise of reasonable diligence that *a cause of action arises from the wrongful conduct* of the defendant. *See id.* at *9 (citing S.C. Code Ann. § 15-3-535 (Supp. 2007); *Burgess v. Am. Cancer Soc'y, South Carolina Div., Inc.*, 386 S.E.2d 798, 800 (S.C. Ct. App. 1989); *Epstein v. Brown*, 610 S.E.2d 816, 818 (S.C. 2005)) (emphasis added). The Court

emphasized that the State's acquisition of bits and pieces of anecdotal information about Zyprexa prior to the filing of its Original Complaint is insufficient to trigger the running of the statute. *Lilly*, slip op. at 11. Without "facts concerning the . . . specified incidences of wrongdoing, of which the State was aware or should have been aware prior to February 27, 2004 or 2005," defendant's argument that the statute had been triggered in 2004, and had run, would fail. *Id.* Indeed, "[t]he burden of establishing the bar of the statute of limitations rests upon the one interposing it" *Turner v. Milliman*, 671 S.E.2d 636, 641 (S.C. Ct. App. 2009). "The limitations period is intended to run against those who are neglectful of their rights and who fail to exercise reasonable diligence in enforcing their rights. However, it is not the policy of the law to unjustly deprive an injured person of a remedy." *Moriarty v. Garden Sanctuary Church*, 534 S.E.2d 672, 679 (S.C. 2000). That same policy applies to the State here in determining Janssen's motion.

Like defendant's failed argument in *Lilly*, Janssen "reveals *no facts* concerning the . . . *specified incidences of wrongdoing*, of which the State was aware or should have been aware," prior to February 2004. *Lilly*, slip op. at 11 (emphases added). Rather, Janssen speculates that "any reader" of the November 2003 "Dear Doctor" letter, including the State, knew or should have known that a cause of action arose from Janssen's willful, deceptive and unfair course of conduct in violation of SCUTPA upon its dissemination, purely because they, allegedly, "had the ability to review the publicly-available published studies to which Janssen pointed them." (Def.'s Mem. at 8-9.)

Fundamentally, Janssen fails to show, as a conclusive fact that would support summary judgment as a matter of law, if and when the State had notice of the November 2003 "Dear

Doctor” letter *at all*—e.g., there is no testimony that the letter was ever received or read by any State official that would even approach “notice” for purposes of triggering the limitations period.

Moreover, the mere fact that the November 2003 “Dear Doctor” letter references “publicly-available published studies” is wholly insufficient to show what the State and its healthcare providers knew, or should have known, relative to Janssen’s misrepresentations *and when they knew it*, so as to trigger the running of the statute. Janssen’s reference to these publications—the majority of which are *Janssen-sponsored*²⁰—has no bearing on the State’s discovery at that time or at any other time thereafter, and, if anything, only advanced the misrepresentations in the November 2003 “Dear Doctor” letter.

In order to charge the State with notice of Janssen’s wrongdoings by way of publication, the referenced publications must be of sufficient “widespread publicity and awareness” to place the State on notice of the *particularized harm* that it seeks to redress. *See Hedgepath v. Am. Tel. & Tel. Co.*, 559 S.E.2d 327, 333-334, 337-338 (S.C. Ct. App. 2001) (holding that plaintiffs’ claims would be barred by the applicable statute of limitations only where “the record is *replete* with *uncontested evidence of widespread publicity and awareness of the alleged [wrongdoing]*,” combined with (1) plaintiffs’ “*affidavits affirm[ing] that [p]laintiffs knew*,”

²⁰ See, e.g., Caro, JJ Ward A, Levinton C and Robinson K. The risk of diabetes during Olanzapine use compared with risperidone use: a retrospective database analysis. *J Clin Psychiatry* 2002; 63:1135-1139 (attached as Exhibit C); Fuller MA, Shermock KM, Secic M and Grogg AL. Comparative study of the development of diabetes mellitus in patients taking risperidone and Olanzapine. *Pharmacotherapy* 2003; 23(8):1037-1043 (attached as Exhibit D); Gianfrancesco F, Grogg A, Mahmoud R et al. Differential effects of antipsychotic agents on the risk of development of type 2 diabetes mellitus in patients with mood disorders. *Clin Therapeutics* 2003; 25(e):1150-1171 (attached as Exhibit E); Gianfrancesco, FD, Grogg AL, Mahmoud, RA et al. Differential effects of risperidone, Olanzapine, clozapine and conventional antipsychotics on type II diabetes: Findings from a large health plan database. *J Clin Psychiatry* 2002; 63:920-930 (attached as Exhibit F).

Other referenced publications are also industry-sponsored by either atypical antipsychotic manufacturer, Eli Lilly and Company, or AstraZeneca Pharmaceuticals, LP. See, e.g., Buse JB, Cavazonni P, Hornbuckle K et al. A retrospective cohort study of diabetes mellitus and antipsychotic treatment in the United States. *J Clin Epidemiology* 2003; 56:164-170 (attached as Exhibit G); Gianfrancesco F, White R, Wang RH and Nasrallah HA. Antipsychotic-induced type 2 diabetes: evidence from a large health plan database. *J Clin Psychopharmacol* 2003; 23(4):328-335 (attached as Exhibit H).

prior to the running of the statute of limitations “of the alleged problems concerning” defendants’ plant emitting environmental pollution, the basis of plaintiffs’ nuisance causes of action; and *affirming that plaintiffs “felt that they had claims arising out of [defendant’s] operation of the facility for injuries to their person and property”*; and, with (2) the “permanency of the claimed property damages”) (emphases added); *see id.* at 333-34 (“widespread publicity” included “widespread . . . community concerns and allegations that the plant was the alleged source of personal injury and property damage in the surrounding areas,” “community forums, town meetings, government involvement, local political debates, door-to-door communications, media coverage, grassroots organization initiated by local citizens groups, and lawsuits brought by hundreds of residents . . . who . . . were friends, neighbors, and, in many instances, relatives of [p]laintiffs,” in the action at bar, *inter alia*). Janssen’s publications, like its Motion, are clearly devoid of evidence of “widespread publicity and awareness” of its illegal conduct in South Carolina.

Further, Janssen’s Motion fails to squarely address *misrepresentations and concealed information in the November 2003 “Dear Doctor” letter*—the very “specified incidences of wrongdoing” of which the State was allegedly aware. *See id.*

In sum, Janssen wholly fails to tie to the State any alleged notice of such *actionable offenses in South Carolina causing the State injury*, or legitimately explain how with reasonable diligence the State should have known of such allegations through the November 2003 “Dear Doctor” letter or otherwise, as it must.

For purposes of the limitations period, the State was arguably not aware of the alleged deception by Janssen, through its labeling, until April 2007 upon the filing of its Original

Complaint.²¹ Janssen has entirely failed to meet its burden to show otherwise in its Motion, and its Motion must be denied.

C. Janssen's Dissemination of the November 2003 "Dear Doctor" Letter Is Actionable Under SCUTPA.

1. S.C. Code Ann. § 39-5-20(b) Does Not Implicate a Reliance Requirement Under S.C. Code Ann. § 39-5-110(a).

Despite the abundance of authority in the alternative, Janssen essentially argues that anomalous federal law and a single decision of the Federal Trade Commission ("FTC") preempt the sound interpretation of S.C. Code Ann. § 39-5-20(a) by South Carolina courts and federal courts *correctly* interpreting FTC decisions. (See Def.'s Mem. at 11 (quoting *Southwest Sunsites, Inc. v. FTC*, 785 F.2d 1431, 1436 (9th Cir. 1986) (citing *In the Matter of Cliffdale Assocs., Inc.*, 103 F.T.C. 110 (1984))).) Citing S.C. Code Ann. § 39-5-20(b), which provides, in pertinent part, "that in construing paragraph (a) of this section the courts will be guided by the

²¹ Even if the Court could find that the State tardily filed its Complaint in this lawsuit—which for clear reasons amply described herein it did not—the doctrines of equitable estoppel and/or equitable tolling nevertheless permit the State to bring its claims. Because Janssen's intentionally deceptive conduct was designed to avoid detection, Janssen is equitably stopped from asserting a limitations defense and/or the applicable limitations period is equitably tolled. See *Hooper v. Ebenezer Senior Servs. & Rehab. Ctr.*, 659 S.E.2d 213, 225 (S.C. Ct. App. 2008) ("A defendant will be estopped to assert the statute of limitations in bar of a plaintiff's claim when the delay that otherwise would give operation to the statute has been induced by the defendant's conduct."). Moreover, "[s]ilence, when it is intended, or when it has the effect of misleading a party, may operate as equitable estoppel." *Hedgepath v. Am. Tel. & Tel. Co.*, 559 S.E.2d 327, 339 (S.C. Ct. App. 2001).

With respect to equitable tolling, the Court of Appeals of South Carolina observed that "[i]t has been held that equitable tolling applies principally if the plaintiff is actively misled by the defendant about the cause of action or is prevented in some extraordinary way from asserting his or her rights." *Hooper*, 659 S.E.2d at 221. "[T]he equitable tolling doctrine does not require wrongful conduct on the part of the defendant, such as fraud or misrepresentation." *Id.*

Janssen's false representations, concealment of material facts, and knowledge of the true facts, intending to mislead the State about any cause of action it may have had against Janssen, demands the application of the equitable estoppel or equitable tolling doctrines here. The State has thoroughly described Janssen's deceptive and manipulative conduct relative to the State and the South Carolina public in the Factual Bases For the Attorney General's Complaint of its Amended Complaint, which is incorporated herein by reference. Given the scope of deceptive activities in which Janssen engaged, the Court should necessarily find that the applicable statute of limitations period is equitably tolled and/or Janssen is equitably estopped from asserting its statute of limitations defense.

interpretations given by the Federal Trade Commission and the Federal Courts to § 5(a)(1) of the Federal Trade Commission Act (15 U.S.C. 45(a)(1)),” Janssen again hopelessly attempts to convince this Court of a causation-based reliance requirement under SCUTPA’s government enforcement provision. *See* S.C. Code Ann. § 39-5-110. Notwithstanding the Federal Trade Commission Act’s (the “FTC Act”) virtually identical enforcement provision to that of SCUTPA, Janssen, relying on a single, inapposite case, advocates a heightened standard of proof under the Act and, likewise, under SCUTPA.²² *Compare* 15 U.S.C. 45(a)(1) (“Unfair methods of competition in commerce, and unfair or deceptive acts or practices in commerce, are declared unlawful.”), *with* S.C. Code Ann. § 39-5-20(a) (“Unfair methods of competition and unfair or deceptive acts or practices in the conduct of any trade or commerce are hereby declared unlawful.”). (*See* Def.’s Mem. at 11 (relying on *Southwest Sunsites*, 785 F.2d at 1436).); *see also* *State ex rel. McLeod v. C & L Corp.*, 313 S.E.2d 334, 338 (S.C. Ct. App. 1984) (noting that section 39-5-20(a) is modeled after section 5(a)(1) of the FTC Act).

Specifically, Janssen claims that consistent with *Southwest Sunsites*, “under the FTC Act, it is not sufficient to allege and argue that a representation or practice is inherently ‘misleading’ or ‘deceptive’; rather, to establish liability under section 5, “probable, not possible, deception,” must be proven, in addition to “likely to mislead,” not a “tendency and capacity to mislead.” (*Id.*) Under Janssen’s absurd, circular, semantics-based reasoning, this “greater burden of proof” supposedly applicable to establishing FTC violations, is also applicable to, and, in fact, required

²² Even if the FTC standard was dissimilar as Janssen contends, South Carolina law prohibits the revocation of “pre-existing South Carolina definitions of unfair or deceptive trade practices,” under SCUTPA, and refuses to “bind[] the Act to the scope of federal law.” *Bostick Oil Co., Inc. v. Michelin Tire Corp.*, 702 F.2d 1207, 1220 (4th Cir. 1983) (emphasis added) (applying South Carolina law, reversing lower court’s dismissal of SCUTPA claims, and cautioning against overly restricting SCUTPA’s coverage to only those practices which would be unlawful under federal law).

to establish violations under S.C. Code Ann. § 39-5-20(a). (*Id.*; *see also id.* at 14 (“A plaintiff must prove more than the ‘possibility’ of deception.”) (citing *Southwest Sunsites*, 785 F.2d at 1436).) Apparently, finding further support in the Lanham Act, 15 U.S.C. § 1125(a), Janssen alleges that a plaintiff must additionally proffer evidence of “actual” impact as proof of violative conduct under *SCUTPA*. (Def.’s Mem. at 15, 17.) Applying this novel, quasi-common law standard to *SCUTPA* and the facts of this case, Janssen confidently concludes that the State has not met its burden of proof, because it did not produce requisite impact evidence or otherwise demonstrate that South Carolina physicians were deceived. (*Id.*) Janssen’s proposed “applicable standard,” is, however, inscrutable and no more applicable to *SCUTPA* than to the FTC Act from which Janssen claims it originates. (Def.’s Mem. at 10.)

Section 39-5-110(a) of *SCUTPA* provides that “[i]f a court finds that any person is willfully using or has willfully used a method, act or practice declared unlawful by § 39-5-20, the Attorney General, upon petition to the court, may recover on behalf of the State a civil penalty of not exceeding five thousand dollars per violation.” S.C. Code Ann. § 39-5-110(a). “For purposes of this section, a willful violation occurs when the party committing the violation knew or should have known that his conduct was a violation of § 39-5-20.” *Id.* § 39-5-110(c). With regard to prohibited acts or practices, section 39-5-20(a) declares unlawful all “[u]nfair methods of competition and unfair or deceptive acts or practices in the conduct of any trade or commerce.” *Id.* § 39-5-20(a).

As the statutes’ plain language evidences and South Carolina courts have made clear, *SCUTPA* does not require proof of fraud or irreparable harm to any consumer or physician but only that misrepresentations have occurred in order to prove violations thereof. *See, e.g., McLeod*, 313 S.E.2d at 338; *Inman v. Hyatt Chrysler Plymouth, Inc.*, 363 S.E.2d 691, 692 (S.C.

1988). Specifically, South Carolina courts “have refused to link proof of unfair or deceptive trade practices to proof of common law fraud.” *McLeod*, 313 S.E.2d at 338; *see, e.g., Inman*, 363 S.E.2d at 692; *see also State ex rel. Medlock v. Nest Egg Soc’y Today, Inc.*, 348 S.E.2d 381, 383-84 (S.C. Ct. App. 1986) (refusing to apply heightened common law standard of actual knowledge relative to “willfulness” under SCUTPA). And, “guided by the interpretations given by the Federal Trade Commission and the Federal Courts to § 5(a)(1) of the [FTC Act],” the court in South Carolina’s seminal government enforcement case under SCUTPA “[held] that the Act creates new substantive rights by making unlawful conduct which was *not actionable under common law*.” *McLeod*, 313 S.E.2d at 338 (emphasis added).

Thus, in its attempts to convince the Court to confer traditional common-law fraud and negligent misrepresentation requisites of proof on statutory causes of action under the FTC Act and SCUTPA, Janssen ignores well-settled precedent under South Carolina law and federal FTC law that makes clear that in demonstrating deceptiveness, “there is no need to show that a claim or representation was intended to deceive, but only that it had the capacity or effect or tendency to deceive.” *Id.* at 338 (citing *Federal Trade Comm’n v. Algoma Lumber Co.*, 291 U.S. 67 (1934); *D.D.D. Corp. v. Federal Trade Comm’n*, 125 F.2d 679 (7th Cir. 1942)). Further, Janssen overlooks that a plaintiff is not required to establish deceptiveness if he demonstrates that the conduct at issue is simply unfair. *See Wright v. Craft*, 640 S.E.2d 486, 498 (S.C. Ct. App. 2006) (citing S.C. Code Ann. § 39-5-20(a) (“The UTPA declares “unfair *or* deceptive acts or practices in the conduct of any trade or commerce . . . unlawful.”) (emphasis added)); *see also Spiegel, Inc. v. Federal Trade Comm’n*, 540 F.2d 287, 293 (7th Cir. 1976) (citing 15 U.S.C. § 45(a)(6) (“The Commission is empowered and directed to prevent persons, partnerships, or corporations . . . from using unfair methods of competition in commerce and unfair *or* deceptive acts or

practices in commerce.” (emphasis added)). To recover for an *unfair* trade practice under SCUTPA, a plaintiff must show only that the defendant engaged in a practice in the conduct of trade or commerce “which is offensive to public policy or which is immoral, unethical, or oppressive.” *Wright*, 640 S.E.2d at 498 (defining “unfair”) (quoting *Wogan v. Kunze*, 623 S.E.2d 107, 120 (S.C. Ct. App. 2005)); see *Bessinger v. Food Lion, Inc.*, 305 F. Supp. 2d 574, 582 (D.S.C. 2003) (construing SCUPTA—per section 39-5-20(b)—in accordance with the Federal Trade Commission Act, under which courts have determined that a practice is *unfair* when it “offends established public policy and when the practice is immoral, unethical, oppressive, unscrupulous, or substantially injurious to consumers”); see also *Spiegel*, 540 F.2d at 293 (“A practice is unfair when it offends established policy and when the practice is immoral, unethical, oppressive, unscrupulous or substantially injurious to consumers.”). In addition, Janssen ignores the crucial distinction between government enforcement of SCUTPA to protect the general public and private actions for individualized damages under section 39-5-140. Compare S.C. Code Ann. § 39-5-140(a), with S.C. Code Ann. § 39-5-110(a).

Further, urging the Court to hold the State to a standard even higher than that prescribed under SCUTPA’s actual damages provision, Janssen again disregards the Court’s prior determinations relative to SCUTPA’s government enforcement provision:

When looking to the purpose of SCUTPA, one comes to the conclusion that *the legislature intended [to] cast a wide net for causes of action in order to prevent and discourage deceit and fraud* perpetrated on both the public at large and the business community of this State. *It is clear that the legislature speaks in broad terms as to the activities that it seeks to make actionable* and allows various avenues of enforcement of its prohibitions.

Lilly, slip op. at 27 (emphases added).

Further, with respect to its impact on the public, this Court has already ruled that labeling, promotions and other such communications by a pharmaceutical manufacturer to the public, including prescribing physicians, are of “considerable importance” to the State, the public and the medical community. *Lilly*, 2007-CP-42-1855, at *18-*20. Beyond that, the State is not required to proffer evidence of the November 2003 “Dear Doctor” letter’s “actual” public impact for its dissemination to be actionable under SCUTPA, as Janssen contends. (Def.’s Mem. at 15, 17.) Rather, under South Carolina law “[a]n impact on the public interest may be shown if the acts or practices have the potential for repetition.” *Wright*, 640 S.E.2d at 501; accord *Dowd v. Imperial Chrysler-Plymouth, Inc.*, 381 S.E.2d 212, 214 (S.C. Ct. App. 1989) (holding that, in order to impact the public interest, unfair or deceptive acts or practices in the conduct of trade or commerce must simply have “the *potential* for repetition”) (emphasis added) (citations omitted). “The potential for repetition may be demonstrated in either of two ways: (1) by showing the same kind of actions occurred in the past, thus making it likely they will continue to occur absent deterrence; or (2) by showing the company’s procedures create a potential for repetition of the unfair and deceptive acts.” *Id.* at 502. Of course, “[t]hese two ways are not the only means for showing the potential for repetition or public impact, and each case must be evaluated on its own merits[.]” *Id.* A “plaintiff need not allege or prove anything further in relation to the public interest[.]” *Crary v. Djebelli*, 496 S.E.2d 21, 23 (S.C. 1998).

Indeed, the purpose of the “public impact” requirement is simply to exempt actions for *private* wrong where the public interest is unaffected. See *Noack Enters., Inc. v. Country Corner Interiors of Hilton Head Island, Inc.*, 351 S.E.2d 347, 349-50 (S.C. Ct. App. 1986); see also *Wright*, 640 S.E.2d at 501 (“Since 1986, South Carolina courts have required that a Plaintiff bringing a private cause of action under UTPA allege and prove the defendant’s actions

adversely affected the public interest.” (quoting *Daisy Outdoor Adver. Co. v. Abbott*, 473 S.E.2d 47, 49 (S.C. 1996))).

