UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF INDIANA
INDIANAPOLIS DIVISION

DEBRA L. TUCKER, Individually and as Personal Representative of the ESTATE OF RICK G. TUCKER,	)	
Plaintiff,	)	
v.	)	**CASE NO. 1:04-cv-1748-DFH-DML**
SMITHKLINE BEECHAM CORP., d/b/a GLAXOSMITHKLINE, a Pennsylvania Corporation,	)	
Defendant.	)	

ENTRY ON DEFENDANT'S MOTION FOR SUMMARY JUDGMENT

Introduction

Plaintiff Debra Tucker has sued defendant SmithKline Beecham Corp. d/b/a GlaxoSmithKline ("GSK") for negligence, strict liability, and breach of express and implied warranty.[1] Plaintiff's brother was Father Rick Tucker, a Roman Catholic priest who committed suicide in September 2002, a few weeks after he began taking Paxil, an anti-depressant drug manufactured and distributed by GSK. Plaintiff Tucker alleges that GSK failed to include in Paxil's packaging and inserts a warning advising doctors and their patients of an

[1]**Effective October 27, 2009, the defendant changed its corporate name to GlaxoSmithKline LLC.**

increased risk of suicide in adults taking Paxil and that GSK's failure to warn proximately caused Father Tucker's death. GSK has moved for summary judgment on the issue of causation. On summary judgment, the court does not engage in fact-finding and does not weigh the credibility of conflicting evidence. Instead, the court must view the conflicting evidence and the undisputed evidence in the light reasonably most favorable to Tucker as the non-moving party, giving her the benefit of all reasonable inferences in her favor. The essential question is "whether the evidence presents a sufficient disagreement to require submission to a jury or whether it is so one-sided that one party must prevail as a matter of law." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 251-52 (1986). The facts in this entry are stated in view of this standard, which requires the court to deny GSK's motion for summary judgment.[2]

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[2]Plaintiff's Tucker's case has narrowly survived two earlier challenges. First, the court held that there are material facts in dispute regarding whether Debra Tucker, as an adult sister of Father Tucker, qualified as his dependent such that she could pursue substantial damages in a wrongful death claim under Indiana law. See *Tucker v. SmithKline Beecham Corp.*, 2006 WL 753128 (S.D. Ind. March 21, 2006). The court later granted defendant's motion for summary judgment based on a theory of federal preemption but then later reversed that decision on reconsideration, see *Tucker v. SmithKline Beecham Corp.*, 596 F. Supp. 2d 1225 (S.D. Ind. 2008), the position later taken by the Supreme Court on that question. See *Wyeth v. Levine*, 129 S. Ct. 1189 (2009).

I. *Undisputed Facts*

A. *GSK and Paxil*

GSK markets, promotes, distributes, and manufactures the prescription drug paroxetine under the trade name Paxil. Paxil is generally classified as a selective serotonin re-uptake inhibitor, or SSRI, and has been approved by the U.S. Food and Drug Administration for the treatment of depression, generalized anxiety disorder, panic disorder, social anxiety disorder, obsessive-compulsive disorder, and post-traumatic stress disorder. GSK Answer ¶¶ 8, 11. SSRIs operate by adjusting the manner in which the neurotransmitter serotonin is processed by brain cells. SSRIs are used to treat depression, along with other conditions.

B. *Father Rick Tucker*

Father Tucker committed suicide on September 18, 2002. He left behind a journal, in which he documented his thoughts and feelings and recorded day-to-day events and activities. In his journal, he wrote about his physical state:

> **"I have discovered that I am diabetic. . . . Whole lifestyle change." Dkt. 99, Ex. 4 at 0620 (June 11, 1999).**
>
> **"Had my visit [with] Dr. Bright. The regular stuff was fine however he discovered a blockage in my carotid artery so he had me take an ultrasound." *Id.* at 0680 (July 18, 2000).**

"July 20, 2000, Thursday, I am to have an MRI done on July 28 then . . . I am to have a stress test done. At first there was such an anxious feeling, but tonight I feel at peace." *Id.* at 0681.

"Aug. 17, 2000, Thursday, Saw Dr. Bright today. There is a problem [with] my heart. So I am to have a heart cath. In the near future. Then I may have angiplasti [sic]. Time will tell. There are days that I feel anxious, but in general very much at peace. . . ." *Id.* at 0683.

"(Undated entry) I had surgery on October 13 [2000]. It was textbook. . . I left the hospital a day ahead of schedule. Spent two weeks at St. Mary Muncie – had great care. Came home and resumed duties full time after a couple of weeks. Much to be thankful for this year." *Id.* at 0684.

Other journal entries describe other outside stressors affecting Father Tucker during this time:

[Regarding sister's allegations of sexual abuse against the Diocese]: "Well today starts the first day we wait to hear from the atty's. Please God, let this be over this week. Let them settle." *Id.* at 1044 (Aug. 12, 2002).

"Debbie's Atty called and said he thought that we might not hear anything until Monday since strictly speaking they had until the end of business Friday to respond. Given their mindset I don't doubt that they will not do it this way. I also think they will fight this in some way." *Id.* at 1044 (Aug. 15, 2002).

"Well, today begins another week of waiting. The Atty's meet Wednesday and map out the strategy to see how they will pursue the law suite [sic]. Mr. Veigh called Wednesday(?) to tell Debbie they were going to meet. There is a little fear in me that they will decide they can't win the case and need to drop it. However, I think that is just the anxiousness inside of me. I hope that when the diocese sees that she is serious, they will settle out of court. Bishop has this image he wants to portray, and I am hoping that plays in our favor." *Id.* at 1046 (Aug. 26, 2002).

In May 1999, Father Tucker began seeing Thomas Bright, M.D., a practicing physician who is board certified in internal medicine, pulmonary disease, and critical care medicine. Dkt. 99 Ex. 1 at 7-9 (Bright Dep.). In September 1999, Dr.

Bright prescribed Trazodone because Father Tucker was having difficulty sleeping. *Id.* at 47. He prescribed Ativan in September 2000 because Father Tucker was feeling anxious about an upcoming carotid artery surgery and pressures related to his work. *Id.* at 57-58.

On July 26, 2002, Father Tucker sought counseling from a psychologist, Dr. Thomas Murray. Dkt. 85 Ex. D at 33 (Murray Dep.). According to Dr. Murray, Father Tucker sought counsel because he had "little or no opportunity" to discuss, vent, or process his emotions. *Id.* Dr. Murray testified that Father Tucker was anxious regarding an upcoming audit by the diocese because he had "advanced himself some monies" and the Church would discover these "irregularities." *Id.* at 34, 46. Dr. Murray also described Father Tucker as "angry and irritated at the diocese for not following through with what he thought they should have done" with regard to his sister's allegations. *Id.* at 34.