Thus, SCUTPA does not condition the prosecution of a government enforcement action under section 39-5-110 upon demonstration of actual public impact or upon deceptiveness. *See Wright*, 640 S.E.2d at 501-02; *Dowd*, 381 S.E.2d at 214.

2. *The State has unequivocally demonstrated that the November 2003 “Dear Doctor” letter is “unfair or deceptive.”*²³

However, as described above, the State has proffered “impact evidence” sufficient to show that the dissemination of the November 2003 “Dear Doctor” letter to thousands of South Carolina prescribing physicians and related deceptive labeling, was offensive to and affected the public interest in misleading the public, and in particular the South Carolina medical community, by “fail[ing] to disclose the addition of information relating to hyperglycemia and diabetes mellitus to the approved product labeling”²⁴; “minimiz[ing] the risk of hyperglycemia-related adverse events, which . . . is associated with serious adverse events including ketoacidosis, hypersmolar coma, and death”²⁵; “fail[ing] to recommend regular glucose control monitoring to identify diabetes mellitus as soon as possible”²⁶; and, “misleadingly claim[ing] that Risperdal is safer than other atypical antipsychotics,”²⁷ despite the FDA’s unequivocal instruction that all product labeling be updated to include information about diabetes mellitus adverse events.²⁸

²³ S.C. Code Ann. § 39-5-20(a).

²⁴ Def.’s Summ. J. Ex. 9 at 1.

²⁵ *Id.*

²⁶ *Id.*

²⁷ *Id.*

²⁸ *See* Def.’s Summ. J. Ex. 1.

In its April 2004 Warning Letter to Janssen, the FDA recognized the significant and detrimental impact of the November 2003 “Dear Doctor” letter on the South Carolina public:

The healthcare community relies on [“Dear Doctor”] letters for accurate and timely information regarding serious risks and associated changes in labeling and the dissemination of this letter at a time critical to educating healthcare providers *is a serious public health issue.*²⁹

Likewise, Janssen’s own competitors, Eli Lilly & Co., acknowledged Janssen’s November 2003 “Dear Doctor” letter as false, misleading and injurious to the public, and the medical community, in particular, in issuing its own “cease and desist” warning letter to Janssen, stating as follows:

We understand that Janssen sales representatives are widely and proactively distributing the [November 2003 “Dear Doctor”] Letter to physicians . . . Janssen’s dissemination of [these] claim[s] [are] improper. It flatly contradicts the weight of relevant medical literature. It also flatly contradicts the new prescribing information adopted by both Lilly and Janssen . . . Therefore, this statement is off-label, false and misleading and likely to result in injury . . . Lilly requests that Janssen immediately cease and desist (1) all use or dissemination of the . . . Letter[.]³⁰

And, despite its current position that the letter is not “false” or “misleading” or of “public impact,” because, allegedly, “the State had the ability to review the publicly-available published studies to which Janssen pointed them and to ‘discover’ any alleged deception” relative to the November 2003 “Dear Doctor” letter, Janssen itself admonished Lilly in 2002 for a similarly misleading “Dear Doctor” letter and promotional materials citing some of the same “publicly-

²⁹ Def.’s Summ. J. Ex. 9 (emphasis added).

³⁰ Letter from Associate General Counsel, Eli Lilly & Co. to Vice President, Law, Janssen Pharmaceutica, Inc. re: Risperdal® (risperidone) Promotion, November 26, 2003, (“Lilly Cease and Desist Letter to Janssen”) (attached as Exhibit I).

available published studies to which Janssen pointed [physicians]” in 2003.³¹ (Def.’s Mem. at 9, 13, 17.) More specifically, Janssen claims that the November 2003 “Dear Doctor” letter cannot constitute an actionable misrepresentation under SCUTPA, because it “cited to each of the published peer-reviewed studies, thereby fully disclosing the entire scientific basis” for the letter’s following conclusion: “a body of evidence from published peer-reviewed epidemiology research¹⁻⁸ suggests that RISPERDAL is not associated with an increased risk of diabetes when compared to untreated patients or patients treated with conventional antipsychotics.”³² (*Id.* at 12.) In other words, from this “body of evidence from published peer-reviewed epidemiology research” cited in the November 2003 “Dear Doctor” letter, Janssen claims the State could have discovered Risperdal’s true safety profile and, thus, “the mailing cannot be considered deceptive.” (*Id.* at 12, 14.)

Aside from the FDA’s clear rejection of that proposition³³ (and Lilly’s),³⁴ Janssen has criticized the very studies it claims are dispositive in the State’s case. Turning to the “VA Healthcare System study,” one of the eight studies cited in Janssen’s November 2003 “Dear Doctor” letter,³⁵ Janssen indentified the study as “flawed” and having severe “limitations” in its

³¹ Letter from Manager Regulatory Affairs, Johnson & Johnson Pharmaceutical Research & Development, LLC, on behalf of Janssen Pharmaceutica Products, LP to FDA, re: Supplementary documentation of unlawful promotion of Zyprexa[®] (olanzapine) by Eli Lilly & Co., Aug. 12, 2002, (“Janssen’s Letter to FDA Regarding Lilly”) (attached as Exhibit J).

³² Def.’s Summ. J. Ex. 7.

³³ *See generally* Def.’s Summ. J. Ex. 9 (April 2004 Warning Letter).

³⁴ *See* Lilly Cease and Desist Letter to Janssen (Ex. I).

³⁵ *See* Def.’s Summ. J. Ex. 7 at 2; Sernyak, MJ, Leslie DL, Alarcon RD *et al.* Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia. *Am. J. Psychiatry* 2002; 159:561-566 (attached as Exhibit K.)

2002 communication to the FDA regarding Lilly's "unlawful promotion of Zyprexa."³⁶ Janssen also identified Lilly's promotional material that, like Janssen's, intentionally minimized the known risks associated with its drug,³⁷ as "yet another example of how Lilly selectively presents or 'cherry-picks' misleading data, relied on flawed studies, and constructs a misleading presentation contradictory to the weight of the evidence regarding antipsychotics and metabolic disturbances."³⁸ Janssen further admitted that the "continued minimization of these serious, labeled adverse events *poses a substantial public health risk*."³⁹ As an aside, this promotional material of Lilly that Janssen chastised as "false" and "misleading" was disseminated *prior to* the FDA's class-wide warning mandate of September 2003, unlike Janssen's, circulated in the wake of the FDA's finding of an increasing prevalence of diabetes-related illnesses associated with atypical antipsychotics.⁴⁰ Lastly, and perhaps most significantly, Janssen condemned Lilly's promotional pieces for the fact that many of the referenced publications were financially, or otherwise, supported by Lilly.⁴¹

Just as "Lilly directly influenced content" of publications referenced in its promotional materials, Janssen, as described above, sponsored the majority of publications that it claims would have allowed the State, or physicians, to "discover" alleged deception in the November

³⁶ Janssen's Letter to FDA Regarding Lilly at 2 (Ex. J).

³⁷ Compare Janssen's Letter to FDA Regarding Lilly at 3 (citing Lilly's claim that "The hazard ratios for developing DM2 on an antipsychotic medication, *compared with individuals not taking antipsychotics*, were *remarkably close*." (emphases added) (Ex. J), with Def.'s Summ. J. Ex. 7 at 1 (November 2003 "Dear Doctor" letter claiming "a body of evidence from published peer-reviewed epidemiology research suggests that RISPERDAL is *not associated with an increased risk* of diabetes *when compared to untreated patients* . . .") (emphases added).

³⁸ *Id.* at 1.

³⁹ *Id.* at 1, 4 (emphasis added).

⁴⁰ See Def.'s Summ. J. Ex. 1.

⁴¹ Janssen's Letter to FDA Regarding Lilly at 1 (Ex. J).

2003 “Dear Doctor” letter.⁴² Those that were not apparently industry-sponsored were otherwise “flawed” and unreliable—even, according to Janssen.⁴³ The State’s expert, Dr. Laura Plunkett, has confirmed the fallibility of the studies referenced in the November 2003 “Dear Doctor” letter.⁴⁴ With respect to the VA Healthcare System study upon which Jansen relied in support of its contention that “RISPERDAL is not associated with an increased risk of diabetes,”⁴⁵ for example, Dr. Plunkett testified that “for patients less than 40 years old, all of the atypical neuroleptics were associated with a significantly increased prevalence of diabetes.”⁴⁶

Relatedly and in further support of its claim that the November 2003 “Dear Doctor” letter is not actionable under SCUTPA, Janssen contends that the State’s “sole witness on ‘deception,’ its expert Dr. Plunkett, acknowledged in her deposition that she has no opinion as to whether the November 2003 mailing, with its statement of opinion as to the scientific evidence, was actually ‘likely to deceive.’ South Carolina physicians.” (Def.’s Mem. at 16.) The State did not intend that Dr. Plunkett testify as to how prescribers viewed or reacted to the November 2003 “Dear Doctor” letter. Nor did the State intend that Dr. Plunkett offer impermissible legal conclusions, as did Janssen’s “regulatory” witness, Sheldon Bradshaw, regarding whether Janssen’s improper labeling “had a ‘tendency to deceive’ or was in fact ‘likely to deceive’ any South Carolina physician.” (Def.’s Mem. at 17.)

⁴² *Id.* at 1; *see supra* n. 20.

⁴³ *Id.* at 2 (identifying the VA Healthcare System study (Sernyak, *et al.*) as “flawed”); *but see* Def.’s Summ. J. Ex. 7 at 2 (November 2003 “Dear Doctor” letter citing the same).

⁴⁴ *See, e.g.*, Dep. of Dr. Laura M. Plunkett, Ph.D., DABT, Oct. 6, 2009, (“Plunkett Dep.”) at 230-238, (attached as Exhibit L).

⁴⁵ Def.’s Summ. J. Ex. 7 at 1; *see also id.* at 2 (citing VA Healthcare System study).

⁴⁶ *See also* Plunkett Dep. at 245-249 (discussing limitations and flaws of other studies cited by Janssen in the November 2003 “Dear Doctor” letter) (Ex. K).

Dr. Plunkett has appropriately opined, however, regarding the perceived unfairness and public impact of the November 2003 “Dear Doctor” letter. In her Expert Report, Dr. Plunkett concluded that “[t]he delays in the changes to Risperdal labeling with regard to metabolic risks was inconsistent with protecting the public health and put patients at increased risk.”⁴⁷ Moreover, she explained, “the language of the November 2003 [“Dear Doctor”] letter was not an accurate reflection of the risks posed by Risperdal.”⁴⁸

Despite that the State has demonstrated that the November 2003 “Dear Doctor” letter tended to deceive the South Carolina public, including prescribers, the State is, in fact, not required to prove that it was “deceptive” at all. To prevail under SCUTPA, the State may show, as it has, that the communication was plainly “unfair,” in that it was “offensive to public policy” or “immoral, unethical, or oppressive.” *Wright*, 640 S.E.2d at 498 (quoting *Wogan*, 623 S.E.2d at 120); *see also Spiegel*, 540 F.2d at 293.

D. The FDA’s April 19, 2004 Warning Letter to Janssen is Competent Summary Judgment Evidence.

Amid an array of evidentiary contentions,⁴⁹ Janssen makes a single dispositive argument relative to the April 2004 Warning Letter—that it is not competent summary judgment evidence of deceptive conduct because it “is merely an ‘informal’ and ‘advisory’ letter which identifies a possible regulatory violation in the hopes of resolving the issue through cooperation.” (Def.’s Mem. at 19.) That argument is, of course, expressly contradicted by Janssen’s own admission,

⁴⁷ Expert Report of Dr. Laura M. Plunkett, Ph.D., DABT, July 7, 2009 (“Plunkett Rep.”) at ¶ 50 (attached as Exhibit M).

⁴⁸ *Id.*

⁴⁹ Janssen’s evidentiary contentions—which are not grounds for summary judgment—are thoroughly addressed in the State’s Response in Opposition to Janssen’s Motion *in Limine* to Preclude the Introduction Into Evidence of the April 19, 2004 DDMAC Letter and Any Evidence of or Reference to the Letter at Trial., which the State incorporates by reference herein as if repeated in full.

which acknowledges that the April 2004 Warning Letter constitutes the “agency’s position” on the issue,⁵⁰ as well as by the *conclusions* the FDA reached in the April 2004 Warning Letter itself—e.g., “[f]ailure to correct the violations . . . may result in FDA regulatory action, including seizure of injunction, *without further notice*”; “DDMAC has concluded that the [November 10, 2003 Letter] is false or misleading in violation of Sections 502(a) and 201(n) of the [FFDCA] (21 U.S.C. 352(a) and 321 (n)); and “DDMAC has concluded that these materials are false, misleading, and/or lacking in fair balance, and in violation of the [FFDCA]”⁵¹ The *Regulatory Procedures Manual* attached to Janssen’s Memorandum (at Exhibit 21) further clarifies that the “Warning Letter was developed *to correct violations of the statutes or regulations*” and “are based on the expectation that most individuals and firms will voluntarily *comply with the law*” as set forth in the Warning Letter. (*Id.* at 4-1 to 4-2 (emphases added).) There is simply no basis for Janssen to argue that the April 2004 Warning Letter is not valid, effective FDA enforcement action of regulatory violations as determined by that agency.

In any event, the State contends that the April 2004 Warning Letter lends support to the State’s claim that the dissemination of the November 2003 “Dear Doctor” letter was violative of SCUTPA. The FDA’s conclusions are indicative of the perceived unfairness of Janssen’s letter as well as its public impact. *See Lilly*, 2007-CP-42-1855, at *18-*20 (considering labeling, promotions and other such communications by a pharmaceutical manufacturer to the public, including prescribing physicians, to be of “considerable importance” to the State, the public and the medical community). At the very least, the April 2004 Warning Letter establishes that the

⁵⁰ Def.’s Mem. in Support of Mot. *in Limine* to Preclude the Introduction Into Evidence of the April 19, 2004 DDMAC Letter and Any Evidence of or Reference to the Letter at Trial at 7 (citing *Regulatory Procedures Manual: Advisory Actions* at 2 (Exhibit C to Def.’s Mem.)).

⁵¹ Def.’s Summ. J. Ex. 9 at 1, 4.

November 2003 “Dear Doctor” letter was, indeed, unfair, or “offensive to public policy.” *Wright*, 640 S.E.2d at 498 (quoting *Wogan*, 623 S.E.2d at 120 (S.C. Ct. App. 2005)); *see also Spiegel*, 540 F.2d at 293 (“A practice is unfair when it offends established policy and when the practice is immoral, unethical, oppressive, unscrupulous or substantially injurious to consumers.”). The April 2004 Warning Letter is, therefore, competent summary judgment evidence that establishes at least a genuine issue of material fact as to Janssen’s SCUTPA violations through its unlawful labeling practices.

**IV.
RELIEF**

For all the foregoing reasons, the State respectfully requests that the Court deny Defendant’s Motion in its entirety.

Respectfully submitted,

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EXHIBIT A

STATE OF SOUTH CAROLINA

COUNTY OF SPARTANBURG

STATE OF SOUTH CAROLINA

Ex. rel. Henry McMaster, in his capacity
as Attorney General of the State of
South Carolina,

Plaintiff,

v.

ELI LILLY AND COMPANY

Defendant.

) IN THE COURT OF COMMON PLEAS

) FOR THE SEVENTH JUDICIAL CIRCUIT

) Case No. 2007-CP-42-1855

) ORDER

MARC KITCHENS

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FILED
CLERK OF COURT
SPARTANBURG COUNTY

ORDER

WHEREAS, the Court has reviewed the following Motions for Summary Judgment in this case, and it is hereby ORDERED:

BACKGROUND

On May 25, 2007, the State of South Carolina initiated this action against Lilly, the manufacturer of the atypical antipsychotic drug Zyprexa, to recover funds expended in purchasing and reimbursing Zyprexa for medically unnecessary uses not covered by the South Carolina Medicaid, the South Carolina Department of Mental Health ("SCDMH"), or the South Carolina Employee's Health Plan ("SHP") as a result of Lilly's false and misleading conduct, and to recover funds expended on the medical treatment of Medicaid, SCDMH, and SHP participants, suffering from Zyprexa-related illnesses as a result of Lilly's false and misleading promotional campaign. (Compl. at ¶ 3).

The State's Complaint asserts the following claims: submission of false and fraudulent claims under the Medicaid program pursuant to SS 43-1-60 and 43-7-60; strict

liability failure to warn and design defect; violation of the South Carolina Unfair Trade Practices Act ("SCUTPA"); negligence; breach of warranty; fraud and misrepresentation; and unjust enrichment. The State's Complaint alleges, *inter alia*, that Lilly: (1) engaged in "pervasive false and misleading marketing, advertising and promotion of Zyprexa," including "actively market[ing] and promot[ing] Zyprexa in several populations where the efficacy and safety of the drug had yet to be established," such as "treatment in the elderly for dementia"; (2) "[i]ntentionally creat[ed] a likelihood of confusion or misunderstanding in the minds of South Carolina prescribers as to whether Zyprexa was safe, effective or medically necessary for Medicaid, SCDMH and SHP participants"; and (3) [m]isrepresent[ed] that Zyprexa is safe and effective for indications for which safety and efficacy had not been demonstrated which caused South Carolina prescribers treating Medicaid, SCDMH and SHP participants to prescribe Zyprexa in inappropriate, non-medically necessary circumstances (Compl. at ¶ 77, 123(a), 123(g)).

LEGAL STANDARD

Summary judgment is a drastic remedy, which should be cautiously invoked so that no person will be improperly deprived of a trial of the disputed factual issues. Doe ex rel. Doe v. Batson, 345 S.C. 316, 322, 548 S.E.2d 854, 857 (citing Baughman v. American Tel. & Tel. Co., 306 S.C. 101, 112, 410 S.E.2d 537, 543 (1991)). Pursuant to South Carolina Rule of Civil Procedure 56(a), a party seeking to recover on a claim may move for summary judgment "upon all or any part thereof". S.C. R. Civ. P. 56(a). A party against whom a claim is asserted may move for a summary judgment "as to all or any part thereof". S.C. R. Civ. P. 56(b). Summary Judgment must be rendered if it is proven that there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as a matter of law. S.C. R. Civ. P. 56(c). See

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also Harris v. Anderson County Sheriff's Office, 381 S.C. 357, 673 S.E.2d 423, 424 (2009). In determining whether any triable issues of fact exist, the evidence and all inferences which can be reasonably drawn from the evidence must be viewed in the light most favorable to the non-moving party. Hansson v. Scalise Builders of S.C., 374 S.C. 352, 355, 650 S.E.2d 68, 70 (2007). It is the duty of the court, on a motion for summary judgment, not to try issues of fact, but only determine whether there are genuine issues of fact to be tried; and, once having found that triable issues exist, must leave those issues for determination at trial." Thomas Sand Co. v. Colonial Pipeline Co., 349 S.C. 402, 408, 563 S.E.2d 109, 112 (Ct. App. 2002) (citing Spencer v. Miller, 259 S.C. 453, 456, 192 S.E.2d 863, 864 (1972)).

The State's Motions for Summary Judgment and Partial Summary Judgment

I. State's Motion for Summary Judgment

- A. *Is Lilly collaterally estopped from re-litigating issues determined by its guilty plea in the United States District Court for the Eastern District of Pennsylvania? (U.S. v. Eli Lilly & Co., Case No. 39-020, January 14, 2009; hereinafter cited as "Plea Agreement").*

South Carolina recognizes that "under the doctrine of collateral estoppel, also known as issue preclusion, when an issue has been actually litigated and determined by a valid and final judgment, the determination is conclusive in a subsequent action whether on the same or a different claim". Zurcher v. Bilton, 379 S.C. 132, 136, 666 S.E.2d 224, 226 (2008). Our courts recently extended the doctrine to include the rule that a person criminally convicted is bound by that adjudication in a subsequent civil proceeding based on the same facts underlying the criminal conviction or plea. Id. at 138. In its plea agreement, Lilly plead guilty to one count, charging it with the introduction into interstate commerce of drugs that were misbranded in violation of 21 U.S.C. § 331(a); § 333(a)(1); and § 352(f)(1). The facts underlying that plea and upon which the plea was based are listed in ¶ 6(A) (1) – (4) of the Guilty Plea Agreement. As to

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the aforementioned facts and under Zurcher, this Court finds and it is therefore ORDERED, that Lilly is collaterally estopped from denying the facts admitted as part of the aforesaid guilty pleas contained in ¶ 6(A) (1) – (4) of the Guilty Plea Agreement in this action.

B. *Is the State entitled to summary judgment as to liability on its SCUTPA claim?*

An act is “unfair,” within the meaning of the South Carolina Unfair Trade Practices Act (SCUTPA) when it is offensive to public policy or when it is immoral, unethical, or oppressive. City of Charleston, S.C. v. Hotels.com, LP, 520 F.Supp.2d 757, 775 (D.S.C., 2007). While Lilly’s guilty plea constitutes an admission of the facts stated in the plea agreement, Lilly has made no admission as to *willfully* using any unfair methods of competition or unfair or deceptive acts or practices in the conduct of its business. Specifically, the Federal statute provisions to which Lilly plead guilty are statutes which do not require any specific level of intent, and are what might be referred to as “status offenses”. As such, the guilty plea does not produce an admission of *willful* conduct on the part of Lilly which would give rise to a violation of the South Carolina Unfair Trade Practices Act as a matter of law. The Court finds and it is ORDERED that there are issues of fact remaining to be determined by a jury at trial as to the relevant matters contained in the statute, therefore, the state’s motion for summary judgment is DENIED.

C. *Is the State entitled to Summary Judgment as to Liability on its Unjust Enrichment Claim for the period between September 1999 and March 2001?*

The State makes the further claim that it is entitled to summary judgment under SCRPC 56 based on its cause of action for unjust enrichment. Equitable relief is generally available only where there is no adequate remedy at law. Santee Cooper Resort, Inc. v. South Carolina Public Service Com’n, 298 S.C. 179, 185, 379 S.E.2d 119, 123 (S.C. 1989). An adequate legal remedy may be provided by statute. Id. The Court is inclined to agree that unjust enrichment may be proper, given the fact that Lilly is collaterally estopped from denying the admissions made in its

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plea agreement. However, at the present time this court finds that the State has not exhausted all adequate remedies at law for injuries and relief complained of. Therefore, it would be improper to allow a cause of action in equity when such legal remedies exist at this time. It may be determined later that the State has no adequate legal remedy, and for that reason, this Court will STAY any final determination of this portion of the State's Motions until a final determination of the State's legal claims has been made.

D. Is the State entitled to Summary Judgment as to Lilly's Fourth, Seventh, Ninth, Tenth, Eleventh, Nineteenth and Twentieth Affirmative Defenses?

Despite the admissions made by Lilly in its guilty plea, the Court finds that those admissions, in and of themselves, do not support granting of summary judgment as to Lilly's Fourth, Tenth, Nineteenth and Twentieth Affirmative Defenses. The Court reminds the parties that for the time period covered in the Guilty Plea, Lilly remains collaterally estopped from denying the admissions contained in that plea. Therefore, the State's Motion for Summary Judgment is DENIED as to Lilly's Fourth, Tenth, Nineteenth and Twentieth Affirmative Defenses

Lilly's Seventh Affirmative Defense asserts that the State's cause of action is preempted by the federal regulatory laws of the Food and Drug Administration. Lilly has admitted to misbranding Zyprexa as part of its plea agreement which is not an approved promotion of the product by the Food and Drug Administration. For that reason the State's Motion for summary judgment is GRANTED as to the Defendant's Seventh Affirmative Defense only for the period of time between September 1999 and March 2001 and only for the issues which were covered in the above referenced plea agreement. Therefore, said Defense is stricken for that limited time period and for the issues covered by the plea agreement.

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Lilly's Ninth Affirmative Defense asserts that it is protected under the commercial speech protections of the First Amendment. With regards to the admissions contained in Lilly's plea agreement and to Lilly's speech in labeling and marketing Zyprexa during that time period covered under the plea, the Court GRANTS the State's Motion for Summary Judgment as to Lilly's Ninth Affirmative Defense only for the period of time between September 1999 and March 2001 and for the issues covered by the plea agreement.

As to Lilly's Eleventh Affirmative Defense of Federal preemption, the Court GRANTS the State's motion for summary judgment based on my decisions concerning the issue of preemption and statutory construction which are discussed in detail below.

II. State's Motion for Non-Jury Determination of Violations and Penalties Under the South Carolina Unfair Trade Practices Act

The South Carolina Unfair Trade Practices Act ("SCUTPA") provides two distinct remedies, both of which the Attorney General in this case has brought an action under. In setting forth which body is to act under each code section, the statute refers to "the Court". S.C. Code Ann. § 39-5-110(a) allows the Attorney General to petition the Court for an assessment of civil penalties. Also, the Attorney General is moving under S.C. Code §39-5-140, an action by an entity to recover damages suffered as a result of a violation of the SCUTPA. From all of the information submitted to this Court, it appears that neither party is contesting the right to a trial by jury under §39-5-140.

At issue here is the State's claim that it is entitled to a determination by the judge, acting alone, under S.C. Code Ann § 39-5-110 that Lilly "has willfully used a method, act or practice declared unlawful by § 39-5-20...upon petition to the Court, may recover on behalf of the State a civil penalty." In its brief, the State cites two cases involving the application of this Code

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section, as indicating the right to a trial without a jury: State ex rel. v. Nest Egg Society Today, Inc., 290 S.C. 124, 348 S.E.2d 381 (Ct. App. 1986) and State exrel. McCleod v. C & L Corp. et. al., 280 S.C. 519, 313 S.E. 2d 334 (Ct. App. 1986). A review of these cases does indicate that they were tried without a jury. However, neither of the above cases directly addresses the issue of whether or not a jury trial is available as to the issues addressed in § 39-5-110 to those who demand such a trial. Parties do have the right to waive a trial by jury. One of the cases cited by the State in support of its position on this matter involved a decision by a "special referee" which is allowed under Rule 53, SCRPC by order of the Court or agreement of the parties. The fact that those two cases were tried by a judge or referee is not conclusive as to this issue.

The Court is aware that the parties in this case have requested a jury trial on all issues triable by jury. Further, Rule 38 of the South Carolina Rules of Civil Procedure states that the right of a trial by jury in the Constitution, or as given by statute in South Carolina, shall be preserved to the parties inviolate. Issues of fact *in an action for the recovery of money only*... must be tried by a jury, unless a jury trial be waived." Rule 38, SCRPC.

A great deal of argument was received by this Court concerning the proper interpretation of the word "court" as used in the code sections. In reading both § 39-5-110 and § 39-5-140, this Court finds that the word "court", when used in these sections, refers to either the judge, the jury or both, depending upon the underlying cause of action which is before the tribunal. The word "court" when used in these code sections must be taken in the context in which it is used. I find that this interpretation will more likely give effect to the Legislature's intent in enacting SCUTPA when the statute is reviewed as a whole.

It appears to this Court that neither party objects in § 39-5-140 to the words "the court" as referring to a judge and jury carrying out their respective responsibilities. This interpretation

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squares with Rule 38, SCRCP which provides for jury trials in actions for the recovery of money and § 39-5-140 involves an action for the *recovery of money*.

However, § 39-5-110 provides for a more punitive relief, that being the assessment of a civil penalty, and it is not designed to allow the "recovery of money" or the restoration of losses through the award of damages. Rule 38, SCRCP. Generally, under South Carolina law, judges acting without a jury assess penalties, criminal or civil in nature, in the form of fines, incarceration, and even civil penalties. Therefore, it is this Court's finding and it is ORDERED that the issue involving whether or not to assess the civil penalties provided for in §39-5-110 should be tried by a judge acting without a jury.

Having made the above Order, this Court, however, is mindful of the fact that courts generally attempt to avoid inconsistent verdicts or outcomes. The practical result of my decision on this issue could be considered as a de-facto bifurcation of the trial. That is one trial conducted by the judge acting alone and one trial before a jury. Under South Carolina Law, "a trial may be bifurcated only if the issues are so distinct that the trial of each alone would not result in an injustice." Fortune v. Gibson, 304 S.C. 279, 281, 403 S.E.2d 674, 675 (Ct. App. 1991). It is clear to this Court that a jury determination of the issues of fact under S.C. Code Ann. § 39-5-140 will be required to make a proper finding concerning *willfulness* and whether or not the conduct complained of constitutes a violation of the Act in order for them to reach a verdict in the case. Also, a judge looking at the same facts would be required to make a ruling as to the *willfulness* of the conduct and the nature of the conduct itself. My ruling on that issue, if given at this time concerning willfulness under § 39-5-110 and the nature of the conduct, could result in inconsistent verdicts given by the judge and jury and as a result an injustice.

Therefore, this Court will reserve its rulings concerning §39-5-110 until after a jury verdict has been issued in this case. This will allow for consistent verdicts from both the jury and the judge as to the willfulness of the conduct as well as to whether or not an act constitutes a violation of the SCUTPA. At that time if the jury verdict is favorable to the State, the Attorney General may petition the judge for an assessment of civil penalties of up to five thousand dollars per violation under § 39-5-110 and such other relief as is allowed by under SCUTPA.

Lilly's Motions for Summary Judgment and Partial Summary Judgment

I. Lilly's Motion for Summary Judgment on Statute of Limitations Grounds

The statute of limitations for a tort action is three years. S.C. Code Ann. § 15-3-530(5) (Supp. 2007) (stating the statute of limitations for "an action for assault, battery, or any injury to the person or rights of another, not arising on contract and not enumerated by law" is three years).

The limitations period begins to run when the facts and circumstances of an injury would be a person of common knowledge and experience on notice that some claim against another party might exist. Burgess v. Am. Cancer Soc'y, South Carolina Div., Inc., 300 S.C. 182, 186, 386 S.E.2d 798, 800 (Ct.App.1989); See also S.C. Code Ann. § 15-3-535 (Supp. 2007) ("[A]ll actions initiated under Section 15-3-530(5) must be commenced within three years after the person knew or by the exercise of reasonable diligence should have known that he had a cause of action."); Epstein v. Brown, 363 S.C. 372, 376, 610 S.E.2d 816, 818 (2005) (noting that under the discovery rule, the statute of limitations begins to run from the date the injured party either knows or should know, by the exercise of reasonable diligence, that a cause of action exists for the wrongful conduct). The standard as to when the limitations period begins to run is objective rather than subjective. Burgess, 300 S.C. at 186, 386 S.E.2d at 800. Moreover, "[t]he statute is not delayed until the injured party seeks advice of counsel or develops a full-blown theory of



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recovery; instead, reasonable diligence requires a plaintiff to act with some promptness.” Maher v. Tietex Corp., 331 S.C. 371, 377, 500 S.E.2d 204, 207 (Ct.App.1998) (internal citations omitted).

As pointed out in the Lilly’s Motion for Summary Judgment on Statute of Limitations grounds, it correctly states that the conduct about which it is complaining in this case is as follows:

1. Medicaid Fraud: the act of concealment by Lilly of its promotion of Zyprexa for medically unnecessary uses and the submission of false claims or same.
2. Unfair Trade Practices: deceptive promotions, misrepresentations and concealment of information about the safety and efficacy of Zyprexa for non-approved uses. This allegedly caused South Carolina physicians to write prescriptions for medically unnecessary purposes.
3. Negligence: This includes the careless and reckless promotion of Zyprexa, such as use in children and the elderly in South Carolina without adequate testing or scientific grounds.
4. Fraud: Intentionally withholding from, and affirmatively misrepresenting, Zyprexa to South Carolina physicians.

The information cited by Lilly stating that the Plaintiff should have been on notice that it had a claim or potentially had a claim is separate and distinct from the wrongs alleged by the State. Knowledge by the State that Zyprexa may have contributed to weight gain, diabetes or related diseases or that some doctors were writing prescriptions for Zyprexa for off-label uses (a practice that is legally permitted) does not place the State on notice that Lilly is involved in any of the enumerated wrongful acts above.

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Further, the antidotal information concerning recruitment of individuals for class actions against Lilly (for unspecified wrongs), or that cases may be being filed against Lilly in inferior courts in other states also does not rise to the level of putting the State on notice that Lilly was involved in any of the above specified wrongs. Lilly in its brief makes no argument and reveals no facts concerning the above specified incidences of wrongdoing, of which the State was aware or should have been aware prior to February 27, 2004 or 2005.

If it is true that Lilly did in fact conceal the evidence of its wrongful and fraudulent conduct, which could and would serve as a basis for an equitable tolling of the Statute of Limitations. Such a course of conduct has been alleged to have been conducted by Lilly from the beginning of its marketing of Zyprexa. If true, this could serve as a basis for equitable tolling of the SOLs. However, because of the Court's findings above, such a determination is not necessary at this time.

In this case at the very least there is a substantial conflict of evidence as to the date upon which the statute of limitation would have begun to run. In such cases "when there is conflicting testimony regarding the time of discovery, it becomes an issue for the jury to decide." Arrant v. Kressler, 489 S.E. 2d 206 (S.C. 1997)

Based on the above foregoing evidence, it is ORDERED that the Defendant's Motion for Summary Judgment on the Statute of Limitations be DENIED.

II. Lilly's Motion for Partial Summary Judgment on Unjust Enrichment Claim

Lilly moves for Partial Summary Judgment on the State's Unjust Enrichment Claim. The primary basis for doing so is that equitable relief is generally available only where there is no adequate remedy at law. Santee Cooper Resort Inc. v. South Carolina Public Service Com'n, 298 S.C. 179, 379 S.E.2d 119 (1989). The Court notes that Lilly has filed motions for summary

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judgment as to all causes of action advanced by the State. These motions have been hotly contested and more than likely this court's rulings will be subject to further review. Based on this Court's rulings, it would appear that the state does have remedies at law; however, should this Court's ruling not be upheld, it could very well be true that the State is without an adequate remedy at law. Actions in equity are triable by a judge sitting without a jury. This Court sees no need for this issue to be fully determined at this time. Therefore, this court stays the cause of action for unjust enrichment until such time as a final adjudication on all other issues in the case are decided. At that time, this Court will then consider this motion as well as the cause of action for Unjust Enrichment in light of the final rulings in this case. Therefore, the Motion for Partial Summary on the Unjust Enrichment is STAYED.

III. Lilly's Motion for Partial SJ on Breach of Warranty

The State asserts breach of express and implied warranty claims. Lilly argues that it is entitled to summary judgment because the State has failed to present evidence that the State is a party to which warranties were made, and that the State cannot identify "a single actual warranty made by Lilly to any actual physician". (Lilly's Mot. for Summary Judgment p. 4). The South Carolina Commercial Code states, "A seller's warranty whether express or implied extends to any natural person who may be expected to use, consume or be affected by the goods and whose person or property is damaged by breach of the warranty. A seller may not exclude or limit the operation of this section." S.C. Code Ann. § 32-2-318. For the purposes of interpretation of the language of the Code, the definition of person "includes an individual or an organization". S.C. Code Ann. § 32-1-201(30). The standard set forth in the Code states that it "shall be liberally construed and applied to promote its underlying purposes and policies." S.C. Code Ann. § 36-1-102(1). Furthermore, South Carolina courts have consistently held that lack of privity is not a

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defense in breach of warranty actions, and that it would be unfair to distinguish between corporate plaintiffs and consumer plaintiffs based on privity. JKT Co., Inc. v. Hardwick, 274 S.C. 413, 418, 265 S.E.2d 510, 512 (S.C. 1980).¹

This Court cannot ignore the language of our State's Commercial Code and the relevant case law. I find that any warranties made by Lilly can be extended to the State as a third party beneficiary since South Carolina was the entity that ultimately paid for portions, if not all, of the costs of prescriptions for Zyprexa through Medicaid reimbursements to doctors and pharmacies, and those prescriptions were consumed and taken by individuals to whom the State owed a duty. In addition, there appears to be a genuine issue of material fact relating to the establishment of and subsequent breach of warranties by Lilly, and therefore, summary judgment is DENIED.

IV. Lilly's Motion for Partial Summary Judgment on Count III (Strict Liability) of the State's Complaint

Lilly moves under SCRCP Rule 56 for Summary Judgment as to Count III of the Complaint which is a cause of action based on a products liability strict liability. S.C. Code Ann. § 15-73-10 codifies the right of a consumer to bring an action based on strict liability. Subsection (1) provides "One who sells any product in a defective condition unreasonably dangerous *to the user or consumer*, or to his property ...". In this case, Lilly argues that the

¹ "South Carolina is in the vanguard in permitting a plaintiff to recover economic loss from a seller with whom he did not deal and who made no express warranties to him. See White & Summers, supra, at page 333. We can perceive no valid reason why we should erect an artificial line distinguishing between consumer plaintiffs and corporate plaintiffs on the issue of privity. It would be patently unfair to allow a manufacturer of a defective product to escape liability via privity when the plaintiff is an individual, so it is unfair to disallow recovery when a corporation brings suit. There is no justifiable reason why an innocent corporate consumer should be denied recovery when a manufacturer places a defective article into commerce. The same rule should apply to corporate transactions as to consumer purchases. JKT Co., Inc. v. Hardwick, 274 S.C. 413, 418, 265 S.E.2d 510, 512 (S.C., 1980).

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State is not a "user or consumer" of the product in question and, therefore, has no standing to sue under §15-73-10.

The State argues that it has the right to sue on behalf of those who may have been affected by the misbranding of Zyprexa under the legal doctrine of *parens patriae*. It argues that the Attorney General has the legal duty and right to bring actions on behalf of the people of the State of South Carolina in order to protect the health and public interests of a significant portion of the citizens of the State. The Attorney General claims to have the duty to "exercise all such power and authority as public interest may, from time to time require, and may institute, conduct, and maintain all such suits and proceedings as he deems necessary for the enforcement of the laws, the preservation of order and the protection of public rights." State ex rel. Condon v Hodges, 349 S.C. 232, 239, 562 S.E.2d 623, 627 (2002).

The cardinal rule of statutory construction is to ascertain and effectuate the intent of the legislature. State v. Pittman, 373 S.C. 527, 561, 647 S.E.2d 144, 161 (2007). Thus, in interpreting statutes, we look to the plain meaning of the statute and the intent of the legislature. State v. Gaines, 380 S.C. 23, 32, 667 S.E.2d 728, 733 (2008). A statute's language must be construed in light of the intended purpose of the statute. Id. at 33, 667 S.E.2d at 733.

Whenever possible, legislative intent should be found in the plain language of the statute itself.

"Where the statute's language is plain and unambiguous, and conveys a clear and definite meaning, the rules of statutory interpretation are not needed and the court has no right to impose another meaning." Pittman, 373 S.C. at 561, 647 S.E.2d at 161 (citing Hodges v. Rainey, 341 S.C. 79, 85, 533 S.E.2d 578, 581 (2000)). See also State v. Bolin, 381 S.C. 557, 673, S.E.2d 885, 886 (S.C. App. 2009).

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Here, it is clear that the legislative intent is to create a cause of action to protect users or consumers of a defective product and be free of common law defenses to such actions such as a lack of privity, etc. It allows redress from the manufacturer of a product for an injury caused by a manufacturing defect in the product done to an individual or entity which used or consumed the product, if the product was defective when placed in the stream of commerce and arrived in the users hands in an unaltered condition. I do not see any effort on the part of the legislature to include the protection of the public as a whole in actions for strict liability or allow state intervention in that right. Unlike actions under the SCUTPA statutes, actions under this code section do not require the elements of potential for repetition or the involvement of a public interest. Therefore, actions for strict liability are personal in nature and do not involve a public protection element.

Lilly argues that to allow the Attorney General to appear as a Plaintiff asserting strict liability cause of action would in effect allow the Attorney General to rewrite the statute since it only created the cause of action for users and consumers. However, this Court's understanding of the *parens patriae* doctrine is that the Attorney General may act as party on behalf of the aggrieved party by standing in the aggrieved party's shoes. I do not find this to be a rewriting of the statute.