C. *Father Tucker's Use of Paxil*

On August 28, 2002, Dr. Bright prescribed Paxil for Father Tucker. Dkt. 85, Ex. C at 61-62 (Bright Dep.). Father Tucker had complained to Dr. Bright "that he had a problem with feeling panicked . . . and said that it was making it difficult for him to perform his duties." *Id.* at 62. Father Tucker advised Dr. Bright that "he was busy with church issues, and with a lawsuit . . . he had things going on at the parish that he felt that he was experiencing these episodes of panic during

the day that were new." *Id.* at 62-63. Father Tucker reported that he was in counseling but that he wanted a prescription as well. *Id.* at 62.

Dr. Bright recommended that Father Tucker begin with a low dose of Paxil during the day. Before he prescribed Paxil, Dr. Bright took into consideration the risks and benefits of treatment. *Id.* at 62, 70. He discussed the potential side effects of the medication with Father Tucker. *Id.* at 64. Dr. Bright selected Paxil because, based upon local practice, it was the SSRI used most commonly for people with panic disorders and it "might be more beneficial." *Id.* at 63. The doctor advised Father Tucker to let him know if he experienced any problems while on the medication or if he was not being benefitted. *Id.* at 64-65. Father Tucker never contacted Dr. Bright to discuss any perceived problems or lack of benefit from Paxil. *Id.* at 65, 66. Dr. Bright has no opinion either way as to whether Paxil caused or contributed to Father Tucker's death. *Id.* at 70.

Dr. Bright testified that prior to prescribing Paxil for Father Tucker, he had reviewed the package insert for Paxil. *Id.* at 34. He stated that in 2002, he was familiar with the package inserts for SSRIs. Dkt. 99, Bright Dec. ¶3. He did not recall any specific warnings in 2002 regarding an association between Paxil and suicide in adults. Nor did Dr. Bright have any independent knowledge in 2002 regarding any association between Paxil and suicide in adults. *Id.*, ¶¶3-4. If he had been provided with a warning that Paxil was associated with suicide, he

would have considered that warning in making his decision to prescribe Paxil to Father Tucker. *Id.*, ¶ 6.

D. *Paxil, Other SSRIs, and Suicidality Generally*

Even before Paxil was approved for use by the FDA, concerns existed that at least one other SSRI might actually cause patients to develop thoughts of suicide. A series of six Harvard case studies published in the American Journal of Psychiatry in February 1990 found that intense, violent, suicidal thoughts appeared to be associated with the use of fluoxetine (Prozac), a drug that operates in a manner similar to Paxil. See Teicher, M. H., et al., *Emergence of Intense Suicidal Preoccupation During Fluoxetine Treatment,* Am. J. Psychiatry 147, 207-10 (1990). In 1991 the FDA convened a meeting of its Psychopharmacological Drugs Advisory Committee to evaluate the possible connection between fluoxetine and suicide. The PDAC and the FDA agreed that no credible evidence existed at the time that fluoxetine caused the "emergence and/or intensification of suicidality and/or other violent behaviors." Dkt. 80, Ex. F at 294.

In evaluating the new drug application for Paxil, the lead FDA safety reviewer reported in June 1991, after reviewing submitted data for the drug, that "there is no signal in this large data base that paroxetine exposes a subset of depressed patients to additional risk for suicide, suicide attempts or suicidal

ideation." Dkt. 80, Arning Aff. Ex. 3 at 25. Another FDA official, Dr. Thomas Laughren, reported:

> **The bottom line here is that none of [the investigations] suggested any greater risk of suicidality for paroxetine than for the other comparator groups and, in fact, paroxetine actually beat the other groups on a number of these variables. So there was no suggestion here of emergence of suicidality with paroxetine.**

Dkt. 80, Ex. 4 at 29-30. The PDAC unanimously concluded that Paxil was safe and effective, and it recommended approval. *Id.* at 153-54. The FDA approved Paxil without requiring any warning associating the drug with suicidality. Dkt. 80, Ex. 5 at 1.

By 2002, when Father Tucker was prescribed Paxil, the prescribing information contained the following warning regarding suicide:

> **PRECAUTIONS: Suicide**
>
> **The possibility of a suicide attempt is inherent in major depressive disorder and may persist until significant remission occurs. Close supervision of high-risk patients should accompany initial drug therapy. Prescriptions for *Paxil* should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose.**
>
> **Because of well-established comorbidity between major depressive disorder and other psychiatric disorders, the same precautions observed when treating patients with major depressive disorder should be observed when treating patients with other psychiatric disorders.**

Dkt. 85, Ex. A at 10 (emphasis in original). Dr. Arvin Schroff, a former employee of the FDA, opined that the information contained in Paxil's label in 2002 was

insufficient to warn physicians adequately about the association between Paxil and suicidality. Dkt. 99, Ex. 2 at 4.

In April 2006, GSK completed an internal analysis of suicidality in patients of all ages using Paxil. GSK's analysis "showed a higher frequency of suicidal behavior in young adults (prospectively defined as aged 18-24 years) treated with paroxetine compared with placebo, although this difference was not statistically significant. In the older age groups (aged 25-64 years and = 65 years), no such increase was observed." Dkt. No. 150, Ex. 1 at 9. GSK's 2006 report went on to note: "In adults with MDD [major depressive disorder] (all ages), there was a statistically significant increase in the frequency of suicidal behaviour in patients treated with paroxetine compared with placebo. However, the majority of these attempts for paroxetine (8 of 11) were in younger adults aged 18-30 years." *Id.* In May 2006, GSK issued a "Dear Doctor" letter advising prescribing physicians of its new findings. Dkt. 83, Ex. 8. Between May 2006 and August 2007, GSK revised Paxil's labeling to include the following language:

> **All pediatric patients being treated with antidepressants for any indication should be observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. Such observation would generally include at least weekly face-to-face contact with patients or their family members or caregivers during the first 4 weeks of treatment, then every other week visits for the next 4 weeks, then at 12 weeks, and as clinically indicated beyond 12 weeks. Additional contact by telephone may be appropriate between face-to-face visits.**
>
> **Adults with MDD or co-morbid depression in the setting of other psychiatric illness being treated with antidepressants should be observed similarly for**

> **clinical worsening and suicidality, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.**
>
> **. . .**
>
> **In adults with MDD (all ages), there was a statistically significant increase in the frequency of suicidal behavior in patients treated with paroxetine compared with placebo (11/3,455 [0.32%] versus 1/1,978 [0.05%]); all of the events were suicide attempts. However, the majority of these attempts for paroxetine (8 of 11) were in younger adults aged 18-30 years. These MDD data suggest that the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24.**

Dkt. No. 99, Ex. 3 at 11-12.

In the meantime, the FDA also engaged in its own evaluation of whether antidepressants were associated with increased risk of suicidality in adults. The FDA announced in July 2005 that it was performing a "complete review of all available data" to determine whether such a link existed. See Dkt. No. 80, Ex. 33. The PDAC convened to review the agency's meta-analysis of suicidality data derived from placebo-controlled trials of antidepressants in adult patients with major depressive disorder and other psychiatric disorders. The PDAC evaluated a pooled analysis of 295 short-term trials covering more than 77,000 patients and eleven different antidepressants. Dkt. No. 149, Ex. B at 2. Based on recommendations from the PDAC, the FDA contacted GSK in May 2007 and instructed GSK to delete the Paxil-specific language in its labeling and to replace it with a class-wide label for all SSRIs. Dkt. No. 149, Ex. C (Letter from Thomas Laughren, M.D., Director of the FDA's Division of Psychiatry Products, to Barbara

Arning, M.D., Senior Director of GSK U.S. Regulatory Affairs). The label for Paxil and all other SSRIs was to include the following warning:

> **Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of [Paxil] or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 or older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior.**

Id. **The FDA's decision was based on an analysis of clinical trials involving more than 77,000 adult patients in 295 antidepressant clinical trials. Dkt. 149, Ex. B at 2. In total, the FDA evaluated more than 372 clinical trials involving more than 100,000 patients. Dkt. 149, Ex. D at 1. Additional facts are stated below, keeping in mind the summary judgment standard.**

II. *GSK's Daubert Motions*

Causation is a required element of each of the plaintiff's claims, and, in pharmaceutical cases, expert testimony is required to prove a causal connection between the drug and its alleged effects. See *Armstrong v. Cerestar USA, Inc.*, 775 N.E.2d 360, 366 (Ind. App. 2002) (under Indiana law, "questions of medical causation of a particular injury are questions of science necessarily dependent on

the testimony of physicians and surgeons learned in such matters"); *Wolfe v. Stork RMS-Protecon, Inc.*, 683 N.E.2d 264, 268 (Ind. App. 1997) ("Proximate cause is an essential element of, and is determined in the same manner in, both negligence and product liability actions."). Along with its motion for summary judgment on causation, GSK filed a motion *in limine* to exclude the testimony of the plaintiff's designated experts on causation, Dr. David Healy and Dr. Joseph Glenmullen, arguing that their testimony is inadmissible under Rule 702 of the Federal Rules of Evidence and the principles of *Daubert v. Merrell Dow Pharmaceuticals., Inc.*, 509 U.S. 579 (1993). Because the admissibility of Dr. Healy's and Dr. Glenmullen's testimony is critical to the plaintiff's tort claims, the court addresses GSK's *Daubert* motions first.

A. *Report of Dr. David Healy*

Dr. David Healy is a psychiatrist and academic neuropsychopharmacologist. He is an accomplished researcher and lecturer. He was awarded his doctorate based on his study and thesis on the subject of the serotonin reuptake system, and he has written many peer-reviewed medical journal articles concerning the SSRI class of drugs, including Paxil, and the risks and benefits of those drugs. He has authored or co-authored seventeen books in the field of mental health and psychiatric drugs, more than 140 peer-reviewed medical journal publications, and more than 160 non-peer reviewed articles, and he has been invited to present his

research and findings on over 200 occasions around the world. Dkt. 105, Healy Dec. ¶¶ 4, 8. His credentials as an expert in this arena are undisputed.

Dr. Healy opined to a reasonable degree of scientific and medical probability, and based on his training and experience and review of relevant literature, that SSRIs, including Paxil, "can make an individual who may not have been likely to commit suicide before taking the pill, more likely to do so while on a course of treatment." Dkt. 83, Ex. 12 at 1 (April 30, 2006 Healy Report). In reaching this conclusion, Dr. Healy relied heavily upon case reports and his own studies and calculations, particularly on his review of GSK's healthy volunteer studies and his meta-analysis of other available data. His opinion is based largely on his ongoing review and analysis of studies relating to SSRIs generally, not Paxil exclusively. In explanation, Dr. Healy stated, "it seems clear that in general these drugs are associated with common profiles of both main effects and side effects. All have received licenses for a similar set of nervous conditions. All produced a set of side effects including extra-pyramidal side effects, which are not generally seen with non-SSRI antidepressants." Dkt. 83, Ex. 12 at 13-14. He also reviewed the mechanisms through which Paxil and other antidepressants could trigger suicide, and he addressed the industry practice of ghostwriting scientific articles, which he said has led to exaggeration of the benefits of drugs and concealment of their risks. Dkt. 83, Ex. 12 at 6.

The healthy volunteer studies Dr. Healy relied on date back to 1958. Not all dealt with Paxil. Of those that did, Dr. Healy reported that GSK's healthy volunteer studies with Paxil used GSK employees and studied the drug's impact on gut physiology, not Paxil's psychotrophic effects. Dkt. 83, Ex. 12 at 7. Because these studies were single dose, Dr. Healy found these studies to be "relatively uninformative." *Id.* at 8.

GSK's multiple dose studies, according to Dr. Healy, showed dropout rates as high as 50%, withdrawal syndromes as high as 85%, mood changes at 25%, agitation at 33%, and sexual dysfunction at 40%. In one study, one volunteer committed suicide following the study. Dkt. 83, Ex. 12 at 8, Appx. 1.

Dr. Healy also reported on his review of various clinical studies and randomized trials involving SSRIs, some involving Paxil. Using a Mantel-Haenszel procedure, Dr. Healy found that the data obtained from randomized trials that was submitted to the FDA showed up to an eight-fold greater rate of suicidal acts among patients on Paxil than among those on a placebo. Dkt. 83, Ex. 12 at 15-16 (Tables 1-2), citing Healy, D. & Aldred G., *Antidepressant Drug Use and the Risk of Suicide*, International Review of Psychiatry 17, 163-172 (2005). He reported that he interpreted these figures differently than GSK did, and he based these differences on GSK's "recoding procedure." Dr. Healy demonstrated that GSK counted suicidal acts committed by three individuals during the run-in/wash-out period and one in the follow up period as suicidal acts by participants in the

placebo group, when suicidal acts by those individuals should have been excluded. Dkt. 83, Ex. 12 at 16-17 (Figures 1, 2). In other words, Dr. Healy believed that GSK artificially inflated the suicidal acts attributable to the placebo group, skewing the results of the trial.