The real issue here is whether or not the doctrine of *parens patriae* authorizes the Attorney General to bring this action on behalf of those users and consumers injured by the alleged defective condition of the product Zyprexa. The doctrine of *parens patriae* applies only to sovereigns asserting at least "quasi-sovereign" interests apart from the interests of particular private citizens. Alfred L. Snapp & Son, Inc. v. Puerto Rico, 458 U.S. 592, 608, 102 S.Ct. 3260, 3269 (1982). Therefore, to allow suit in this case the State would have to be protecting some

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quasi-sovereign interest. In this case, the Plaintiff asserts that it seeks to protect the health and welfare of the portion of the population who were allegedly subjected to ingesting medically unnecessary prescriptions with potentially dangerous side effects. Further, the State claims an interest since state programs and funds were subverted to allow Zyprexa to be consumed by these individuals to their detriment.

Further, it should be noted that Article 12 § 1 of the South Carolina Constitution states, "The health, welfare, and safety of the lives and property of the people of this State and the conservation of its natural resources are matters of public concern. The General Assembly shall provide appropriate agencies to function in these areas of public concern and determine the activities, powers, and duties of such agencies." Based on this and other constitutional provisions the General Assembly provided authority to the Attorney General in the following form, " He shall appear for the State in the Supreme Court and the Court of Appeals in the trial and argument of all causes, criminal and civil, in which the State is a party or interested, and in these causes in any other court or tribunal when required by the Governor or either branch of the General Assembly." S.C. Code Ann. § 1-7-40.

Our courts have recognized the authority of the Attorney General to appear in the courts of this state in *parens patriae*. In one case involving the intervention by the Attorney General in a street closing issue, the court recognized the Attorney General's authority to appear on behalf of the citizens of the state, but the Supreme Court refused to delineate the extent of his authority to do so by saying, "In the light of the view we take of the proof, we find it unnecessary to delicately determine the authority of the Attorney General and to precisely define that authority. For the purpose of the opinion we will assume that he had authority to institute the proceeding." State v. Beach Co., 271 S.C. 425, 248 S.E.2d. 115, 118 (S.C. 1978).

There appears to be no judicial decision which would allow the Attorney General the right to bring a civil suit for damages under the doctrine of *parens patriae*, and there is no authority which prevents it as well. This therefore is a novel issue. In many of the cases reviewed by this court from various jurisdiction there seems to be agreement the extent to which the public interest are affected by the conduct alleges is one of the deciding factors as to whether or not the State is allowed to proceed in *parens patriae*. Our courts have said, "Summary judgment is not appropriate where further inquiry into the facts of the case is desirable to clarify the application of the law." Gadson v. Hembree, 364 S.C. 316, 320, 613 S.E.2d 533, 535 (2005); Montgomery v. CSX Transp., Inc., 362 S.C. 529, 608 S.E.2d 440 (Ct.App. 2004). "Even when there is no dispute as to evidentiary facts, but only as to the conclusions or inferences to be drawn from them, summary judgment should be denied." Nelson v. Charleston County Parks & Recreation Comm'n, 362 S.C. 1, 5, 605 S.E.2d 744, 746 (Ct.App. 2004); Bennett v. Investors Title Ins. Co., 370 S.C. 561, 635 S.E.2d 660 (Ct.App. 2006).

This Court finds that a further development of the facts as to the scope and severity issues involved in this case, the potential damages cause by he public problem and the degree to which victims of the alleged conduct are able to assert their own protection is necessary, and therefore summary judgment is DENIED.

V. Lilly's Motion for Partial Summary Judgment on State's Negligence Claim

Lilly moves for Summary Judgment as to Plaintiff's cause of action on negligence. It argues that in order to sustain a cause of action the State must establish (1) that Lilly owed a legal duty to the State, (2) that Lilly breached the duty owed to the State, (3) that the State suffered damages as a proximate result of the breach of the duty owed by Lilly. Lilly takes the position that there was no relationship between itself and the State that would give rise to a duty

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under the law since their relationship was too remote. The State takes the position that Lilly is one of primary providers of anti- psychotic drugs to clients of the State programs involved in this suit. Annually the state reimburses the costs of these drugs to the providers of them, who in turn rely upon representations made by Lilly in the marketing of these drugs.

“The question of whether or not a duty exists as the result of a given factual situation is resolved by the judge, not the jury. There exists no general test or rules for how a court determines the existence of a duty.” F. P. Hubbard and R.L. Felix, 2 South Carolina Law of Torts 42 (3rd Ed. 2004).

There is no formula for determining duty: a duty is not sacrosanct in itself, but only an expression of the sum total of those considerations of policy which lead the law to say that a particular plaintiff is entitled to protection. Suffice it to say that a number of factors come into play when courts contemplate the question of duty. Those factors include the policy of deterring future tortfeasors, the moral culpability of the tortfeasor and numerous other conceivable factors; duty is seen in general terms as requiring a person or corporation to conform his or its conduct to a standard which is adequate to protect others from unreasonable risk of harm.

Araujo v. Southern Bell Tel. & Tel. Co., 291 S.C. 54, 57-58 (Ct. App. 1986).

In this case there is some evidence in the record that; 1) Lilly marketed its drug Zyprexa in a false and misleading manner not approved by the regulatory agencies, (2) it promoted its drug for uses for which it was not approved, (3) it withheld scientific studies that would have informed the public, its own sales force and the regulatory agencies of adverse effects of the use of the drug resulting in unnecessary cases of obesity and diabetes, (4) its marketing scheme took direct action to obtain favorable legislation so that prescriptions for Zyprexa would not be scrutinized (open access) (5) intentionally mislead prescribers concerning the side effects and the proper uses of the drug. Lilly took all of these actions while being aware that one of the primary sources of the funds for payment for these prescriptions would be the various programs paid for and operated by the State of South Carolina. This Court finds that policy considerations

involved in the above factors, which if true, would be of considerable importance to the State and its agencies. Such conduct, if true, involves massive and costly frauds perpetrated upon the public, regulatory agencies, payers, the public and the medical community. This Court should consider that this activity (if true) is such that those who would have been foreseeably affected by them should be entitled to protection under the law in the form of a recognition of a duty owed to those who might be affected by the perpetrator.

Lilly takes the position that it bears no direct relationship with the state in these transactions, and therefore owes no duty to the State. Our State Supreme Court has recognized that a direct relationship is not required between parties for a duty to be found. In South Carolina State Ports Authority v. Booz-Allen & Hamilton, 289 S.C. 373, 346 S.E.2d 324 (1986), a duty was found to exist owed by the Defendant consulting firm to the S.C. Ports Authority for misstatements made in a consulting report prepared for the Georgia Ports Authority. That was true even though the South Carolina agency had no direct relationship with the Defendant consulting firm. In the above referenced case the court reasoned that, "Liability for negligence in preparing reports has been extended to parties other than those who were parties to the contract in certain circumstances." 57 Am. Jur.2d Negligence, § 51. Consultants such as BAH may be found liable in negligence to non-contracting parties who have reasonably relied on their reports in taking some action. Stagen v. Stewart-West Coast Title Company, 149 Cal.App.3d 114, 196 Cal.Rptr. 732 (2d Dist, 1983); Carlotta v. T.R. Stark & Associates, Inc., 57 Md.App. 467, 470 A.2d 838 (1984). We hold a duty to use due care, running from a consultant to the commercial competitor who is being critiqued, arises when the consultant undertakes to objectively analyze and compare the attributes of commercial competitors for the purpose of giving one a market advantage over

the other. South Carolina State Ports Authority v. Booz-Allen & Hamilton, Inc., 289 S.C. 373, 377, 346 S.E.2d 324, 326 (S.C. 1986).

This Court finds a similar duty runs from a party who undertakes to inform the public and prescribing physicians concerning the proper considerations in deciding if the drug is question is “medically necessary” for treatment and for State reimbursement plans. That duty runs to those who would be foreseeably affected by those decisions. When considering the factor of the allegations made in this case as stated above, public policy requires such a duty to be recognized. Foreseeability of injury to the State in this case exists. The motion is DENIED.

VI. Lilly’s Motion for Partial Judgment on State’s SCUTPA Claim

Lilly moved for Summary Judgment under SCRCP, Rule 56 as to the claim by the State that Lilly violated the South Carolina Unfair Trade Practices Act (“SCUTPA”) contained in S.C. Code § 39-5-10. Lilly claims that the motion should be granted as to all of the following reasons. The State opposes the motion as to all of the stated reasons.

- 1) The State cannot establish that Lilly engaged in any unfair or deceptive acts.
- 2) An FDA approved label cannot constitute a violation of SCUTPA.
- 3) The claims of the State interfere with the FDA’s regulation of prescription drugs.
- 4) There is no private right of action under the Food Drug & Cosmetics Act.
- 5) Imposing a penalty under SCUTPA for the period of time from 1996 through 2007 would constitute a violation of Lilly’s due process rights.
- 6) That the imposition of civil penalties would offend Lilly’s substantive due process rights.

A) *The State cannot establish that Lilly engaged in any unfair or deceptive acts.*

Lilly argues that the record is void of any evidence that it engaged in any unfair or deceptive acts and goes through a description of what types of acts would be considered deceptive or unfair. It states that the State was aware of off-label prescriptions being written by

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South Carolina prescriptions and of the adverse effects that the drug Zyprexa could cause. Therefore, the State or its agencies could not have been deceived by Lilly's alleged actions.

The State argues that Lilly has admitted to conduct which would constitute an unfair or deceptive act in its Guilty Pleas in Federal Court in January of this year. Further, that the State alleges that it has produced evidence of Lilly's deceptive conduct in withholding scientific research from its staff and regulators, it has produced Lilly call notes which reflect deceptive practices in its dealings with physicians practicing in this State, and testimony from a South Carolina physician that he was deceived by Lilly's marketing efforts. As to off-label prescribing of Zyprexa by South Carolina physicians, the State argues that such activity by doctors is not illegal. Doctors have a legal right to issue such prescriptions. However, the State says that such activity does not in and of itself put the State on notice as to the allegedly deceptive and unfair practices that might be precipitating such activity.

This Court notes that this is a motion for Summary Judgment, and as such, the limits of this court's inquiry have been previously stated. Based on a careful review of the evidence presented and taking all inferences that can be gleaned from that evidence in the light most favorable to the non-moving party, I find that there are genuine issues of fact as to relevant matters in controversy as to this issue.

B) An FDA approved label cannot constitute a violation of SCUTPA.

Lilly argues that under the plain language of SCUTPA, the FDA approved Zyprexa label does not constitute a violation of the act. They make this statement based on the contention that the use of an FDA approved label cannot be the "willful" use of a false or deceptive trade practice.

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The State argues that Lilly had the right and the opportunity to change its labeling at any time. It alleges that federal law allows a drug manufacturer to amend its label at any time when there is a reasonable association made with the drug Zyprexa and a serious hazard. 21 C.F.R. §201.57. In addition, 21 CFR §201.80(e) requires a manufacturer to amend its label when safety of the public dictates such a change. The State has produced evidence that Lilly had in its possession studies and adverse reaction reports that it alleges should have made Lilly aware of needed changes to the indications for which the drug should be offered and the warnings that should have been issued. The State points out that Lilly cites no authority for the proposition that an FDA approved label can never constitute a SCUTPA violation.

It appears to this Court that the activities about which the State is complaining is the failure of Lilly to make the FDA aware of the studies and adverse reaction reports that it allegedly had in its possession so that its label might amended to add more restrictions as to the drug's uses. Also, the State alleges that Lilly failed to take advantage of the federal regulations that allowed it to voluntarily and unilaterally amend its labeling so as to make warning about the drug or uses of the drug more restrictive. The U.S. Supreme Court in Wyeth v. Levine recently noted:

There is, however, an FDA regulation that permits a manufacturer to make certain changes to its label before receiving the agency's approval. Among other things, this "changes being effected" (CBE) regulation provides that if a manufacturer is changing a label to "add or strengthen a contraindication, warning, precaution, or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product," it may make the labeling change upon filing its supplemental application with the FDA; it need not wait for FDA approval. §§ 314.70(c)(6)(iii)(A),(C).

Wyeth v. Levine, 129 S. Ct. 1187 at 1197 (2009).

Based upon Lilly's ability to make unilateral amendments to its labeling and the further facts concerning their marketing and labeling methods which have been demonstrated to this

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Court as being in controversy this Court finds as a matter of law that the fact that an FDA approved label is in effect does not bar an action under the SCUTPA.

C) The claims of the State interfere with the FDA's regulation of prescription drugs.

Rather than go through a detailed discussion of this portion of Lilly's motion, the Court notes that it has reviewed the recent decision in the Wyeth case cited above, and based upon my understanding of that case and the legal principles stated therein, this Court finds Lilly's position concerning this point to be without merit, and therefore, this portion of the motion is DENIED.

D) There is no private right of action under FDCA.

Rather than restate each party's position in regard to this issue, to the extent that the Plaintiff in this case might be seeking to bring a private cause of action based of the FDCA the motion would be granted. However it is clear to this Court that the Plaintiff is not seeking to do so. In one of the cases cited by the Defendant, In re Epogen & Aranesp Off-Label Mktg. & Sales Practices Litig., the California District Court stated "To the extent that the Plaintiffs allege that the defendants made false statements or deliberately concealed material facts in order to mislead health care professionals and consumers about the safely of [the drug at issue], those claims are viable...". 590 F. Supp. 2d 1282, 1291 (C.D. Cal. 2008). In the present case, Lilly failed or refused to inform this Court of this portion of the holding in this case in its arguments to the Court. The State's case, in which it bases its allegations upon false and misleading actions of the Defendant Lilly in marketing the drug Zyprexa, is exactly the type of claim being made in the above noted Epogen decision. This Court refuses to find that the Plaintiff is seeking to bring a private cause of action under the U.S. Food Drug and Cosmetics Act. Therefore, this portion of the motion is DENIED.

E) Imposing a penalty under SCUTPA for the period of time from 1996 through 2007 would constitute a violation of Lilly's due process rights.

F) *That the imposition of civil penalties would offend Lilly's substantive due process rights.*

As to the above issues raised by the Defendant, it is this Court's finding that they are not ripe for argument or decision at this time and will be preserved until such time as the court might be in a position to decide the issue of SCUTPA penalties

VII. *Lilly's Motion for Partial Summary Judgment on its SCUTPA Claim based on Statutory Construction*

Lilly moves for partial Summary Judgment based on the construction of the SCUTPA. It argues the following issues in that regard:

A) *Lilly's alleged actions are exempt from liability under SCUTPA because they were allowed and authorized by the FDA.*

Lilly argues that SCUTPA does not apply to "actions or transactions permitted under laws administered by any regulatory body or officer acting under authority of the State or the United States...." S.C. Code Ann. § 39-5-40(a). The primary case that it asserts in support of its position on this issue is InMed Diagnostic Services, LLC v. MedQuest Associates, Inc., 358 S.C. 270, 594 S.E. 2d 552, (Ct. App. 2004). In InMed, the Plaintiff sued the defendant under SCUTPA for having misrepresented information submitted to SCDHEC in an application for a certificate of need to be issued by that agency. The court barred the SCUTPA claim on the basis that SCDHEC had in place regulatory procedures to handle the application in question. It further found that the application process should be the proper means for resolving that issue rather than by the court. Lilly argues that the same reasoning should apply in this case since Zyprexa's labeling was FDA approved and therefore the FDA is the proper body to regulate that labeling.

The State argues that South Carolina abandoned the "general activities" test in considering the exemption from SCUTPA contained in §39-5-40(a), citing the opinion in Ward

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v. Dick Dyer & Associates, 304 S.C. 152, 403 S.E. 2d 310 (1991). It argues that the activities that it is complaining of are not authorized or permitted by the federal regulatory scheme, and therefore, are not protected from application of SCUTPA.

This Court does not find the InMed case to be particularly useful in this analysis. It is clear that when dealing with false information contained in an application document submitted directly to a state regulatory agency for the purpose of having that agency act upon that application, that such matters would be within the regulatory jurisdiction of that agency. The issues involved in this case revolve around the alleged systematic misrepresentation of the usefulness of a drug, its side effects on the using public as well as the agencies that paid for the drug, and for the consequences of the side effects. These are consumer protection issues which are precisely the issues concerning which the South Carolina Legislature enacted SCUTPA.

Ward abandoned the "general activities" test, and subsequently adopted the language of a Tennessee case stating:

In Skinner v. Steele, 730 S.W.2d 335 (Tenn.App.1987), the Tennessee court construed a similar statutory exemption and found that only those activities which were specifically authorized by a regulation or another statute were exempt. In discussing this ruling, the court explained as follows: The purpose of the exemption is to insure that a business is not subjected to a lawsuit under the Act when it does something required by law, or does something that would otherwise be a violation of the Act, but which is allowed under other statutes or regulations. It is intended to avoid conflict between laws, not to exclude from the Act's coverage every activity that is authorized or regulated by another statute or agency. Virtually every activity is regulated to some degree. The defendant's interpretation of the exemption would deprive consumers of a meaningful remedy in many situations. We find this reasoning persuasive and applicable to our statutory exemption...

Ward v. Dick Dyer and Associates, Inc. 304 S.C. 152, 156, 403 S.E.2d 310, 312 (S.C. 1991).

The FDA does not allow or authorize the illegal or deceptive activities that the Plaintiff alleges to have occurred in this case. Further, it would appear that Lilly had the right to update its labeling, without regulatory approval, when information in its possession would indicate that

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such an update was necessary to protect any member of the public who might be affected by the sale, distribution or use of Zyprexa. See 21 CFR §201.57.

This Court does not interpret the SCUTPA to create a "safe harbor" for the alleged activities of Lilly in the marketing and labeling of its drug Zyprexa. The exemption of §39-5-40(a) does not bar this claim. Therefore, this portion of Lilly's Motion for Summary Judgment is DENIED.

B) *The Attorney General lacks standing to seek actual and treble damages under the SCUTPA.*

Lilly argues that the only relief that the Attorney General may pursue in this case is the relief that is authorized under Sections 39-5-50 and 39-5-100 of the SCUTPA. In Section 50, the Attorney General may seek an injunction to prevent the violation of the Act, and the court may order as a result thereof restoration of losses and costs and fees. Section 100 requires compliance with the act in the event of an investigation by the Attorney General and allows for an assessment of civil penalties for individuals who fail to cooperate.

The State argues that the Attorney General may, through the exercise of its authority under the *parens patriae* doctrine bring action on behalf of the effected persons. It alleges that this is not a suit being brought in a "representative" capacity which is prohibited under SCUTPA Section 39-5-140(a). That section states:

Any person who suffers any ascertainable loss of money or property, real or personal, as a result of the use or employment by another person of an unfair or deceptive method, act or practice declared unlawful by Section 39-5-20 may bring an action individually, but not in a representative capacity, to recover actual damages. If the court finds that the use or employment of the unfair or deceptive method, act or practice was a willful or knowing violation of Section 39-5-20, the court shall award three times the actual damages sustained and may provide such other relief as it deems necessary or proper. Upon the finding by the court of a violation of this article, the court shall award to the person bringing such action under this section reasonable attorney's fees and costs.

S.C. Code Ann. § 39-5-140(a)

For purposes of this discussion the court refers to its discussion on p. 15, Section D of this Order (Lilly's Motion for Partial Summary Judgment on Count III) concerning the right of the Attorney General to sue as *parens patriae*. I would add to that discussion that "*parens patriae*" means "parent of his or her country", and refers to the state in its capacity as the provider of protection to those unable to care for themselves." 72 Am. Jur.2d States § 90 (May 2009).

In this case, I am surprised by the fact that most of the members of the public who involved in this case are economically disadvantaged individuals who suffer from such debilitating conditions as schizophrenia, bi-polar mania, alzheimers, children, and dementia. They were in these programs because they could not pay for or arrange for their own care. In other words, they were unable to care for themselves.

When looking to the purpose of SCUTPA, one comes to the conclusion that the legislature intended cast a wide net for causes of action in order to prevent and discourage deceit and fraud perpetrated on both the public at large and the business community of this state. It is clear that the legislature speaks in broad terms as to the activities that it seeks to make actionable and allows various avenues of enforcement of its prohibitions. Once a deceptive or unfair act in the commerce of is state is identified as affecting the public interest as a whole, and as such, the act is capable of repetition; then it would seem that the legislature seeks broad enforcement of the act.