Similarly, Dr. Healy contended that data submitted to the British regulatory authorities showed an increased risk of suicidal acts or suicides in patients taking Paxil (1 patient in 8,481) as compared to those taking a placebo (0 patients in 5,808). Dkt. 83, Ex. 12 at 22 (Table 3), citing Expert Working Group Report on SSRIs and Suicide, issued by the Medicines and Healthcare Devices Regulatory Agency, Dec. 6, 2004. From papers presented to the Expert Working Group, Dr. Healy extrapolated the occurrence of one suicide on Paxil and none on the placebo, bringing the relative risk of suicide on treatment to 2.66 with a 95% confidence interval of .90 to 7.90; p = .067. Dkt. 83, Ex. 12 at 24. Dr. Healy also relied on the Fergusson study, which was a cumulative meta-analysis of suicidal acts from clinical trials of SSRIs generally. That study showed an approximate doubling of suicidal acts among patients on SSRIs as compared to those on a placebo in studies conducted as early as 1988. Dkt. 83, Ex. 12 at 19-20 (Fig. 5), citing Fergusson, D., et al., *The Association Between Suicide Attempts and SSRIs: A Systematic Review of 677 Randomized Controlled Trials Representing 85,470 Participants*, British Medical Journal 330(7488), 396 (2005).

Citing the healthy volunteer studies he previously referenced, Dr. Healy also reported that "figures are also available for the relative risk of suicide in patients exposed to these agents in trials for anxiety indications compared to placebo . . . in these studies, FDA reviews point to 11 suicides in 12,914 patients versus 0 suicides in 3,875 patients on placebo. From this it would seem that the risk is even greater in patients who are not classically depressed." Dkt. 83, Ex. 12 at 25. He also asserted that this analysis is borne out by an FDA analysis of the data on suicides from placebo-controlled trials, which, Dr. Healy noted, may include the data on suicides from Paxil. *Id.* at 25. That 2003 analysis, reported by Dr. Tarek Hammad, studied suicides in randomized controlled trials of patients with major depressive disorder. *Id.*, citing Hammad, T., et al., *Incidence of Suicides in Randomized Controlled Trials of Patients With Major Depressive Disorder*, Pharmacoepidemiology & Drug Safety 12, S156 (2003).

In analyzing data from randomized clinical trial data sources stemming from a working paper of the British regulatory body examining Paxil, Dr. Healy concluded that "it is reasonable to state that patients taking Paxil show an excess of suicide related events that is consistent with the rates found with other SSRI agents." Dkt. 83, Ex. 12 at 27. In a table entitled "Suicide Related Events in Paxil Placebo Controlled Adult and Pediatric Trials: on Therapy and 30 days post Taper (Study 057 Removed)," Dr. Healy provided two sets of numbers. Dkt. 83, Ex. 12 at 26 (Table 6). In the first, he showed an overall odds ratio of 1.59 for suicidal events on Paxil compared to a placebo during the 30-day period following taper

and cessation of treatment. Among depressed trial subjects, those taking Paxil had a 1.91 greater odds ratio of a suicidal event (68 of 3665 subjects on Paxil compared to 22 of 2266 subjects on a placebo), and all other trial subjects still showed an odds ratio of 0.96 (23 of 5423 subjects taking Paxil compared to 18 of 4053 subjects taking a placebo). He excluded one "placebo suicide" from his analysis because that event occurred after other psychotropic agents were introduced. Dkt. 83, Ex. 12 at 26. In his second set of data, Dr. Healy found slightly higher odds ratios in each category (1.66 overall, 1.99 for depressed subjects, and 1.01 for other subjects) under the assumption that two suicidal acts attributed to the placebo group, one in the depression studies and one from the non-depression studies, were also misclassified. *Id.*

In both sets of figures Dr. Healy omitted "Study 057," because Dr. Healy believed it to be an anomaly, or, as he put it, "distinctly odd." Dkt. 83, Ex. 12 at 26. Overall, the data showed 65 suicide events in 14,022 patients. Study 057, by itself, showed 56 suicide events in 267 patients, and 17 suicide events in 2 patients. Its 50-fold greater increase in the rate of suicide-related events over other studies was so far out of synch from the other, more homogenous studies that Dr. Healy decided to exclude it from his analysis.

Dr. Healy explained why his results differ from the results of the Expert Working Group report, which included Study 057 and found that there were 27 suicide related events on Paxil and 29 on placebo across the studies they

reviewed. He listed certain patient discrepancies that he found to explain this difference:

> **057.012.1321 is listed as a suicide attempt in GSK's report to FDA on 2/6/03, but no such patient exists in my "057" folder.**
>
> **057.012.1536 is a suicide attempt in the "057" folder, but not listed in the 2/6/03 report to FDA.**
>
> **One so-called placebo suicide comes from this study but inspection reveals that this case occurred on the 33rd day post treatment (patient 057.012.057). This event should have been excluded from further analysis.**

Dkt. 83, Ex. 12 at 26. Dr. Healy also stated, based on this data:

> **Overall Paxil placebo controlled trials show a rate of approximately 3 suicide related or hostility events per thousand. The true figure is likely to be higher as events in the 30 post taper phase were not recorded systematically in early trials. It is also the case that events in real life may be quite a bit higher than this as subjects are stopped or stop abruptly from a 20 mg dose or higher, because no-one has warned them about the potentially lethal risks from withdrawal. It is of some interest that these events occur in both depression and non-depression trials and therefore cannot be put down to any one disorder.**

Dkt. 83, Ex. 12 at 27.

Dr. Healy then discussed the Jick studies, which were a meta-analysis of data in the British General Practice Research Database. The data he discussed from July 2004 was published in Jick, H.S., et al., *Antidepressants and the Risk of Suicidal Behaviors*, Journal of the American Medical Association 292, 338-43 (2004). Jick's September 2004 data was presented on September 13 and 14, 2004 at the Meeting of the Psychopharmacologic Drugs Advisory Committee with the

Pediatric Sub-Committee of the Anti-Infective Drugs Advisory Committee. Dr. Healy reported that, with a confidence interval of 95%, the July data showed that Paxil had a 1.29 odds ratio of a suicidal act (compared to a .83 odds ratio for Amitriptyline, and 1.16 for Prozac). The September data showed a 1.55 odds ratio for a suicidal act on Paxil (compared to 1.21 for Dothiepin and 1.46 for Prozac). Dkt. 83, Ex. 12 at 27 (Table 7).

Dr. Healy also addressed a study by Didham in New Zealand, who found an increased odds ratio of completed suicides on Paxil of 2.98 compared to non-SSRI antidepressants, with a 95% confidence interval. The study showed that the odds ratio of suicide for SSRIs as a group (Paxil and Prozac, mainly) was 2.32 compared to non-SSRIs. Dkt. 83, Ex. 12 at 28, citing Didham R.C., et al., *Suicide and Self-Harm Following Prescription of SSRIs and Other Antidepressants: Confounding By Indication*, British Journal of Clinical Pharmacology 60, 519-25 (2005).