In reviewing the above issues I found that the discussion in City of Charleston, S.C. v. Hotels.com, LP, 520 F.Supp.2d 757 (D.S.C. 2007) is relevant concerning the broad enforcement of SCUTPA. In that case the City of Charleston brought action against Hotels.com under the

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SCUTPA for charging consumers, on a national basis, a hospitality tax which it represented to be for a City tax. Instead of remitting the funds to the City (which it was under no apparent obligation to do in the first place) Hotels.com kept the funds thus collected as additional profit. Charleston was not a party to the transactions, had no right to collect the tax, and had no contractual connection with Hotels. In determining the legislative intent of SCUTPA and whether it would apply to this relationship, Judge Duffy held that the Defendants are clearly involved in trade and commercial activity of the type that legislators intended to regulate by enacting SCUTPA. He took this action in spite of the lack of close connection between the City and the defendant and the fact that the victims could have protected themselves. It appears he looked to the nature of the wrong and its relationship to public policy considerations in finding the City could proceed. In reviewing SCUTPA as a whole it is clear to me that the legislature intended to provide many avenues for the enforcement of its prohibitions. Therefore, I find that the Attorney General is given enforcement authority under SCUTPA by acting in *parens patriae*.

Also, the action before the Court is an attempt to recover on behalf of the agencies that were allegedly directly affected by the alleged unfair and deceptive conduct of the Lilly in its marketing scheme. Under the SCUTPA a "person" includes "natural persons...and any other legal entity" S.C. Code Ann. § 39-5-10(a). I find that it is clear that the Attorney General has the right and authority, if not the duty to bring actions on behalf of state agencies in just such situations as are alleged here.

Motion is DENIED.

VIII. Lilly's Motion for Summary Judgment regarding State's Medicaid Claims

The State is seeking penalties and damages against Lilly under the false claims provision of South Carolina's Medicaid Fraud Statute, based on the alleged submission of false and

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fraudulent claims under the State Medicaid Program. Lilly argues it is entitled to summary judgment on these claims because the State has failed to present evidence that it is a "provider" under the statute and that subrogation is the only remedy afforded to the State by statute.

A) *Is Lilly entitled to Summary Judgment because it does not fall under the definition of "provider" under the SC Medicaid False Claims Act?*

South Carolina's Medicaid False Claims Act makes it unlawful "for a provider of medical assistance, goods, or services to knowingly and willfully make or cause to be made a false claim, statement or representation of a material fact...and knowingly and willfully to conceal or fail to disclose any material fact, event, or transaction...". S.C. Code Ann. § 43-7-60. Section 43-7-60(A)(1) states that a "provider" includes "a person who provides goods, services or assistance and who is entitled or claims to be entitled to receive reimbursement, payment or benefits under the state's Medicaid program. 'Provider' also includes a person acting as an employee, representative, or agent of the provider. S.C. Code Ann. § 43-7-60(A)(1). The General Assembly defines "person[s]" to include "firms, companies, associations and corporations..." S.C. Code Ann. § 2-7-30. Further, the statute makes "it unlawful for a provider of medical assistance, goods or services to knowingly and willfully make or cause to be made a false claim, statement, or representation of material fact..." S.C. Code Ann. § 43-7-60(B).

A choice of language in a act will not be construed with literality when to do so will defeat the lawmakers' manifest intention, and a court will reject the ordinary meaning of words used in a statute when, to accept the ordinary meaning, will lead to a result so plainly absurd that it cannot possibly have been intended by the legislature. Hodges v. Rainey, 341 S.C. 79, 85-88, 533 S.E.2d 578, 581 - 582 (S.C. 2000); citing South Carolina Board of Dental Examiners v. Breeland, 208 S.C. 469, 480, 38 S.E.2d 644, 650 (1946) (citations omitted). If the language of an act gives rise to doubt or uncertainty as to legislative intent, the construing court may search

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for that intent beyond the borders of the act itself. Morgan, 352 S.C. at 367, 574 S.E.2d at 207; See also Wade v. Berkeley County, 348 S.C. 224, 229, 559 S.E.2d 586, 588 (2002) (“[W]here a statute is ambiguous, the Court must construe the terms of the statute.”). An ambiguity in a statute should be resolved in favor of a just, beneficial, and equitable operation of the law. City of Sumter Police Dep't v. One 1992 Blue Mazda Truck, 330 S.C. 371, 376, 498 S.E.2d 894, 896 (Ct.App.1998). In construing a statute, the court looks to the language as a whole in light of its manifest purpose. State v. Dawkins, 352 S.C. 162, 166, 573 S.E.2d 783, 785 (2002); Adams v. Texfi Indus., 320 S.C. 213, 217, 464 S.E.2d 109, 112 (1995).

This Court finds that the statute at issue is sufficiently broad to include Lilly as a provider, since ultimately Lilly received benefits in the form of profits as a result of its marketing Zyprexa in South Carolina. In addition, the statute also indicates that it is sufficiently broad to include providers who “knowingly and willfully make or cause to be made a false claim, statement or representation of material fact”. S.C. Code Ann. § 43-7-60(B). Lilly allegedly engaged in false and misleading advertising of the drug Zyprexa to prescribers across South Carolina, which in turn realized enormous profits for Lilly. Again, Section 43-7-60(A)(1) states that a “provider” includes “a person who provides goods, services or assistance and who is entitled or claims to be entitled to receive reimbursement, payment, or benefits under the state’s Medicaid program”. There is evidence that Lilly realized profits through the misleading advertising and lobbying efforts of its very own employees. I find that Lilly falls within the ambit of the statute as a “provider”, since there is evidence that Lilly knowingly marketed and lobbied Zyprexa for unapproved, off-label uses through its employees to South Carolina prescribers and legislators, and in-turn realized profits. This Court cannot overlook that Lilly ultimately, although indirectly, received benefits through the Medicaid program. In light of the

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evidence presented to this Court, I find that the Medicaid False Claims Act is sufficiently elastic to support a cause of action by the State against Lilly.

B) *Is Lilly entitled to Summary Judgment because subrogation is the only remedy afforded to the state by statute?*

The doctrine of *expressio unius est exclusion alterius*, provides that “to express or include one thing implies the exclusion of another, or of the alternative.” Black’s Law Dictionary 602 (7th ed. 1999). See also Hodges v. Rainey, 341 S.C. 79, 86-87, 533 S.E.2d 578, 582 (S.C. 2000). Lilly argues that the doctrine of *expressio unius est exclusion alterius* precludes the State from pursuing any other remedy outside of subrogation, as afforded under Section 43-7-410. This Court disagrees with Lilly’s contention.

Section 43-7-410 provides the Department of Health and Human Services an “automatic” remedy to seek reimbursement from a third party or private insurer on behalf of an “applicant or recipient” under the Medicaid program. This section is intended to be a separate and distinct avenue (from the remedies afforded under the Medicaid Fraud Statute § 43-7-60) for the state to essentially “close the loophole” and avoid an windfall or double payment where recipients eligible for Medicaid also receive payment for the same medical procedure or service by their own private insurer. Section 43-7-410 gives the Department of Health and Human Services the ability to seek reimbursement, “only to the extent of the amount of medical assistance paid by Medicaid”, from a third party or private insurer when an applicant or recipient has received payment or benefits from a third party or private insurer. Thus, it is this Court’s interpretation that § 43-7-410 expressly grants the Department the right to subrogation, in order to prevent applicants or recipients of State Medicaid benefits from receiving any windfall. Lilly’s argument that the State is precluded from bringing action under the Medicaid Fraud Statute is without merit. It is this Court’s opinion that the subrogation and fraud statutes are intended to work

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interchangeably, to promote efficiency, provide a remedy in light of overpayment of benefits to the applicant or recipient of Medicaid, and provide a cause of action and damages for defrauding the Medicaid system.

In light of the foregoing reasons, Defendant Lilly's motion for summary judgment as to the State's Medicaid Claims is DENIED.

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IX. Lilly's Motion for Summary Judgment on State's Failure to Prove Causation Claim

Lilly moves for Summary Judgment against the Plaintiff for the failure to prove causation. First, Lilly argues that the State should not be allowed to rely on "aggregate proof" in meeting its burden of proof as to causation. Secondly, Lilly argues that the learned intermediary doctrine breaks the causal chain of proof. They argue that the State had knowledge that physicians were writing off-label prescriptions and that aggregate proof does not excuse the fact that the State was aware of Lilly's on and off-label promotions. Finally, Lilly argues that aggregate proof does not account for the highly unique issues relating to an individual's diagnosis of diabetes and other related diseases.

In its brief in opposition to this motion, the State in points out that it has offered the testimony of Dr. John Abramson who will testify about the causal relationships between the conduct of Lilly and the damages claimed by the State. In the State's brief, Dr. Abramson opines that if the allegations concerning Lilly's abuses in the promotion of the drug Zyprexa are true that the behavior resulted in the over prescribing of the drug as well as increased off-label

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prescribing of the drug for medically unnecessary reasons. Also, Dr. Abramson stated that Lilly's marketing scheme resulted in Lilly expanding of the market for Zyprexa well beyond what it would have been if it were not marketed in the manner in which the Plaintiff alleges.

Concerning the use of aggregate proof to establish causation in tort litigation in South Carolina, there appears to be no case in the State directly on point. The court does note that there are federal cases cited by both sides in this case that go both ways on the subject. The court does note to deny the Plaintiff the right to present aggregate proof concerning massive programs involving perhaps hundreds of thousand incidents would most probably result in effectively denying the State the right for redress by making the proof so massive and cumbersome that no court or jury could comprehend the case. This court is convinced that the use of aggregate proof in this case is proper when coupled with proper expert testimony and analysis for the consideration by a jury in reaching a determination of fault, causation and damage issues. See Plaintiff's Response in Opposition to Lilly's Motion for Partial Summary Judgment on Causation, pages 12-20 for a discussion of this issue as this Court finds it to be.

"As a general rule cause-in-fact is a jury issue and the burden is upon the plaintiff. The plaintiff need not show that it is certain that the defendant's breach of duty was the cause-in-fact. It is only necessary to show by the preponderance of the evidence that it was reasonably probable or reasonably inferable that the breach was the cause-in-fact."

F. P. Hubbard and R.L. Felix, 2 South Carolina Law of Torts 139 (3rd Ed. 2004).

The above referenced rule applies to the trial of a case. In considering a motion for summary judgment a Plaintiff need not show by a preponderance of the evidence that causation exists, but rather that there is some genuine issue of fact as to the question to be considered by the jury at trial.

As to Lilly's learned intermediary issue and the State's knowledge as to off-label prescriptions on causation, this Court finds that the testimony of Dr. Abramson, when coupled with the evidence presented to this Court as to the content of the call notes and deposition testimony of Lilly's own detail sales representatives, create a genuine issue of fact for the jury to determine on that issue.

In short, this Court finds that there exists sufficient evidence in the record of this case at this time as to causation and proximate cause such that when all inferences that can be drawn from that evidence as made in favor of the Plaintiff that the motion for summary judgment is hereby DENIED.

X. Lilly's Motion for Partial Summary Judgment regarding State's Fraud and Misrepresentation Claims

Summary Judgment is proper only when there is no genuine issue as to any material fact. All fact placed into the record and any inferences that can be drawn from those facts must be viewed in the light most favorable to the non moving party. After a careful review of the facts placed in the record and cited in the respective party's briefs this court finds that a genuine issue as to the material facts exists, and therefore, the motion is DENIED.

IT IS SO ORDERED.

Spartanburg, South Carolina

September 22, 2009


Roger L. Couch
Presiding Judge

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EXHIBIT M

EXPERT REPORT OF
Laura M. Plunkett, Ph.D., DABT
July 7, 2009

I. Training and Qualifications

1. I am a pharmacologist, toxicologist, United States Food and Drug Administration (FDA) regulatory specialist and principal of a consulting company known as Integrative Biostrategies, LLC. Integrative Biostrategies, based in Houston, Texas, is a consulting firm that works at the interface of biological science, regulatory affairs and business decisions to provide its clients with science-based solutions to issues associated with product development and stewardship. Before joining Integrative Biostrategies in 2001, I was head of the consulting firm known as Plunkett & Associates.

2. I am board-certified as a Diplomate of the American Board of Toxicology. I am a member of several professional organizations and have authored or co-authored numerous scientific publications. I have over twenty years of experience in the areas of pharmacology and toxicology and have worked in both government and academic research. I have taught pharmacology and toxicology at the undergraduate and postgraduate levels.

3. I received a B.S. degree in 1980 from the University of Georgia and a Ph.D. in pharmacology from the University of Georgia, College of Pharmacy in 1984. My doctoral research was focused in the area of cardiovascular pharmacology and specifically dealt with delineating neurochemical mechanisms responsible for the cardiac toxicity of digitalis glycosides.

4. From June 1984 through August 1986, I was a Pharmacology Research Associate Training (PRAT) fellow at the National Institute of General Medical Sciences, Bethesda, Maryland. I worked in a neurosciences laboratory of the National Institute of Mental Health. My research focused on the role of various brain neurochemical systems involved in the control of autonomic nervous system and cardiovascular function.

5. From September 1986 to June 1989 I was an Assistant Professor of Pharmacology and Toxicology in the medical school at the University of Arkansas for Medical Sciences, Little Rock, Arkansas, where I performed basic research in the areas of neuropharmacology and toxicology as well as cardiovascular pharmacology and toxicology. I taught courses for both medical students and graduate students in pharmacology and toxicology as well as the neurosciences. During this time, I studied drugs of all classes that affect brain function, including anti-psychotic drugs. As a pharmacologist, my work was directed towards understanding the biologic mechanisms of drug actions. Much of my focus was on drugs that affect brain function, which includes anti-psychotics.

6. From December 1989 to August 1997, I worked for ENVIRON Corporation, first in the Arlington, Virginia office and then in the Houston, Texas office. I worked specifically within the health sciences group and most of my projects dealt with issues surrounding products or processes regulated by the FDA. During my consulting career (ENVIRON, Plunkett & Associates, and Integrative Biostrategies), I have worked on a variety of projects dealing with the regulation of products by the FDA, including human drugs, veterinary drugs, biologics, medical devices, consumer products, dietary supplements and foods. I have advised my clients on regulatory issues and strategies for their products (relating to both Canadian and American regulations), designed preclinical and clinical studies for both efficacy and safety, advised clients on issues related to statements regarding efficacy and warnings for their products based on the current labelling regulations and generally acted as a regulatory affairs staff for small companies in their early stages of product development. A tool common to all work my work as a consultant would be risk assessment, including many projects where risks and benefits of human therapeutics were at issue. Attached here in Appendix A is a copy of my curriculum vitae.

II. Information Reviewed

7. During the course of work on this case, I have reviewed the following materials:
- a) scientific literature relating to the pharmacology and toxicology of anti-psychotic drugs in general and risperidone (Risperdal) in particular;
 - b) labelling for Risperdal as provided by the Physician's Desk Reference;

c) regulations of the U.S. Food and Drug Administration (FDA) relating to the development, approval, labelling and marketing of prescription drug products; and

d) internal company documents relating to the development, approval and marketing of Risperdal by the defendants in these cases.

III. Summary of Bipolar Disorder and Schizophrenia

8. Schizophrenia is a major mental illness described by the Diagnostic and Statistical Manual of Mental Disorders ("DSM IV") as a psychotic disorder that is a chronic, severe and disabling brain disease. The hallmark of schizophrenia is disordered thought and perception. Typical symptoms include delusions and hallucinations. While most people diagnosed with schizophrenia are not gainfully employed, a substantial minority do have gainful employment.

9. Bipolar disorder is described by the DSM IV as a mood disorder. Bipolar disorder is a major mental illness, the hallmark of which is manic episodes marked by a euphoric, irritable or expansive mood. Patients with bipolar disorder usually also experience major depressive episodes.

IV. Atypical Anti-psychotics

10. The primary class of drugs used to treat symptoms of schizophrenia and bipolar disorder is known as anti-psychotics. Additionally, mood stabilizers or anti-depressants may also be used to treat bipolar disorder.

11. Anti-psychotics fall into two general categories: the newly developed atypical anti-psychotics and the older, conventional or typical anti-psychotics. The term "atypical" is applied to the newer drugs mainly because of the lower risks of adverse neurological effects known as extrapyramidal effects. As a general rule, because many atypical anti-psychotics (which until recently included Risperdal) still have patent protection, generic versions are not available and as such they are more expensive to purchase and, as a result, more profitable to the manufacturer.

12. Conventional, or typical, anti-psychotics as a group include drugs of a number of different chemical classes. These drugs have efficacy to treat both bipolar disorder and schizophrenia. Although it has often been asserted that a disadvantage of the typical drugs is their side effect profile, which includes risk of acute and long-term neurological side effects, including extrapyramidal effects, more recent analyses have demonstrated that differences in the side effect profiles of typical and atypical anti-psychotic drugs are not as clear.

13. Atypical anti-psychotic drugs have been considered as having less of a risk of producing extrapyramidal side effects, the unwanted neurological effects that are characterized by changes in movement. In fact, the goal of introducing atypical anti-psychotics to the marketplace was to provide an effective treatment that also improved the quality of life of the patient. Recent analyses have cast some doubt on the perceived advantage of atypical anti-psychotic agents in terms of adverse effect profiles. While the exact mechanisms responsible for the pharmacological differences between typical and atypical anti-psychotics have not yet been clearly defined, differences have been identified in the pattern of brain neurotransmitter receptor systems affected by the various drugs, effects that can be seen in responses elicited in animal models and/or effects that relate to the pharmacological and toxicological responses in humans.

14. Anti-psychotics will only treat the symptoms of schizophrenia and bipolar disorder; there is no "cure" for such disorders. The etiology of schizophrenia and bipolar disorder also remains to be elucidated, although genetics appears to play some role in these disorders.

15. Risperidone, marketed in the U.S. under the trade name of Risperdal, is a widely prescribed prescription drug product that was approved by the FDA in 1993 for the treatment of schizophrenia. Risperdal was subsequently approved for management of acute manic episodes associated with bipolar disorder in 2003, for irritability in autistic children aged 5-16 years of age in 2006, and for treatment of schizophrenia in 13-17 year old children and management of acute manic episodes associated with bipolar disorder in 10-17 year old children, both in 2007. I believe that Risperdal is also widely prescribed for off-label uses, including the treatment of sleep disorders, control of agitation, anxiety, aggression and behavioural disturbances.

16. The psychotic symptoms treated with atypical anti-psychotic drugs such as Risperdal include disordered thought processes, disorganized and/or irrational behaviour, and degrees of altered mood, from severe agitation to severe withdrawal. Other drugs that have been or are used in the treatment of psychotic disorders include phenothiazines (e.g., chlorpromazine, also known as Thorazine; thioridazine, also known as Mellaril), thioxanthines (e.g., chloprothixene, also known as Taractan; thiothixene, also known as Navane), haloperidol (Haldol), clozapine (Clorazil), aripiprazole (Abilify), loxapine (Loxitane), molindrone (Moban), pimozide (Orap), olanzapine (Zyprexa), quetiapine (Seroquel), and ziprasidone (Geodon). The optimum therapy for treating schizophrenia and bipolar disorder is chosen for each patient based on the patient's medical history, including any risks of known side effects of the drug, and the patient's response to the drug in relation to the drug's efficacy and adverse events.

17. The pharmacology of Risperdal and other similar anti-psychotic drugs is described in many textbooks and review articles (e.g., *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, 11th edition. 2006. Brunton, L.L. et al. (eds.), McGraw-Hill: New York, chapter 18). Risperdal produces its therapeutic and adverse effects through its activity on various receptor systems in the brain and throughout the body. Risperdal is known to be an antagonist of D₂, D₁, 5-HT₂, 5-HT_{1A}, 5-HT_{1C}, 5-HT_{1D}, H₁, α_1 , and α_2 receptors. The efficacy of Risperdal and other atypical anti-psychotic drugs has been linked to dopaminergic and serotonergic system antagonist activity. However, the exact mechanism by which atypical anti-psychotic drugs produce their effects in schizophrenia and bipolar disorders is not known.