Dr. Healy believed that more patients taking Paxil commit suicidal acts because Paxil induces agitation or akathisia, emotional blunting, and/or psychotic decompensation. In support of his belief that Paxil causes akathisia, he referred to the five percent dropout rate of clinical trials due to "agitation," "hyperkinesis," or other coding terms. Dr. Healy contended that if akathisia were properly defined and diagnosed by the reviewers, the results would support his five percent estimate for akathisia-related dropout. Dkt. 83, Ex. 12 at 29-30. Dr. Healy also attested that SSRIs can cause emotional blunting, claiming that his assertion is

supported by the clinical trials and a growing body of case studies that "make it clear that the emotional blunting SSRIs produce, the fear reduction, can proceed too far and become an abnormal absence of fear that has consequences for behavior." Dkt. 83, Ex. 12 at 30, citations omitted. Dr. Healy also noted that a "regular feature" of SSRI testing is a showing that patients at risk of psychotic decompensation became worse on the drugs. *Id.* at 31, citations omitted.

Finally, Dr. Healy went on the offensive against the larger scientific community. He asserted that "a significant proportion of the studies undertaken by SSRI companies have not been published and that in those that have been published not all the data has been published. This holds true for GlaxoSmithKline's studies on Paxil. . . . The situation has become so extreme that it can now be statistically demonstrated that the greatest determinant of the outcome of a published study lies in the identity of the sponsor." *Id.* at 31-32, citing Freemantle N., et al., *Predictive Value of Pharmacological Activity for the Relative Efficacy of Antidepressants Drugs. Meta-Regression Analysis*, British Journal of Psychiatry 177, 292-302 (2000); Gilbody S.M., Song F., *Publication Bias and the Integrity of Psychiatry Research*, Psychological Medicine 30, 253-58 (2000). Additionally, Dr. Healy contended that an increasing proportion of the pharmacotherapeutic literature is biased because it is ghost-written in communication agencies, appears in unreviewed supplements or in journals whose editors are consultants to the SSRI companies, or is written in-house by the companies themselves. *Id.* at 32.

B. *Report of Dr. Joseph Glenmullen*

Dr. Joseph Glenmullen is a graduate of Harvard Medical School and serves as a Clinical Instructor in Psychiatry at Harvard Medical School. He is on the staff of the Harvard Law School Health Services and also treat patients in private practice. Dkt. 83, Ex. 27 at 1 (May 1, 2006 Glenmullen Report). He has authored two books, entitled "Prozac Backlash: Overcoming the Dangers of Prozac, Zoloft, Paxil, and Other Antidepressants with Safe, Effective Alternatives" and "The Antidepressant Solution: A Step-by Step Guide to Safely Overcoming Antidepressant Withdrawal, Dependence, and Addiction" published in 2000 and 2005, respectively. GSK does not challenge Dr. Glenmullen's credentials as an expert in his field.

In the debate over the risks and benefits of antidepressants, Dr. Glenmullen described himself as a "moderate" who has prescribed antidepressants but believes that such drugs have become over-prescribed for mild conditions and that patients were not adequately warned of the possible side effects. Dkt. 83, Ex. 27 at 2. He believes that published research or reports involving antidepressants other than Paxil were relevant to the issue of antidepressants triggering suicide. *Id.* In preparing his report, he interviewed plaintiff Debra Tucker and Linda Kwiatkowski, Pat Boyle, and Pat Perry, who were friends of Father Tucker. *Id.* He discussed the case with plaintiff's counsel and reviewed discovery responses, witness declarations, and deposition transcripts. He also reviewed Father

Tucker's medical records, employment records, journal and calendar entries, the records of the Dunkirk Police Department and Jay County EMS, and Father Tucker's suicide letters and autopsy report, among other documents. *Id.* at 3-4. He relied on his experience as a physician treating patients with antidepressant-induced suicidality and on relevant medical literature. *Id.* at 4.

Dr. Glenmullen believes to a reasonable degree of medical probability that Father Tucker's death was a Paxil-induced suicide. Dkt. 83, Ex. 27 at 1, 25. He believes that after Father Tucker began taking Paxil, he "developed classic symptoms of antidepressant-induced worsening of his condition, including akathisia, insomnia, worsening anxiety, paranoia, agitation, restlessness, sweating, out-of-character behavior, and ultimately irresistible suicidal urges." Dkt. 83, Ex. 27 at 1.

Briefly, Dr. Glenmullen discussed his belief that SSRIs, including Paxil, could cause some patients to experience suicidality. He based that belief on his own experience as a treating physician, FDA warnings on the risk of suicide and other possible side effects of SSRIs, GSK's "Dear Doctor" letter proposed in April 2006, and academic journal articles. He opined that the possible side effects associated with SSRIs, including "anxiety, agitation, panic attacks, insomnia, irritability, hostility, akathisia, manic-like reactions, and hypomanic-like reactions," and "paranoia and psychotic reactions," "form a cluster of over-stimulating antidepressant side effects that can cause or exacerbate suicidality"

and that "have long been linked to drug-induced suicidality in reports and studies published in medical journals going back decades." *Id.* at 6.

Specifically, akathisia, according to Dr. Glenmullen, had "two sides, or faces: outer, objective restlessness and inner, subjective agitation." *Id.* at 7. Of the two, the inner, subjective side was the more dangerous and could include anxiety, tension, irritability, hostility, paranoia, rage, and violence. *Id.* In determining whether a patient was suffering from an antidepressant-induced side effect, and in evaluating Father Tucker's case, Dr. Glenmullen looked for evidence of the over-stimulating side effects of antidepressants – either the appearance of a side effect that was not present previously or the sudden deterioration of the patient's condition. Dr. Glenmullen believed that the most dangerous times for these side effects to cause antidepressant induced suicidality are at the beginning of therapy and with a change in dosage. *Id.*

In Father Tucker's specific case, Dr. Glenmullen found that Father Tucker had no history of mental health treatment prior to 2002, and any depressed moods he experienced lasted only one to three days, never rising to the level of clinical depression. *Id.* at 9. He established Father Tucker's pre-Paxil state of mind through his journal, which, according to Dr. Glenmullen, revealed Father Tucker to have been "an extremely kind, thoughtful, sensitive man who took great joy in his faith and his work." The journal documented "days when Father Tucker was stressed over his sister's health, the sexual abuse scandal engulfing the

Catholic Church, or his unrelenting responsibilities for his parishioners." Dr. Glenmullen also found that the journal shows that Father Tucker was not clinically depressed until after he began taking Paxil. *Id.* at 10.

Dr. Glenmullen recounted that Father Tucker began treating with Dr. Thomas Murray, a psychotherapist, in the summer of 2002 while his sister's lawsuit against the Catholic Diocese for sexual abuse was pending. Dr. Murray diagnosed Father Tucker with adjustment disorder with depressed mood, but not clinical depression. He was stressed about his sister's allegations but was otherwise doing well. *Id.* at 11. On August 28, 2002, Father Tucker called his primary care doctor, Dr. Bright, to say he was feeling anxious, had gotten into psychotherapy, and was interested in medication. Dr. Bright prescribed 10 milligrams of Paxil daily. It is believed that Father Tucker had taken 22 daily pills before killing himself on September 18, 2002. *Id.* at 12.

According to Dr. Glenmullen, Father Tucker's journal also shows his "precipitous decline." *Id.* at 12. On August 30, 2002, Father Tucker wrote, "Things have gotten behind and I do not know how to catch up. I want to live, but I want out of the pain. I feel like I am in an ocean and I can't swim to the top for air. . . . I can see no way out of it. I know that if I follow through with the thoughts that come to my mind, there will be people hurt. . . . Debra I am sorry." Dr. Glenmullen believed that Debra Tucker's deposition testimony corroborated Father Tucker's decline. She said that, "within probably two or three days, he

became like a different person. . . . He, he was very, sweating profusely. He made the comment to me that, he said I feel like I'm crawling out of my skin." Dr. Glenmullen wrote that feeling like "crawling out of one's skin" is a classic description of akathisia, the antidepressant side effect most closely linked to suicidality. *Id.* at 13.

Dr. Glenmullen also observed that Father Tucker became much more anxious on Paxil, as shown by his reaction to a scheduled audit of the parish books in September 2002. Based on Father Tucker's conversations with friends as those conversations were reported to Dr. Glenmullen, Father Tucker became "obsessively preoccupied" with the audit and "paranoid that the Bishop was out to get him." Father Tucker became convinced that he would lose his parish and be demoted because he had paid himself early, and in the last week of his life, he convinced himself that he had paid himself twice in one month. He had asked his friend Pat Boyd to review the parish finances with him. Boyd told Dr. Glenmullen that she double-checked everything and did not find any overpayments, but that Father Tucker could not be convinced that everything would be fine. *Id.* at 14. When the audit was performed, it uncovered no irregularities. Dr. Glenmullen believed that "Father Tucker's increasing anxiety, paranoia, and obsessive preoccupation with the pending audit are striking symptoms of his Paxil-induced decompensation." *Id.* He did not believe that Father Tucker became frankly psychotic, "but his thinking became increasingly distorted and out of touch with reality." *Id.*

Dr. Glenmullen also recounted interviews with Father Tucker's friends Linda Kwiatokowski and Pat Perry, who noticed changes in his behavior, appearance, and his worsening mental condition. Father Tucker had told each of them that, although he was taking his medication, he was getting worse instead of better. *Id.* at 15-17.

Dr. Glenmullen used a process called "differential diagnosis" in which he arrived at a final diagnosis by ruling in or out all the possible diagnoses that might have accounted for Father Tucker's suicide. *Id.* at 21. Dr. Glenmullen considered the factual information contained in the documents, the testimony he reviewed, and the information he obtained from the plaintiff and from Father Tucker's friends, and he considered and ruled out all other possible diagnoses except Paxil-induced suicidality. He eliminated clinical depression because no evidence suggested that Father Tucker was clinically depressed, and even if he had been clinically depressed, that would not necessarily have meant that he was suicidal. *Id.* at 21. Dr. Glenmullen ruled out general anxiety because Father Tucker was never formally diagnosed with an anxiety disorder. Prior to taking Paxil, any anxiety he had was mild, and he was doing well in spite of it. Dr. Glenmullen wrote, however, that Father Tucker's anxiety level increased when he took Paxil and that increased anxiety was one of the side effects that led to his death. *Id.* at 21.

Dr. Glenmullen also ruled out the pending audit, which found no irregularities. *Id.* at 21-22. Instead, Dr. Glenmullen believed that Father Tucker's heightened anxiety and paranoia about the audit were caused not by realistic concerns but by his Paxil-induced decompensation. He also ruled out Father Tucker's sister's allegations of sexual abuse against the church. Father Tucker began dealing with his sister's allegations several years before his death, and during that time he did not show any symptoms of suicidality. *Id.* at 22.

Dr. Glenmullen also ruled out Father Tucker's history of insomnia, a concurrent psychotic disorder, alcoholism, or substance abuse, a character disorder, a concurrent psychiatric condition, a concurrent medical condition, or another prescription medication. *Id.* at 22-24. Father Tucker's preexisting insomnia worsened after he began taking Paxil. Dr. Glenmullen believed that severe insomnia was another Paxil-induced side effect. Also, prior to taking Paxil, Father Tucker had not been diagnosed with a psychotic disorder that might have accounted for his suicide, and while his paranoia and distorted thinking related to the audit were out of touch with reality, Dr. Glenmullen did not believe that Father Tucker suffered from a psychotic disorder. *Id.* at 22. Father Tucker had no history of alcoholism or substance abuse, and he had no alcohol or illicit drugs in his blood when he died. He had never been diagnosed with a character disorder; there was no indication that Father Tucker suffered from a concurrent psychiatric condition; and none of his concurrent medical conditions could account for any of the dramatic personality changes he exhibited in the weeks

prior to his death. *Id.* at 23. Finally, none of the other prescription medications Father Tucker was taking at the time he died was associated with an increased risk of suicide.

Dr. Glenmullen also identified protective factors that would have reduced the likelihood that Father Tucker would commit suicide and other risk factors that would have increased his likelihood of committing suicide without accounting for his ingestion of Paxil. *Id.* at 24. Of those factors, Father Tucker has six of seven factors protecting him from suicide and only two of seventeen risk factors. Based on this analysis, Dr. Glenmullen believed that before taking Paxil, Father Tucker was strongly protected against suicide and at low risk.

C. *Standards for Admissibility Under Rule 702 and Daubert*

GSK argues that the opinions of Dr. Healy and Dr. Glenmullen do not meet the reliability requirement of Rule 702 of the Federal Rules of Evidence, as articulated by the Supreme Court in *Daubert v. Merrel Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), and should be excluded as unreliable and irrelevant. Rule 702 provides:

> **If 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, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied**

the principles and methods reliably to the facts of the case.