V. Background Information on Risperdal

18. Risperdal is well absorbed following oral administration, with peak concentrations of the parent compound achieved in the blood within one hour, and an elimination half-life in the range of 3 hours. It is widely distributed in the body and steady state blood levels are achieved within a few days. Following oral administration, Risperdal is extensively metabolized and its major metabolite, 9-hydroxyrisperidone, is pharmacologically active. The 9-hydroxyrisperidone metabolite is formed through activity of the CYP2D6 enzyme in the liver. It has been established that some individuals are classified as "extensive CYP2D6 metabolizers"

while others are classified as “poor CYP2D6 metabolizers”. This leads to very different pharmacokinetic profiles for Risperdal, with an elimination half-life for the parent compound of 3 hours in “extensive metabolizers” as compared to an elimination half-life of 20 hours in “poor metabolizers”. A similar pattern of prolonged elimination half-life is also seen for 9-hydroxyrisperidone, where the elimination half-life in “poor metabolizers” is in the range of 30 hours, as compared to 20 hours in “extensive metabolizers”. This difference in metabolism among the general population has implications for the safe use of the drug.

19. Risperdal use has been associated with deaths, including deaths in elderly patients with dementia. Its adverse effects include, but are not limited to hyperprolactinemia, gynecomastia, galactorrhea, amenorrhea, impotence, orthostatic hypotension, ketoacidosis, diabetes mellitus, weight gain, hyperglycemia, cerebrovascular events (stroke), and somnolence. Other serious injuries associated with Risperdal use include: a potentially fatal condition known as neuroleptic malignant syndrome (NMS); tardive dyskinesia, which can cause potentially irreversible, involuntary movements; and other serious health problems associated with the onset of diabetes including heart disease, blindness, coma, seizures and death. These adverse health effects have been reported following both short-term and longer-term use of Risperdal. Additionally, Risperdal treatment was associated with cancer in rodents, producing tumors of the pituitary gland, the mammary gland, and pancreatic islet cells. As a result, Risperdal use in patients at risk for breast cancer in particular has been a concern, as well as the potential for Risperdal to cause tumors of the pituitary gland.

20. Some of the adverse health effects associated with Risperdal use have been attributed to activity of the drug on certain receptor systems in the body. For example, orthostatic hypotension seen in some patients administered Risperdal is thought to be attributed to α_1 -adrenergic antagonist activity of the drug while somnolence has been attributed to antagonism of histamine type 1 (H_1) receptors by Risperdal. The effect of Risperdal to produce hyperprolactinemia has been linked to the D_2 receptor antagonist activity of the drug.

21. While Risperdal is similar in basic pharmacological profile to other atypical anti-psychotic drugs, including olanzapine and quetiapine, the potency of these drugs as an antagonist

at D₂ and 5-HT_{2A} receptors differs. Differences in potency as an antagonist at certain receptor types may explain some of the differences observed among the various atypical anti-psychotics in terms of both efficacy and toxicity.

VI. Risperdal and Effects on Prolactin

22. There is a great deal of literature describing the effects of Risperdal on prolactin levels in humans and the serious outcomes that can be associated with elevated levels of prolactin, or hyperprolactinemia.

23. Prolactin is a hormone secreted by specialized cells in the anterior pituitary gland, known as lactotrophs. It is normally secreted with a circadian trend in a series of daily pulses. The main biological role for prolactin is milk induction and lactation in women, but it also plays a role in mammary gland development, parental behaviour and immune system responsiveness. Levels of prolactin in blood are maintained in a "homeostasis" by the activity of a variety of mediators. The most important of these factors is dopamine. Dopamine secreted from the hypothalamus reaches the anterior pituitary gland and inhibits secretion of prolactin by binding to D₂ receptors on the membrane of lactotroph cells. Other factors that inhibit prolactin release include the neurotransmitters GABA, somatostatin, acetylcholine, and norepinephrine. Factors that stimulate prolactin release or "prolactin-releasing factors" include serotonin, thyroid-releasing hormone, estrogen, histamine, vasopressin, neurotensin, opioids, oxytocin, as well as a variety of other substances. Additionally, a variety of drugs that act through one of more of the mediators can also affect prolactin release.

24. Hyperprolactinemia is defined as an abnormally high circulating level of prolactin in blood. In women it has been defined as fasting levels at least 2 hours after waking of greater than 25 ng/ml and in men of greater than 20 ng/ml (Torre and Falorni. 2007. *Ther. Clin. Risk Manage.* 3:929-951). Symptoms of prolonged hyperprolactinemia usually involve reproductive system function (*i.e.*, lack of ovulation, menstrual irregularities such as amenorrhea, infertility, decreased libido, impotence, erectile dysfunction). Other consequences of sustained hyperprolactinemia include galactorrhea, breast enlargement, decreased bone mineral density and osteoporosis, depression, anxiety, psychosis, and increased risk of cardiovascular disease.

One of the most serious consequences of chronic hyperprolactinemia may be the risk of cancer. The published medical literature has focused in particular on the risks of breast cancer. Hyperprolactinemia also has been associated with a risk for pituitary tumors.

25. The mechanisms underlying the various physiological effects or disorders associated with hyperprolactinemia are well-established. There are many review papers describing the complex interactions of prolactin with various target organs and systems in the body and how prolactin levels are regulated (e.g., Bostwick et al. 2009. *Pharmacotherapy* 29:64-73; Byerly et al. 2007. *J. Clin. Psychopharmacol.* 27:639-661; Compton and Miller. 2002. *Psychopharmacol. Bull.* 36:143-164; Haddad and Wieck. 2004. *Drugs* 64:2291-2314; Halbreich and Kahn. 2003. *J. Psychiatr. Pract.* 9:344-353). All of these reviews have discussions or diagrams showing that antagonism of dopamine receptors in the anterior pituitary gland by a drug, such as Risperdal, leads to a cascade of events where prolactin secretion from the pituitary lactotroph cells results in an inhibition of release of hypothalamic gonadotrophic releasing hormone (GnRH), which leads to decreased levels of gonadotrophs, leading to decreased levels of estrogen and testosterone, and finally to symptomatic hyperprolactinemia. In the case of chronic hyperprolactinemia, increased risks of breast cancer and pituitary tumors have been linked directly to the increased levels of prolactin circulating, while an increased risk of osteoporosis is linked to the chronic hypogonadism produced with the hyperprolactinemic state. Additionally, hyperprolactinemia has been identified as risk factor for cardiovascular disease due to the effects of the hormone on estrogen levels (e.g., Halbreich and Kahn. 2003. *J. Psychiatr. Pract.* 9:344-353).

26. It is well-established that Risperdal increases circulating levels of prolactin, producing hyperprolactinemia that persists with chronic administration of the drug (see labelling for Risperdal; dozens of published references e.g., Torre and Falorni. 2007. *Ther. Clin. Risk Manage.* 3:929-951; Bostwick et al. 2009. *Pharmacotherapy* 29:64-73; Anderson et al. 2007. *Biol. Psychiatry* 61:545-550; Hellings et al. 2005. *J. Child Adolesc. Psychopharmacol.* 15:885-892; Abraham et al. 2003. *Am. J. Psychiatry* 160:1618-1620; Yasui-Furukori et al. 2002. *Psychopharmacology* 162:63-66; Duval et al. 2008. *Psychoneuroendocrinology* 33:255-259).

Moreover, the effects of Risperdal on prolactin levels have been known since the drug was first developed and marketed (e.g., Bowden et al. 1992. *J. Pharmacol. Exp. Ther.* 262:699-706).

27. The body of data available on Risperdal and hyperprolactinemia demonstrate that the risk of hyperprolactinemia is greater with Risperdal than some other anti-psychotic drugs. For example, Compton and Miller (2002. *Psychopharmacol. Bull.* 36:143-164) provided an estimate of the relative propensities for certain anti-psychotics to induce clinically significant elevations in prolactin. They ranked the drugs listed as follows: conventional anti-psychotics = Risperdal > olanzapine > ziprasidone > clozapine = quetiapine (see Table 1). Additionally, there are clinical data showing that Risperdal increases serum prolactin levels to a greater extent than some other atypical anti-psychotics (e.g., Abraham et al. 2003. *Am. J. Psychiatry* 160:1618-1620; Knegtering et al. 2003. *Psychoneuroendocrinology* 28(suppl. 2):109-123; Breir et al. 1999. *Am. J. Psychiatry* 156:294-298; Volavka et al. 2004. *J. Clin. Psychiatry* 65:57-61; Kelly and Conley 2006. *Psychoneuroendocrinology* 31:340-346; Kinon et al. 2003. *Psychoneuroendocrinology* 28(suppl. 2):55-68; Kim et al. 2002. *J. Clin. Psychiatry* 63:408-413; Potkin et al. 2003. *Arch. Gen. Psychiatry* 60:681-690; Conley and Mahmoud. 2001. *Am. J. Psychiatry* 158:765-774; Byerly et al. 2004. *J. Sex Marital Ther.* 30:325-332; Riedel et al. 2005. *Eur. Arch. Psychiatry Clin. Neurosci.* 255:432-437). Therefore, the weight-of-the-evidence demonstrates that the risk of hyperprolactinemia and the consequences of this disorder are not equivalent across atypical anti-psychotics, with Risperdal posing a greater risk to patients for this adverse effect than many of the other drugs.

28. After reviewing a variety of company documents, it is clear that the defendants in these cases were aware of the risks associated with hyperprolactinemia as well as the unique nature of Risperdal to produce significant hyperprolactinemia in patients (see for example JJRE00423468 through 469; JJRE00116082 through 271; JJRE05756531 through 532). The defendants were aware of the fact that patients administered Risperdal were more likely to exhibit hyperprolactinemia than patients taking other atypical anti-psychotics (for example JJRE00116082).

29. When considered as a whole in a weight-of-the evidence assessment, the available scientific data indicate that Risperdal can cause hyperprolactinemia that then causes a variety of conditions, including abnormal menstrual cycles and amenorrhea in women, decreased libido, galactorrhea and breast enlargement in men, and decreased bone density. The scientific data include case reports (e.g., Chung and Eun. 1998. *Int. J. Neuropsychopharmacol.* 1:93-94; Popli et al. 1998. *Ann. Clin. Psychiatry* 10:31-33; Dickson and Glazer. 1999. *J. Clin. Psychiatry* 60:125; Kim et al. 1999. *J. Clin. Psychiatry* 60:315-317; Haddad et al. 2001. *J. Psychopharmacol.* 15:293-295; Hariharan and Mohsin. 2002. *WMJ* 101:41-43; Meany and O'Keane. 2003. *J. Psychopharmacology* 17:455-458; Madhusoodanan and Moise. 2006. *J. Clin. Psychiatry* 67:1110-1113; Afzal et al. 2007. *CNS Spectr.* 12:818-820), a survey of adverse drug reports (Szarfman et al. 2006. *Pharmacotherapy* 26:748-758), human clinical and epidemiological data (e.g., Brunelleschi et al. 2003. *Pharm. Res.* 48:405-409; Saito et al. 2004. *J. Child Adolesc. Psychopharmacol.* 14:350-358; Bushe and Shaw. 2007. *Psychopharmacol.* 21:768-773; Addington et al. 2009. *Can. J. Psychiatry* 54:46-54; Holzer and Eap. 2006. *J. Clin. Psychopharmacol.* 26:167-171; Kearns et al. 2000. *Endocrin. Pract.* 6:425-429; Kinon et al. 2003. *Psychoneuroendocrinology* 28(suppl. 2):55-68; Knegtering et al. 2003. *Psychoneuroendocrinology* 28:109-123; Greenspan et al. 1986. *Ann. Intern. Med.* 104:777-782), and mechanistic data collected in humans, animals or *in vitro* (e.g., Melkersson, K.I. 2006. *Human Psychopharmacol.* 21:529-532; Wu et al. 2000. *Neuropsychopharmacology* 23:676-689). Each source of information is important in the analysis of the risks associated with use of Risperdal, and is consistent with accepted methods for establishing causation in a weight-of-the-evidence analysis (Hill, A.B. 1965. *Proc. Royal Soc. Med.* 58:295-300). It is important to note as well that the biologic mechanism underlying the effects of Risperdal is well-established based on the known biology of increased levels of prolactin (see reviews such as Bostwick et al. 2009. *Pharmacotherapy* 29:64-73; Byerly et al. 2007. *J. Clin. Psychopharmacol.* 27:639-661; Compton and Miller. 2002. *Psychopharmacol. Bull.* 36:143-164; Haddad and Wieck. 2004. *Drugs* 64:2291-2314; Halbreich and Kahn. 2003. *J. Psychiatr. Pract.* 9:344-353; Montejo, A. 2008. *Eur. Neuropsychopharmacol.* 18(suppl. 2):S108-S114).

30. Also in a weight-of-the-evidence assessment, the available scientific data indicate that hyperprolactinemia that is produced by drugs such as Risperdal is an independent risk factor

for breast cancer and pituitary tumors. The scientific data include case reports (e.g., Mendhekar et al. 2004. *Pharmacopsychiatry* 37:41-42), a survey of adverse drug reports (Szarfman et al. 2006. *Pharmacotherapy* 26:748-758), epidemiological data (e.g., Hankinson et al. 1999. *J. Natl. Cancer Instit.* 91:629-634; Wang et al. 2002. *Arch. Gen. Psychiatry* 59:1147-1154; Halbreich et al. 1996. *Am. J. Psychiatry* 153:559-560; Tworoger and Hankinson. 2006. *Cancer Lett.* 243:160-169), and mechanistic data collected in humans, animals and *in vitro* (e.g., Melkersson, K.I. 2006. *Human Psychopharmacol.* 21:529-532; Wu et al. 2000. *Neuropsychopharmacology* 23:676-689; Welsch and Nagasawa. 1977. *Cancer Res.* 37:951-963; Pearson et al. 1969. *Trans. Assoc. Am. Physicians* 82:225-238; Risperdal cancer data in rodents discussed in labelling see PDR 2008). Each source of information is important in the analysis of the risks associated with use of Risperdal, and is consistent with accepted methods for establishing causation in a weight-of-the-evidence analysis (Hill, A.B. 1965. *Proc. Royal Soc. Med.* 58:295-300). It is important to note as well that the biological mechanism underlying the effects of Risperdal is well-established based on the known biology of increased levels of prolactin (see reviews such as Bostwick et al. 2009. *Pharmacotherapy* 29:64-73; Byerly et al. 2007. *J. Clin. Psychopharmacol.* 27:639-661; Haddad and Wieck. 2004. *Drugs* 64:2291-2314; Halbreich and Kahn. 2003. *J. Psychiatr. Pract.* 9:344-353; Montejo, A. 2008. *Eur. Neuropsychopharmacol.* 18(suppl. 2):S108-S114).

31. Although it has been argued in some company documents that the laboratory animal cancer data are not relevant to assessing risks in humans, this is not correct. It is true that rodent mammary tumors develop by mechanisms that are not directly relevant to human breast cancer. However, the animal data are important in demonstrating that high levels of prolactin can lead to carcinogenesis in certain tissues in mammals. Therefore, when examining the animal data in the context of human health risk assessment the animal data are relevant to cancer risk in humans in tissues that are sensitive to prolactin. For example, increased prolactin levels have been linked to human cancer of the breast, prostate, ovary, endometrium, and the colon (e.g., Clevenger et al. 2003. *Endocr. Rev.* 24:1-27; Levina et al. 2009. *Cancer Res.* 64:5226-5233). As a result, it is not scientifically defensible to assert that the cancer data in animals is not relevant to human health risk assessment and in particular cancer risk assessment. Prolactin is a hormone that is involved in carcinogenesis in prolactin-responsive tissues and acts through a threshold mechanism to exert its effects.

VII. Risperdal and Adverse Metabolic Effects

32. It has been known for decades that many anti-psychotic drugs have effects to alter metabolism that can lead to weight gain and effects on glucose metabolism (e.g., Baldessarini, R.J. 1980. Drugs and the treatment of psychiatric disorders. In: *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, 6th edition. A.G. Gilman et al. (Eds.), chapter 19, MacMillan Publishing Co.: New York). However, it has been recognized more recently (since about 1999) that there appear to be differences among the various anti-psychotic drugs in terms of their propensity for inducing weight gain and changes in glucose metabolism, as well as the onset of diabetes (e.g., Melkersson, K. and M-L. Dahl. 2004. *Drugs* 64:701-723; American Diabetes Association et al. 2004. *Diabetes Care* 27:596-601; Allison, D.B. et al. 1999. *Am. J. Psychiatry* 156:1686-1696; Bobes, J. et al. 2003. *Schizophr. Res.* 62:77-88; Wetterling, T. 2001. *Drug Saf.* 24:59-73; Buse, J.B. et al. 2003. *J. Clin. Epidemiol.* 56:164-170). Moreover, it has now been recognized that clinically significant hyperglycemia and diabetic complications can occur during anti-psychotic treatment both with and without changes in body weight (Newcomer, J.W. et al. 2002. *Arch. Gen. Psychiatry* 59:337-345; Newcomer, J.W. 2005. *CNS Drugs* 19(S1):1-93). Because of the differences apparent among different anti-psychotic agents in terms of risks of diabetes and weight gain, the effects of Risperdal cannot be considered simply a "class" effect for atypical anti-psychotic drugs (Newcomer, J.W. 2005. *CNS Drugs* 19(Suppl. 1):1-93). Different anti-psychotic drugs, including the second generation atypical anti-psychotic agents, have different toxicological profiles.

33. Between 1993 and 2002, numerous adverse drug event reports were submitted to the FDA. These reports indicated that patients consuming Risperdal experienced significant adverse health effects, including hyperglycemia, diabetes, exacerbation of pre-existing diabetes, ketoacidosis, and death. These adverse event reports were discussed in an article by Koller *et al.* (2003. *Pharmacotherapy* 23:735-744). The authors concluded that use of Risperdal may unmask or precipitate hyperglycemia in patients.

34. Case reports linking Risperdal use with hyperglycemia and/or diabetes appeared in the published literature as early as 2000 (e.g., Croarkin et al. 2000. *Psychosomatics* 41:369-370).

35. A large study involving the U.S. Veterans' Administration (Sernyak, M.J. et al. 2002. *Am. J. Psychiatry* 159:561-566) was performed in 1999 where records from all patients being treated nationally with anti-psychotics were examined. The authors reported that there was an increased risk of diabetes with exposure to certain anti-psychotic drugs. One of the drugs shown to be associated with an increased risk was Risperdal.

36. Following this 2002 publication, other epidemiological studies appeared in the scientific literature that also reported an association of Risperdal with an increased risk of diabetes (e.g., Cavazzoni et al. 2002. *Int. J. Neuropsychopharmacology* 5(S1):S168; Buse et al. 2003. *J. Clin. Epidemiol.* 56:164-170; Feldman et al. 2004. *J. Am. Med. Dir. Assoc.* 5:38-46; Lambert et al. 2006. *Am. J. Epidemiol.* 164:672-681; Sacchetti et al. 2005. *Int. Clin. Psychopharmacol.* 20:33-37; Guo et al. 2006. *J. Clin. Psychiat.* 67:1055-1061; Guo et al. 2007. *Pharmacotherapy* 27: 27-35).

37. When considered as a whole in a weight-of-the evidence assessment, the available scientific data indicate that Risperdal can cause physiological effects known to be risk factors for diabetes, including increased body weight and other metabolic effects, and can cause diabetes itself. The scientific data include case reports (e.g., Fukui and Murai. 2002. *Clin. Neuropharmacol.* 25:269-271; Wirshing et al. 2001. *Biol. Psychiatr.* 50:148-149; Croarkin et al. 2000. *Psychosomatics* 41:369-370; Mallya et al. 2002. *J. Clin. Psychiatr.* 63:453; Lauwers et al. 2006. *Tijdschr. Psychiatr.* 48:331-335; Lu and Yan. 2009. *Diabetes Res. Clin. Pract.* 83:e66-e77; Sato et al. 2008. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 32:577-578), a survey of adverse drug reports (Koller, E.A. et al. 2003. *Pharmacotherapy* 23:735-744), epidemiological data assembled since 2002 (e.g., Sernyak, M.J. et al. 2002. *Am. J. Psychiatry* 159:561-566; Cavazzoni et al. 2002. *Neuropsychopharmacology* 5(S1):S168; Hedenmalm et al. 2002. *Drug Safety* 25:1107-1116; Buse et al. 2003 *J Clin Epidemiol.* 56:164-170; Feldman et al. 2004. *J. Am. Med. Dir. Assoc.* 5:38-46; Lambert et al. 2006. *Am. J. Epidemiol.* 164:672-681; Sacchetti et al.