The district court's role in applying Rule 702 is to be a gatekeeper. *Naeem v. McKesson Drug Co.*, 444 F.3d 593, 607 (7th Cir. 2006). In fulfilling this role, the court must consider both the relevance and reliability of the proffered evidence. *Kumho Tire Co., Ltd. v. Carmichael*, 526 U.S. 137, 141 (1999), citing *Daubert*, 509 U.S. at 597. For an expert opinion to satisfy the reliability requirement, the expert must be qualified in the relevant field, and the expert's opinion must be based on sound scientific or other relevant methodology. *Smith v. Ford Motor Co.*, 215 F.3d 713, 718 (7th Cir. 2000). Generally, "a court should consider a proposed expert's full range of practical experience as well as academic or technical training when determining whether that expert is qualified to render an opinion in a given area." *Id.* The court's role is not to decide whether the expert is actually correct, however. "Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence." *Daubert*, 509 U.S. at 596, citing *Rock v. Arkansas*, 483 U.S. 44, 61 (1987).

The court's role as "gatekeeper" requires the court to ensure that scientific testimony is grounded in the "methods and procedures of science." *Deimer v. Cincinnati Sub-Zero Products, Inc.*, 58 F.3d 341, 344 (7th Cir. 1995), quoting *Daubert*, 509 U.S. at 590. In evaluating the soundness of an expert's methodology, the court should avoid passing judgment on the "factual

underpinnings of the expert's analysis and the correctness of the expert's conclusions," a role better left to the fact-finder. *Smith*, 215 F.3d at 718; accord, *Daubert*, 509 U.S. at 595 (court must focus on the methodology, not on the conclusions generated by the methodology); *Walker v. Soo Line Railroad Co.*, 208 F.3d 581, 587 (7th Cir. 2000) (affirming admission of expert's opinion where it was "appropriate for [him] to rely on the tests that he administered and upon the sources of information which he employed.").

The line between methodology and conclusion can be subtle and even elusive in some cases. For the opinion to be admissible, the court must determine that the data supports the expert's opinion by more than merely the say-so of the expert. *General Electric Co. v. Joiner*, 522 U.S. 136, 146 (1997). The testimony cannot simply be "subjective belief or unsupported speculation." *Daubert*, 509 U.S. at 590. An opinion becomes speculative when too wide an analytical gap exists between the data and the opinion provided. *Target Market Publishing, Inc. v. ADVO, Inc.*, 136 F.3d 1139, 1144-45 (7th Cir. 1998) (affirming exclusion of expert opinion on expected revenues using unrealistic assumptions), citing *Joiner*, 522 U.S. at 146; see also *Beachler v. Amoco Oil Co.*, 112 F.3d 902, 909 n.6 (7th Cir. 1997) (affirming exclusion of opinion that refiner's assignment of service station franchise agreements would harm dealers; testimony was speculative and not supported by any factual foundation).

In *Daubert*, the Supreme Court identified factors that might be considered to determine the reliability of a scientific expert's opinion, including whether the opinion can be tested or falsified, whether the opinion has been subjected to peer review and publication, any known rate of error of the methodology employed, and the degree of general acceptance of the opinion or its methodology within the relevant field. 509 U.S. at 593-94. In *Kumho Tire*, the Court made clear that strict adherence to the four *Daubert* factors is not necessary; rather, the factors are examples of criteria that a trial court may use to determine whether the expert, in offering the opinion, acted as would an expert in the field. 526 U.S. at 151-52. As a result, "the *Daubert* framework is a flexible one that must be adapted to the particular circumstances of the case and the type of testimony being proffered." *Mihailovich v. Laatsch*, 359 F.3d 892, 919 (7th Cir. 2004). Ultimately, the object of the court's Rule 702 reliability inquiry is to ensure that the opinions expressed by testifying experts "adhere to the same standards of intellectual rigor that are demanded in their professional work." *Rosen v. Ciba-Geigy Corp.* 78 F.3d 316, 318 (7th Cir. 1996). At the end of the day, the only absolute requirements imposed on expert testimony are reliability and relevance.

D. *Dr. Healy's General Causation Opinion*

GSK argues that Dr. Healy's opinion is unreliable and therefore inadmissible under *Daubert*. Specifically, GSK argues that most of the data on which Dr. Healy relied was derived from studies of drugs other than Paxil, and that, in any case,

Dr. Healy mischaracterized the data. GSK asserts further that Dr. Healy's opinions are not generally accepted in the scientific community and that there are no controlled, statistically significant, epidemiological studies establishing an association between Paxil and suicide. Finally, GSK suggests that Dr. Healy's proposed testimony is unreliable because he is driven by litigation.

1. *Reliance on Non-Paxil Data*

GSK asserts that Dr. Healy relied on data from studies of other (non-Paxil) SSRIs, other non-SSRI anti-depressants, and on a "composite hypothetical risk" in forming his opinion. Dkt. 83 at 18. GSK contends that although this practice is not problematic when the goal is to generate a hypothesis, it is problematic when drawing conclusions regarding causation. See Dkt. 83 at 18, Ex. 2 at 6-7 (Rothschild Report) (while SSRIs are classed together "due to their shared therapeutic mechanism of action . . . each of [them] has a distinct chemical composition and structure," which confer "different pharmacodynamic and pharmacokinetic properties").

The court recognizes that Paxil is a unique chemical compound, but the court is not persuaded that Dr. Healy's use of extrapolation or his reliance on data for SSRIs as a class renders his methodology in and of itself unreliable. "Trained experts commonly extrapolate from existing data." *Joiner*, 522 U.S. at 146. Notably here, although the FDA has recognized a variation in risk of suicidality amongst SSRIs, it has handled the drugs as a class, going so far as to have required GSK to drop Paxil's specific label in favor of a class-wide label in May 2007. Dkt. No. 149, Exs. A, B, C; see also Dkt. 105, Healy Dec. at ¶¶ 26, 27. SSRIs are discussed as a class in a majority of the articles and studies relied on by the parties' experts, including many of those not written by Dr. Healy. See

generally Dkt. 83, Ex. 2(B) (Rothschild Report literature).[3] Based on the fact that SSRIs are commonly treated as a class by the scientific and medical communities and in the literature, the court finds that Dr. Healy did not undermine the admissibility of his opinion by considering research regarding SSRIs generally in support of his conclusions regarding Paxil. GSK is certainly entitled to attack Dr.