2005. *Int. Clin. Psychopharmacol.* 20:33-37; Guo et al. 2006. *J. Clin. Psychiat.* 67:1055-1061; Guo et al. 2007. *Pharmacotherapy* 27: 27-35), and mechanistic data collected in animals and *in vitro* (e.g., Ader et al. 2005. *Diabetes* 54:862-871; Dwyer and Donohoe 2003. *Pharmacol. Biochem. Behav.* 75:255-260; Ardizzone et al. 2001. *Brain Res.* 923:82-90; Cope et al. 2005. *Int. J. Obesity* 29:607-614; Vestri et al. 2007. *Neuropsychopharmacology* 32:765-772; Savoy et al. 2008. *Schizophr. Bull.* Epub Aug 14; Chintoh et al. 2009. *Schizophr. Res.* 108:127-133). Each source of information is important in the analysis of the risks associated with use of Risperdal, and is consistent with accepted methods for establishing causation in a weight-of-the-evidence analysis (Hill, A.B. 1965. *Proc. Royal Soc. Med.* 58:295-300).

38. It is my opinion that the available scientific data demonstrate that Risperdal consumption and use can cause adverse metabolic effects that include, but are not limited to an increased risk of clinically significant body weight gain, hyperglycemia, altered glucose metabolism, and an increased risk of diabetes and diabetes-related complications. It should be remembered that diabetes-related complications include an increased risk of stroke and cardiovascular disease, events that have been associated with Risperdal use in elderly patients and that are listed on Risperdal labelling as a Black Box warning.

39. Although the exact molecular mechanisms responsible for the metabolic effects of Risperdal have not been established, there are data that describe the basic mechanisms that lead to the effects of Risperdal on body weight gain and altered glucose metabolism, and eventually diabetes. However, weight gain is not a prerequisite for atypical anti-psychotic drug-induced effects on glucose metabolism and induction of type II diabetes (Newcomer, J.W. 2004. *Clin. Ther.* 26:1936-1946; Newcomer, J.W. 2005. *CNS Drugs* 19(S1):1-93; Dwyer, D.S. and D. Donohoe. 2003. *Pharm. Biochem. Behav.* 75:255-260; Ardizzone, T.D. et al. 2001. *Brain Res.* 923:82-90; Dwyer, D.S. et al. 1999. *Prog. Neuro-Psychopharmacol. Biol. Psychiat.* 23:69-80; Newcomer, J.W. et al. 2002. *Arch. Gen. Psychiat.* 59:337-345; Koller, E.A. and P.M. Doraiswamy. 2002. *Pharmacotherapy* 22:841-852; Koller, E. et al. 2001. *Am. J. Med.* 111:716-723; Ebenbichler, C.F. et al. 2003. *J. Clin. Psychiat.* 64:1436-1439).

40. Clinically significant body weight gain is often seen with administration of Risperdal to patients (many published studies, e.g., Saddichha et al. 2008. *Schizophr. Res.* 101:266-272; Saddicha et al. 2007. *J. Clin. Psychiatry* 68:1793-1798; Perez-Iglesias et al. 2007. *J. Clin. Psychiatry* 68:1733-1740; Farwell et al. 2004. *J. Gen. Intern. Med.* 19:1200-1205). The effects of atypical anti-psychotics on weight gain have been shown to be attributable to both increased caloric intake (increased appetite) and decreased energy expenditure (Gothelf, D. et al. 2002. *Am. J. Psychiatry* 159:1055-1057; Virkkunen, M. et al. 2002. *Pharmacopsychiatry* 35:124-126). These mechanisms for increased body weight gain are consistent with the fact that Risperdal has effects on neurotransmitter systems in the brain that affect appetite and mood. It is well-established in the medical literature that a clinically significant increase in body weight is a risk factor for diabetes (e.g., Foster, D.W. 1994. Diabetes mellitus. In: *Harrison's Principles of Internal Medicine*, 13th edition. K.J. Isselbacher et al. (Eds.), chapter 337, McGraw-Hill: New York). Therefore, any effect of Risperdal to increase body weight is a significant risk for the development of diabetes.

41. Although available studies have focused on the association of type II diabetes with Risperdal treatment, as well as treatment with other atypical anti-psychotic drugs, the toxicity of these drugs, which includes altered glucose metabolism, obesity, and hyperglycemia, would also be significant risk factors for individuals with undiagnosed type I diabetes or a genetic predisposition for type I diabetes. Type I diabetes is characterized by a loss of insulin secretion capacity due to the loss of beta cells in the pancreas. The loss of insulin secretion capacity means that type I diabetics would need to rely on exogenous sources of insulin to control blood glucose levels. Therefore, it is only common sense that any effects of a drug such as Risperdal to affect glucose metabolism or blood glucose levels would be a greater risk for individuals who already are at risk of type I diabetes or who are not yet exhibiting clinical signs and symptoms of type I diabetes.

42. In 2003, a consensus conference was held that examined the available data on risk of diabetes and use of anti-psychotic drugs, in particular the atypical anti-psychotic drugs. It was sponsored jointly by the American Diabetes Association and the American Psychiatric Association. After a review of company documents, it is clear that manufacturers of atypical

anti-psychotic drugs, including Janssen (the defendants) had significant input into much of the process of selecting panel participants, as well as having had the chance to discuss issues with conference participants before the conference was held (see for example JJRE0032554; JJRE01147159; JJRE01147840; JJRE02222737; JJRE02236338; JJRE02256370; JJRE03965541; JJRE06826665; JJRE14166945; JJRE14166998; JJRE14167015; JJRE14167017). Although a review of these company documents reveals that the defendants' position was that Risperdal was associated with less risk of metabolic effects, including diabetes, as compared to other atypical anti-psychotic drugs, the conference consensus was that Risperdal use was associated with some risk of diabetes. The ranking proposed by the conference was that olanzapine and clozapine posed the most risk. However, the consensus was that quetiapine and Risperdal each posed a risk of diabetes as well. The findings of the consensus panel are consistent with my opinions regarding the risk of various atypical anti-psychotic drugs, including Risperdal.

VIII. Risperdal Risks Versus Benefit

43. It is important to remember that although clinical trials had been performed with Risperdal as part of the drug development process, such trials are limited in their ability to identify risks associated with drug use by the general population. This is because such drug development clinical trials are performed in either healthy volunteers or in patients that have often been pre-screened for the propensity to develop adverse effects, with such patients then usually excluded from studies. It is only after a drug has been placed on the market, and wider exposure is seen, that a true picture of the adverse effects associated with a drug can be observed. As a result, I believe that companies have the duty to carefully monitor their drugs after approval and during marketing for either the existence of new adverse events or a higher than expected incidence of known adverse effects.

44. Scientific studies have established that there are apparent differences among anti-psychotic drugs in terms of risks of hyperprolactinemia and the metabolic effects discussed above. As a result of these differences, and differences in toxicological profiles, I believe that side effects arising through the consumption of Risperdal cannot be described as a "class effect" for all atypical anti-psychotic drugs. Further, the defendants were aware of the unique adverse

health risks associated with Risperdal, most importantly its effects to produce hyperprolactinemia (see for example JJRE00423468 through 469; JJRE00116082 through 271; JJRE05756531 through 532) as well as hyperglycemia and diabetes.

45. When considering the adverse health effects associated with use of Risperdal, it is important to realize that Risperdal is not unique in terms of its efficacy. Studies have shown that other anti-psychotic drugs have similar effectiveness to Risperdal but have less risk for hyperprolactinemia and related adverse effects, as well as adverse metabolic effects (hyperglycemia, weight gain, and diabetes). Therefore, there are alternative therapies that could be used that would also provide for effective treatment but with fewer side effects.

46. For example, in the CATIE Schizophrenia Trial, a trial sponsored by the National Institute of Mental Health which is the largest trial conducted to date comparing efficacy and safety of some of the most prescribed anti-psychotic drugs, it was shown that clozapine was more effective than other atypical anti-psychotics (*i.e.*, Seroquel, Zyprexa, Risperdal). Further, when all of the atypical agents studied were examined, including Risperdal, none of the agents was more effective or better tolerated than the typical anti-psychotic, perphenazine (Manschreck, T.C. and R.A. Boshes. 2007. *Harv. Rev. Psychiatry* 15:245-258; Nasrallah, H.A. 2007. *J. Clin. Psychiatry* 68(suppl. 1):5-11).

IX. Regulatory Issues

47. Risperdal is marketed as a prescription drug product in the United States and worldwide. Here in the United States, the development, approval and marketing of Risperdal are regulated by the FDA. FDA is concerned with both assuring that products being developed are safe and effective for their labelled indications as well as assuring that once a product is marketed it continues to be safe and effective as labelled.

48. In the case of Risperdal, a review of company documents shows that the company was aware of the risks of hyperprolactinemia and the unique nature of Risperdal in terms of its propensity to induce hyperprolactinemia even before the drug was approved by the FDA in 1993. With respect to cancer risks and Risperdal, a 1993 document shows that the defendants were

aware of the potential concern of Risperdal exposure in patients either with breast cancer or at risk of breast cancer (see JJRIS02250277). A “white paper” on the topic of hyperprolactinemia also shows that the defendants were aware of the risks of hyperprolactinemia in susceptible populations such as children and adolescents (see JJRE12145922). With respect to adverse metabolic effects and Risperdal, the defendants worked to avoid labelling of their product as it related to diabetes risk (see for example JJRE01147840; JJRE02222737).

49. A significant issue with use of Risperdal by physicians is off-label uses. Off-label use of a prescription drug is any use that is not listed in the product labelling. The FDA assesses efficacy and safety of prescription drugs based on uses in defined populations of patients with specific diseases. It is only these uses that have been deemed as “safe and effective” by FDA review and approval. As a result, off-label use of drugs, which can involve uses in very different populations of patients than the population of patients covered by labelled indications, also can pose very different risks to patients. Attached in Appendix B is a table I have prepared that shows the indications for which Risperdal was approved since it was first marketed. In the case of Risperdal, there was a large amount of use off-label in both the elderly and in children and adolescents. It is well-established that age is a factor in drug pharmacokinetics and pharmacodynamics. A review of company documents shows that Risperdal was being prescribed in these populations and was even a focus of marketing. Thus, the lack of data to support the safety and efficacy of off-label uses of Risperdal in the elderly and children is of particular importance. It is interesting to note that the defendants were aware of the lack of data for Risperdal for off-label uses, even referring to it as “an Achilles heel” (see JJRE02490472).

50. The labelling for prescription drug products contains warnings for physicians and patients that relate to the most serious health risks associated with use of a drug. Drug labelling is regulated in terms of what information must be included on the labelling as well as how that information is presented. Drug labelling must not be false or misleading and if the FDA determines that information in a drug label is false or misleading, the company must change the language of the label as directed by the FDA. In the case of Risperdal, the defendants received several warning letters from the FDA that related to warnings for metabolic risks and false or misleading statements in the labelling. In 2003, manufacturers of atypical anti-psychotic drugs

were required to adopt “class” labelling language that related to risks of hyperglycemia and diabetes. However, the defendants failed to change the language of their label as directed by FDA and in fact in November 2003 the defendants sent physicians a “Dear Health Care Provider” letter and a new package insert for Risperdal that modified the FDA-mandated label language. As a result of this action, FDA sent the defendants a Warning Letter that concluded that the November communications with physicians were false and misleading. The delays in the changes to the Risperdal labelling with regard to metabolic risks was inconsistent with protecting public health and put patients at increased risk. Moreover, the language of the November 2003 “Dear Health Care Provider” letter was not an accurate reflection of the risks posed by Risperdal.

51. From the time Risperdal was first approved by the FDA in 1993 and up until 2007, hyperprolactinemia was mentioned in the Precautions section of the label (see table in Appendix B). The language in the labelling linked hyperprolactinemia with all drugs that antagonize D₂ receptors. A review of company documents demonstrates that the company was aware of the unique nature of Risperdal and the risks related to increased prolactin levels (JJRE00423468), even describing the issues in detail in a white paper dated August 2004 (JJRE00116082). It is my opinion that the Risperdal labelling failed to adequately convey the risks posed by Risperdal that the defendants knew were related to hyperprolactinemia. For example, the discussion of hyperprolactinemia fails to acknowledge the association of hyperprolactinemia and Risperdal with cancers in prolactin-responsive tissues.

52. A review of the product labelling for Risperdal that is available to health professionals demonstrates that, in my opinion, the warnings related to risks of hyperglycemia and diabetes in particular are not adequate to convey the risks posed by Risperdal itself. The discussion of hyperglycemia and diabetes is put forth as an effect of anti-psychotics in general.

53. As a result, the Risperdal product warnings were wholly inadequate to warn physicians and their patients of the significant adverse effects associated with the consumption of Risperdal. This is of special concern since the drug is used in children as well as adults. Nonetheless, Risperdal was marketed heavily as safe and effective for the treatment of bipolar

disorder and schizophrenia, promising fewer side effects than other similar treatments including the other atypical anti-psychotics on the market. Further, Risperdal has been prescribed by physicians for treatment of conditions other than bipolar disorder and schizophrenia (off-label use), use that was known by Janssen.

X. Conclusion

54. In conclusion, based on my training and experience as a pharmacologist, toxicologist, and risk assessor, it is my opinion that Risperdal can cause hyperprolactinemia as well as variety of adverse effects that ensue following establishment of the hyperprolactinemic state in the patient. It is also my opinion, based on my training and experience as a pharmacologist, toxicologist, and risk assessor, that Risperdal can cause adverse metabolic effects such as weight gain, hyperglycemia and diabetes. The adverse health effects associated with the consumption and use of Risperdal were predictable based on the known pharmacological profile of the drug. Moreover, the adverse health effects associated with Risperdal consumption and use can be serious, life-threatening conditions that have been recognized in the published medical literature. Finally, it is my opinion that the labelling for Risperdal failed to adequately convey the real risks posed by the drug, risks that needed to be conveyed to patients taking the drug. All opinions expressed in this report are based on a reasonable degree of scientific certainty.

XI. Compensation

55. My compensation by plaintiff's attorney in this matter is at the rate of \$300.00 per hour for review of documents and materials related to the case and \$400.00 per hour for testimony.

A handwritten signature in black ink, appearing to read "Laura M. Plunkett", written over a horizontal line.

Laura M. Plunkett, Ph.D., DABT

APPENDIX A

CURRICULUM VITAE

Laura M. Plunkett, Ph.D., D.A.B.T

OFFICE ADDRESS 1223 Melford Drive
Houston, TX 77077-1544

EDUCATION

1984	Ph.D.	Pharmacology	University of Georgia
1980	B.S.	Zoology	University of Georgia

PROFESSIONAL EXPERIENCE

President. Integrative Biostrategies (IB) LLC, 2001- present

Consultant to a variety of clients in areas of pharmacology, toxicology, risk assessment and regulatory strategy. Focus on products regulated by the U.S. Food and Drug Administration. Provides litigation support services as both consulting expert and testifying expert.

Owner. Plunkett & Associates, Houston, Texas, 1997 – 2001

Consultant to a variety of clients in areas of pharmacology, toxicology, risk assessment and regulatory strategy. Focus on products regulated by the U.S. Food and Drug Administration. Provided litigation support services as both consulting expert and testifying expert.

Manager. ENVIRON Corporation, Houston, Texas, 1992 – 1997

Consultant to a variety of clients in areas of pharmacology, toxicology, risk assessment and regulatory strategy. Focus on products regulated by the U.S. Food and Drug Administration. Provided litigation support services as both consulting expert and testifying expert.

Manager. ENVIRON Corporation, Arlington, Virginia, 1989 – 1992

Consultant to a variety of clients in areas of pharmacology, toxicology, risk assessment and regulatory strategy. Focus on products regulated by the U.S. Food and Drug Administration.

Assistant Professor. University of Arkansas for Medical Sciences, Department of Pharmacology and Toxicology, 1986 – 1989

Taught medical and graduate student courses in pharmacology (lecture and laboratory), neurosciences, cardiovascular pharmacology, and neuropharmacology. Performed basic research in area of autonomic control of cardiovascular function and neurochemical systems involved in autonomic function. Recipient of extramural funding from the Arkansas Heart Association (principal investigator).

Postdoctoral fellow. National Institute of General Medical Sciences, Pharmacology Research Associate Training Program, 1984 – 1986

Performed basic research in area of neurochemical control of cardiovascular function and neurochemical systems involved in autonomic function.

Research Assistant. University of Georgia, College of Pharmacy, Department of Pharmacology and Toxicology 1980 – 1984

Taught laboratory courses in pharmacology to pharmacy students as part of graduate student assistantship responsibilities.

HONORS AND AWARDS

Chosen for PRAT program at National Institutes of Health. Pharmacology Research Associate Training Program, 1984-1986.

Rho Chi. The University of Georgia, College of Pharmacy, Initiated, 1984.

Recipient of Excellence in Graduate Research Award. The University of Georgia, College of Pharmacy, 1983.

Alpha Lambda Delta. The University of Georgia Chapter, 1978.

PROFESSIONAL CERTIFICATION

Diplomate, American Board of Toxicology, 1993 to present.

Registered patent agent, 1999.

PROFESSIONAL MEMBERSHIPS

Member, Society for Toxicology 1992 - present

Member, American College of Toxicology, 1997 - present

Member, Society for Risk Analysis, 2007- present

President, Lone Star Chapter of the Society for Risk Analysis, 1998

Counselor, Lone Star Chapter of the Society for Risk Analysis, 1999-2000

Member, Society for Neuroscience 1985 - present

Member, American Association for Pharmaceutical Sciences 1992 - present

Member, Society for Environmental Geochemistry and Health 1992 - present

Member, ASTM Committee E06, 1990 - present

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37. Plunkett LM, Vallner JJ, Tackett RL. Prazosin lowers plasma digoxin levels. American Heart Assoc, pp 15, Savannah, GA, 1983.
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39. Bayoumi SM, Gokhale R, Plunkett L, Vallner JJ. Pharmacokinetics of clortrimazole in dogs. *Acad. Pharmaceut. Sci* 1983;13(2):204, (Miami meeting).
40. Plunkett LM, Tackett RL. Central alpha receptors and their role in digitalis cardiotoxicity. *The Pharmacologist* 1982; 24:489A.
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PRESENTATIONS

1. Plunkett LM. Regulatory primer for pharmacy students: focus on human therapeutics. Invited speaker for the AAPS Visiting Scientist Program, Texas A&M University, College of Pharmacy, Kingsville, TX, May 1, 2009.
2. Plunkett, LM. Strategies for reducing adverse drug reactions: Science versus regulatory considerations. Invited speaker for the AAPS Visiting Scientist Program, Texas A&M University, College of Pharmacy, Kingsville, TX, May 1, 2009.

3. **Plunkett L.M.** Novelty requirement of §102. Lecturer at Drexel University School of Law. September 22 and 24, 2008.
4. **Plunkett L.M.** Novelty requirement of §102. Lecturer at Rutgers School of Law, Camden Campus. September 22 and 24, 2008.
5. **Plunkett L.M.** Strategies for reducing adverse drug reactions: Science versus regulatory considerations. Invited speaker for the AAPS Visiting Scientist Program, Florida A&M University, Tallahassee, FL, October 26, 2006.
6. **Plunkett L.M.** The guidance as currently implemented: experience with Minnesota's draft risk levels. Presented at the ISRTP workshop entitled: EPA's New (Proposed) Guidance for Assessing Cancer Risks from Early Life Exposures. Genotoxic Mode of Action and Implications for Human Health-Based Standards. Baltimore, MD February 10, 2005.
7. **Plunkett L.M.** An overview of the regulation of products of biotechnology: Who's in charge? Lecturer at University of Houston at Clearlake, November 17, 2004.
8. **Plunkett L.M.** Moderator of the symposium entitled "Regulation of genetically modified cells, foods, organisms and animals for consumer and therapeutic use. Meeting of the American Association of Pharmaceutical Sciences (AAPS), Baltimore, MD, November 11, 2004.
9. **Plunkett L.M.** A Road map to the US Food And Drug Administration Regulations. Invited Speaker and Session Co-chair, Federation of European Biochemical Societies (FEBS), Istanbul, Turkey, October 20-24, 2002.
10. **Plunkett L.M.** An overview of the regulation of products of biotechnology: Who's in charge? Lecturer at University of Houston at Clearlake, November 2001.
11. **Plunkett L.M.** Differences and Similarities Between Children and Adults in their Exposure and Response to Environmental Chemicals: An Update Since 1992. Invited Speaker at ToxFORUM, Aspen CO, July 2001.
12. **Plunkett L.M.** Do current FIFRA guideline tests protect infants and children? Lead as a case study. Invited speaker at the Sixteenth International Neurotoxicology Conference, Pesticides and Susceptible Populations: Who is at Risk and When? Little Rock, Arkansas, September 13-16 1998
13. **Plunkett L.M.** An overview of biotechnology regulations: the USFDA and the USEPA. Lecturer at University of Houston at Clearlake, October 16 1998.

14. Rodricks JV, Santamaria AB, Plunkett LM. Risk Assessment as a Tool in Litigation: A Discussion of the Uses and Their Limits [Presented by Plunkett LM]. Society for Risk Analysis, , New Orleans, LA. December 10 1996.
15. Plunkett LM. Current Issues in Lead Exposure and Risk Assessment. Symposia at the annual meeting of The American College of Toxicology, Valley Forge, PA. November 9 1996.
16. Plunkett LM . An Overview of Biotechnology Regulations: Environmental Regulations. Lecturer at the South Texas School of Law, October 1995.
17. Plunkett LM. An Overview of Biotechnology Regulations: FDA Regulations. Lecturer at the South Texas School of Law, October 1995.
18. Plunkett LM . A Discussion of Toxicokinetics. Featured speaker at a symposium at the Int. Congress of Toxicol., July 5 1995.
19. Plunkett LM. Chutes and Ladders: The Hazardous Journey for R&D to Market. Featured speaker at the Futurist's Conference, Irvine, CA, June 28, 1995.

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1. Rodricks JV, Frankos VH, Plunkett LM. 1995. Food Additives. In: Regulatory Toxicology. C.P. Chengelis, J.F. Holson and S.C. Gad (eds.) Raven Press, New York, New York, 51-82.
2. Plunkett LM, Turnbull D, Rodricks JV. 1992. Differences between adults and children affecting exposure assessment. In: Similarities and Differences Between Children and Adults: Implications for Risk Assessment. P.S. Guzelian, C.J. Henry and S.S. Olin (eds.) ILSI Press, Washington D.C., 79-96.
3. Saavedra JM, Plunkett LM, Correa FMA, Israel A, Kurihara M, Shigematsu K. 1986. Quantitative autoradiography of angiotensin and atrial natriuretic factor binding sites in brain nuclei of spontaneously hypertensive rats. In Brain Peptides and Catecholamines in Cardiovascular Regulation in Normal and Disease States.

MISCELLANEOUS

1. Plunkett LM, Brett SM. 1991. A new look at lead: sources, exposures, and uptake in populations at risk. ENVIRON Report. 5:6-9.
2. Plunkett LM, Frankos VH. 1991. FDA re-examines the safety of silicone gel-filled breast implants. ENVIRON Report. 5:10-13.

APPENDIX B

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
Dec. 1993	Management of the manifestations of psychotic disorders (<i>i.e.</i> , schizophrenia)	Hypersensitivity to Risperdal	Neuroleptic Malignant Syndrome (NMS), Tardive Dyskinesia (TD), and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Metabolic and Nutritional Disorders Infrequent Diabetes Mellitus (DM) and weight gain ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal	

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
March 1994	Management of the manifestations of psychotic disorders (i.e., schizophrenia)	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent DM and weight increase ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial	N

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
August 1994	Management of the manifestations of psychotic disorders (i.e., schizophrenia)	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM Postintroduction reports of DM aggravated Cerebrovascular Disease ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular	Y In Adverse Rxns section, "diabetes mellitus" has word "aggravated" following it as related to postintroduction reports; First mention of Cerebrovascular disease as part of postintroduction reports

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
Dec. 1994	Management of the manifestations of psychotic disorders (i.e., schizophrenia)	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM Postintroduction	N

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					reports of DM- aggravated Cerebrovascular Disease ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation,	

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects: (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
April 1995	Management of the manifestations of psychotic disorders (i.e., schizophrenia)	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM Postintroduction reports of DM aggravated Cerebrovascular disease ECG Changes Infrequent: Palpitation,	N

**Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia,
Cardiovascular and Cerebrovascular Events)**

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure	

**Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia,
Cardiovascular and Cerebrovascular Events)**

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Rare: Gynecomastia Male breast pain	
April 1996	Management of the manifestations of psychotic disorders (i.e., schizophrenia)	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial	Y (Change from 1994) First mention of "Diabetic Ketoacidosis" in Adverse Rxns section as related to postintroduction reports

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
July 1996	Management of the manifestations of psychotic disorders (i.e., schizophrenia)	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM	N

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation,	

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
September 1996	Management of the manifestations of psychotic disorders (i.e., schizophrenia)	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder ECG Changes Infrequent: Palpitation, Hypertension,	N

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare:	

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Gynecomastia Male breast pain	
July 1997	Management of the manifestations of psychotic disorders (i.e., schizophrenia)	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions,	N

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
November 1997	Management of the manifestations of psychotic disorders (i.e., schizophrenia)	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM DM aggravated	N

**Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia,
Cardiovascular and Cerebrovascular Events)**

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Diabetic Ketoacidosis Cerebrovascular disorder ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea,	

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
July 1998	Management of the manifestations of psychotic disorders (i.e., schizophrenia)	Hypersensitivity to Risperdal	NMS, TD ,and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder ECG Changes Infrequent: Palpitation, Hypertension, Hypotension,	N

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia	

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Male breast pain	
May 1999	Management of the manifestations of psychotic disorders (i.e., schizophrenia)	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions,	N

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia, Male breast pain	
December 2000	Management of the manifestations of psychotic disorders (i.e., schizophrenia)	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM DM aggravated Diabetic Ketoacidosis	N

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Cerebrovascular disorder ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain,	

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects: (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
November 2001	Treatment of schizophrenia	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder that includes cerebrovascular accidents ECG Changes Infrequent: Palpitation,	Y Indication language changed Adverse Rxns section under postintroduction reports now includes "cerebrovascular disorder, including cerebrovascular accident"

**Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia,
Cardiovascular and Cerebrovascular Events)**

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure	

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Rare: Gynecomastia Male breast pain	
February 2002	Treatment of schizophrenia	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder, including cerebrovascular accident ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia,	N

**Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia,
Cardiovascular and Cerebrovascular Events)**

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
July 2002	Treatment of schizophrenia	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders	Y First mention of "hyperglycemia" in the Adverse Rxns

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
March 2003	Treatment of schizophrenia	Hypersensitivity to Risperdal	NMS, TD, and Proarrhythmic Effects Cerebrovascular Adverse events, including stroke, in elderly patients with dementia	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight Increase and DM DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder, including cerebrovascular	Y Includes cerebrovascular events in warning section

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Infrequent weight increase and DM DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder, including cerebrovascular accident Hyperglycemia ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression,	section under postintroduction reports

**Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia,
Cardiovascular and Cerebrovascular Events)**

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					accident Hyperglycemia ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain,	

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
December 2003	Treatment of schizophrenia Short-term treatment of acute mania or mixed episodes associated with Bipolar I disorder	Hypersensitivity to Risperdal	Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia Hyperglycemia Diabetes Mellitus NMS and TD	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM Postintroduction reports include DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder, including cerebrovascular accident Hyperglycemia ECG Changes	Y Added indication of use for short-term treatment of acute mania or mixed episodes associated with Bipolar I disorder Hyperglycemia, and D M added to Warnings section as well (language change too) Removes potential for proarrhythmic

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent:	effects from Warnings section

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Ejaculation failure Rare: Gynecomastia Male breast pain	
2004	Treatment of schizophrenia Short-term treatment of acute mania or mixed episodes associated with Bipolar I disorder	Hypersensitivity to Risperdal	Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia Hyperglycemia Diabetes Mellitus NMS and TD	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM Postintroduction reports include DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder, including cerebrovascular accident Hyperglycemia ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block,	N

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	

**Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia,
Cardiovascular and Cerebrovascular Events)**

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
2005	Treatment of schizophrenia Short-term treatment of acute mania or mixed episodes associated with Bipolar I disorder	Hypersensitivity to Risperdal	Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia Hyperglycemia Diabetes Mellitus NMS and TD	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM Postintroduction reports include DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder, including cerebrovascular accident Hyperglycemia ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular	N

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
December 2006	Treatment of schizophrenia	Hypersensitivity to Risperdal	Cerebrovascular Adverse Events, Including Stroke, in	Hyperprolactinemia, Orthostatic Hypotensions	Weight Changes Weight Gain Metabolic and	Y Appearance of Black

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
	Short-term treatment of acute mania or mixed episodes associated with Bipolar I disorder Treatment of irritability associated with autistic disorder in children and adolescents		Elderly Patients with Dementia Hyperglycemia Diabetes Mellitus NMS TD Appearance of "Black Box" warning re: death in elderly patients with dementia		Nutritional Disorders Infrequent weight increase and DM Postintroduction reports include DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder, including cerebrovascular accident Hyperglycemia ECG Changes Infrequent: Palpitation, Hypertension, Hypotension, AV block, Myocardial Infarction Rare: Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions,	Box warning for death in elderly patients New language in section in Precautions on "Hyperprolactinemia" indicating Risperdal raises prolactin higher than other antipsychotic drugs. Added new indication of treatment of irritability associated with autistic disorder in children and adolescents

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Ventricular Extrasystoles, ST Depression, Myocarditis (F) Infrequent: Nonpuerperal Lactation, Amenorrhea, Female breast pain, Dysmenorrhea (M) Frequent: Erectile dysfunction, Infrequent: Ejaculation failure Rare: Gynecomastia Male breast pain	
June 2007	Treatment of schizophrenia in adults and adolescents (13-17 years). Short-term treatment of	Hypersensitivity to Risperdal	Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia Hyperglycemia Diabetes Mellitus Hyperprolactinemia	NOTE: At this time upon compliance with new label format, the "Warnings" and "Precautions" sections are now merged into one	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM Postintroduction reports include DM	Y New indication age groups added for schizophrenia and Bipolar I disorder. No mention of

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
	acute mania or mixed episodes associated with Bipolar I disorder in adults, children and adolescents (10-17 years). Treatment of irritability associated with autistic disorder in children and adolescents		NMS TD Orthostatic Hypotension "Black Box" warning re: death in elderly patients with dementia	larger section covering both	aggravated Diabetic Ketoacidosis Cerebrovascular disorder, including cerebrovascular accident Hyperglycemia Change in ECG Hypotension Postural, Hypotension Gynecomastia AV Block, Bundle Branch Block Tachycardia (F) Amenorrhea, Lactation Nonpuerperal (M) Ejaculation disorder, Ejaculation Failure	dysmenorrhea, hypertension, male or female breast pain, Ventricular Tachycardia, Angina Pectoris, Premature Atrial Contractions, T Wave Inversions, Ventricular Extrasystoles, ST Depression, Myocarditis, or Myocardial Infarction First mention of Bundle Branch Block, Postural Hypotension,
August 2008	Treatment of schizophrenia in adults and adolescents (13-17 years).	Hypersensitivity to Risperdal	Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia Hyperglycemia	NOTE: At this time upon compliance with new label format, the "Warnings" and "Precautions"	Weight Changes Weight Gain Metabolic and Nutritional Disorders Infrequent weight increase and DM	Y New label format implemented making label appear different although language of

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
	Short-term treatment of acute mania or mixed episodes associated with Bipolar I disorder in adults, children and adolescents (10-17 years). Treatment of irritability associated with autistic disorder in children and adolescents		Diabetes Mellitus Hyperprolactinemia NMS TD Orthostatic Hypotension "Black Box" warning re: death in elderly patients with dementia	sections are now merged into one larger section covering both	Postintroduction reports include DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder, including cerebrovascular accident Hyperglycemia Change in ECG Hypotension postural, Hypotension Tachycardia, Arrhythmia, AV Block, Bundle Branch Block, Ejaculation Failure, Lactation Nonpuerperal, Amenorrhea Gynecomastia	sections of interest were the same. Arrhythmia added to Adverse Reactions

**Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia,
Cardiovascular and Cerebrovascular Events)**

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
The following are concerned with long-acting injections						
January 2004	Treatment of schizophrenia	Hypersensitivity to Risperdal	Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia Hyperglycemia Diabetes Mellitus NMS TD	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Metabolic and Nutritional Disorders Infrequent hyperglycemia and DM DM aggravated Diabetic Ketoacidosis Cerebrovascular disorder, including cerebrovascular accident Hyperglycemia ECG Changes Hypertension Frequent: Hypotension Infrequent: Postural	

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Hypotension (F) Frequent: Amenorrhea Infrequent: Nonpuerperal lactation, Dysmenorrhea, Breast Pain (M) Infrequent: Ejaculation Failure Infrequent: Gynecomastia, Myocardial Infarction, Myocardial Ischemia, Angina Pectoris	
March 2007	Treatment of schizophrenia	Hypersensitivity to Risperdal	Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia Hyperglycemia Diabetes Mellitus NMS	Hyperprolactinemia, Orthostatic Hypotension	Weight Changes Metabolic and Nutritional Disorders Infrequent hyperglycemia and DM DM aggravated	Y Weight gain not considered infrequent Hyperglycemia considered infrequent in adverse

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
			TD First appearance of "Black Box" warning re: death in elderly patients with dementia		Diabetic Ketoacidosis Cerebrovascular disorder, including cerebrovascular accident Hyperglycemia ECG Changes Hypertension Frequent: Hypotension Infrequent: Postural Hypotension (F) Frequent: Amenorrhea Infrequent: Nonpuerperal lactation, Dysmenorrhea, Breast Pain (M) Infrequent: Ejaculation Failure Infrequent:	reactions Wording change in hyperprolactinemia section of Precautions

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Gynecomastia, Myocardial Infarction, Myocardial Ischemia, Angina Pectoris	
February 2008	Treatment of schizophrenia	Hypersensitivity to Risperdal	Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia-Related Psychosis Hyperglycemia Diabetes Mellitus Hyperprolactinemia NMS TD "Black Box" warning re: death in elderly patients with dementia	Hyperprolactinemia, Orthostatic Hypotension	Weight Increase Metabolic and Nutritional Disorders Infrequent hyperglycemia Diabetic Ketoacidosis Hyperprolactinemia Hypertension ECG Changes Frequent: Hypotension Infrequent: Postural Hypotension (F) Frequent: Amenorrhea Infrequent:	Y Hyperprolactinemia added to Adverse Rxns section Postintroduction reports listed are different in not including cerebrovascular accidents, DM aggravated, and hyperglycemia

Summary of Risperdal Labeling Changes Related to Selected Adverse Effects (Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia, Cardiovascular and Cerebrovascular Events)						
Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
					Nonpuerperal Lactation, Dysmenorrhea, Breast Pain (M) Infrequent: Ejaculation Failure Infrequent: Myocardial Ischemia, Angina Pectoris, Myocardial Infarction Gynecomastia	
February 2009	Treatment of schizophrenia	Hypersensitivity to Risperdal	Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia- Related Psychosis Hyperglycemia Diabetes Mellitus Hyperprolactinemia NMS TD Orthostatic Hypotension "Black Box" warning	Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia-Related Psychosis Hyperglycemia Diabetes Mellitus Hyperprolactinemia NMS TD Orthostatic Hypotension	Cerebrovascular Adverse Events, Including Stroke Hyperglycemia Diabetes Mellitus Hyperprolactinemia Changes in body weight Weight Gain ECG Changes Tachycardia, Atrioventricular block first degree,	Y Removal of hypertension from Adverse Reactions and no mention anywhere else No mention of hypotension or postural hypotension No mention of Female Breast Pain, Nonpuerperal

**Summary of Risperdal Labeling Changes Related to Selected Adverse Effects
(Extrapyramidal Effects, Hyperprolactinemia and Associated Events, Weight Gain, Diabetes, Hyperglycemia,
Cardiovascular and Cerebrovascular Events)**

Month and Year of Label	Approved Indications	Contraindications	Warnings	Precautions	Adverse Reactions	Change from Last Label (Y/N)
			re: death in elderly patients with dementia		Palpitations, Sinus Bradycardia, Bundle Branch Block Left, Bradycardia, Sinus Tachycardia, Bundle Branch Block Right Amenorrhea, Erectile Dysfunction, Galactorrhea, Sexual Dysfunction, Gynecomastia	Lactation or Dysmenorrhea. First mention of Galactorrhea No mention of Ejaculation failure; First mention of Erectile Dysfunction and Sexual Dysfunction First mention of Atrioventricular Block First Degree, Sinus Bradycardia, Bundle Branch Block Left and Bradycardia

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SUPPLEMENTAL EXPERT REPORT OF
Laura M. Plunkett, Ph.D., DABT
August 4, 2010

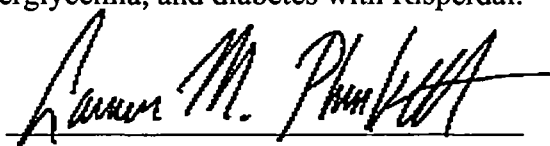
I have been asked by plaintiffs' counsel to supplement my expert witness report dated July 7, 2009 concerning Risperdal to elucidate aspects of my earlier report. The statements and observations made in this Supplemental Report are based on my knowledge, training, and experience described in my earlier report at pages 1-2 and other places in the report.

56. As I described in my previous report, the development, approval, and marketing of Risperdal are regulated by the FDA in the United States. In particular, Risperdal's drug labeling is regulated by the FDA in terms of what information must be included on the labeling and how that information is presented. Expanding upon my earlier observations, an example of the regulations concerning the content of drug labeling is contained in section 352(f) of title 21 of the United States Code, which requires that a drug's labeling must contain "adequate directions for use," including a statement of all conditions, purposes, and uses for which the drug is intended. Section 352(f) also requires that a drug's labeling must contain "adequate warnings against use" when taking or administering the drug may be dangerous. In addition, section 352(a) requires that a drug's labeling have fair balance and not be false or misleading in any particular. If a drug's labeling does not satisfy such requirements, the drug is deemed misbranded under section 352 and may not be distributed in interstate commerce under section 331 of the United States Code. For example, a drug that is promoted for a use that has not been found to safe and effective by the FDA does not contain adequate directions for use because the unapproved use is not included in the FDA-approved labeling for the drug.

57. In my earlier report, I stated that a company must change the language of its drug's labeling as directed by the FDA if the FDA determines that information in a drug label is false or misleading. Expanding upon that statement, section 321(n) of title 21 of the United States Code provides that, when "an article is alleged to be misbranded because the labeling or advertising is misleading, then in determining whether the labeling or advertising is misleading

there shall be taken into account (among other things) not only representation made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual." In addition, under section 201.57(e) of title 21 of the Code of Federal Regulations (2006), a drug's labeling "shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved." While a drug's labeling is considered to include promotional or marketing materials for the drug, specific provisions of the FDA statutes and regulations address the content of promotional or marketing materials for a drug, such as section 352(n) of title 21 of the United States Code and section 202.1 of the Code of Federal Regulations.

58. Based upon my knowledge, training, experience, and observations in my earlier report, it is my opinion that Risperdal's labeling was and is false and misleading, lacks fair balance, and did not bear adequate directions for use or warnings against use, and that Risperdal's labeling should have been revised because there was reasonable evidence of an association of hyperprolactinemia, weight gain, hyperglycemia, and diabetes with Risperdal.

A handwritten signature in black ink, appearing to read "Laura M. Plunkett", written over a horizontal line.

Laura M. Plunkett, Ph.D., DABT