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[3]Citing, *e.g.*, Barbui C., et al., *Antidepressant Drug Use in Italy Since the Introduction of SSRIs: National Trends, Regional Differences and Impact on Suicide Rates*, Social Psychiatry and Psychiatric Epidemiology 34(3), 152-56 (1999); Benazzi F., *Do SSRIs Cause Suicide?*, Psychotherapy and Psychosomatics 72(6), 358-59 (2003); [author reply] 359-60; Caley C. F., *Extrapyramidal Reactions and the Selective Serotonin-Reuptake Inhibitors*, The Annals of Pharmacotherapy 31(12),1481-89 (1997); Casey P., *SSRI and Suicide*, Psychotherapy and Psychosomatics 10, 259-60 (2004); Donovan S., et al., *Deliberate Self-Harm and Antidepressant Drugs. Investigation of a Possible Link*, British Journal of Psychiatry 177, 551-56 (2000); Fergusson D., et al., *Association Between Suicide Attempts and Selective Serotonin Reuptake Inhibitors: Systematic Review of Randomised Controlled Trials*, British Medical Journal 330(7488), 396 (2005), Erratum in: British Medical Journal 330(7492), 653 (2005); Furlan P.M., et al., *SSRIs Do Not Cause Affective Blunting in Healthy Elderly Volunteers*, American Journal of Geriatric Psychiatry 12(3), 323-30 (2004); Grunebaum M. F., et al., *Antidepressants and Suicide Risk in the United States, 1985-1999*, Journal of Clinical Psychiatry 65(11), 1456-62 (2004); Gunnell D., Ashby D., *Antidepressants and Suicide: What is the Balance of Benefit and Harm*, British Medical Journal 329(7476), 34-8 (2004); Hammad T. A., et al., *Antidepressant Use and Suicidality in Pediatric Patients: a Meta-Analysis*, Pharmacoepidemiology and Drug Safety 14, S54 (2004); Hammad T. A., et al., *Suicide Rates in Short-Term Randomized Controlled Trials of Newer Antidepressants*; Journal of Clinical Psychopharmacology 26(2), 203-7 (2006); Hammad T. A., *Incidence of Suicide in Randomized Controlled Trials of Patients with Major Depressive Disorder*, Pharmacoepidemiology and Drug Safety 12, S156 (2003); Leo R. J., *Movement Disorders Associated with the Serotonin Selective Reuptake Inhibitors*, Journal of Clinical Psychiatry 57(10), 449-54 (1996); Simon G. E., et al., *Suicide Risk During Antidepressant Treatment*, American Journal of Psychiatry 163(1)m 41-7 (2006); Teicher M. H., et al., *Antidepressant Drugs and the Emergence of Suicidal Tendencies*, Drug Safety 8(3), 186-212 (1993); Wessely S., Kerwin R., *Suicide risk and the SSRIs*, Journal of the American Medical Association 292(3), 379-81 (2004); Wilson K, Mottram P., *A Comparison of Side Effects of Selective Serotonin Reuptake Inhibitors and Tricyclic Antidepressants in Older Depressed Patients: a Meta-Analysis*, International Journal Geriatric Psychiatry 19(8), 754-62 (2004).

Healy's methods and conclusions with vigorous cross-examination and contrary evidence on this basis, but Dr. Healy's opinion of general causation is not inadmissible on this basis.

2. *Contrary Evidence and Dr. Healy's Interpretation of Available Data*

GSK also argues that Dr. Healy's thesis, that Paxil can induce suicidality among adults, has been repeatedly tested and rejected by regulatory agencies and researchers. Dkt. 83 at 10-13. For example, GSK argues that the FDA has repeatedly stated that it has not definitively found an association between suicidality and Paxil compared to a placebo. Dkt. 83, Ex. 4 (FDA June 19, 2003 Questions and Answers on Paxil); Ex. 5 at 190-91 (Sept. 13, 2004 Advisory Committee Transcript). Similarly, GSK argues that the December 2004 report of the British Expert Working Group ("EWG") found that the incidence of events that might be related to suicide in patients taking Paxil was similar to the incidence of suicidal events in patients taking a placebo, and was lower than the incidence in the patients taking other antidepressants. Dkt. 83, Ex. 10 at 74-75 (EWG Report).[4] GSK's expert, Dr. Anthony Rothschild, discussed scientific literature

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[4]**Overall, the EWG report stated: "there is no strong evidence of an increased risk of suicidal events for adult patients with depression exposed to paroxetine compared to placebo, *although the point estimates and confidence intervals are consistent with a possible increase in risk*." Dkt. 83, Ex. 10 at 82 (emphasis added). The report also states that "whilst the results provide no clear evidence of an increased risk, the range of risk ratios included within the 95% confidence intervals are consistent with the possibility of a small increased risk of suicidal events for patients exposed to paroxetine compared with those exposed**

(continued...)

that tested the hypothesis that Paxil and other SSRIs are associated with suicidality, reporting that the bulk of that literature did not find evidence of such an association. Dkt. 83, Ex. 2 at 10-12.

GSK criticizes the results Dr. Healy reached in his re-analysis of the available data. For example, Tables 1 and 2 of Dr. Healy's report show up to an eight-fold greater rate of suicidal acts for patients on Paxil instead of a placebo. Dkt. 83, Ex. 12 at 14-16 (Tables 1-2). GSK attacks this finding by arguing that Dr. Healy failed to account for a 14-fold difference between the time of exposure to Paxil compared to the placebo, which artificially inflated the reported suicide rate in Paxil patients. Dkt. 83 at 15-16. Dr. Healy's findings, reprinted from an article he co-wrote called *Antidepressant Drug Use and the Risk of Suicide* published in 2005 in the International Review of Psychiatry, are based on data from the FDA's safety review of the original new drug application for Paxil conducted by Dr. Martin Brecher. Dkt. 83, Ex. 13 (Brecher Report). Brecher himself found no such increase in the risk of suicidality. Dkt. 83 at 15-16, citing Brecher Report at 25 (finding "no signal . . . that paroxetine exposes a subset of depressed patients to additional risk for suicide, suicide attempts or suicidal ideation").

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[4](...continued)
to placebo." *Id.* at 83. Dr. Healy explained in his report that his results differ from those of the EWG because he excluded Study 057, which he believed to be an anomaly. Dkt. 83, Ex. 12 at 26.

GSK's argument regarding exposure time assumes that the rate of suicide in patients exposed to Paxil is identical to the rate in patients exposed only to placebo, an assumption that an internal GSK document shows may be false. Dkt. 103, Ex. 54 at 11-12 (Dunbar, G. C, Mewett, S., *Suicidal Thoughts and Acts with Paroxetine*, SmithKline Beecham Pharmaceuticals, Feb. 15, 1991). And, in May 2006, when GSK voluntarily issued a Dear Doctor letter and amended Paxil's label, it included language suggesting that patients taking Paxil are at the highest risk for suicidal events when treatment begins or when the dose of the drug is chamged, lending credence to the idea that exposure time may have less of an impact on risk than GSK's argument (and a lay judge's instincts) would suggest. See Dkt. No. 83, Ex. 8; Dkt. No. 99, Ex. 3 at 12 ("Adults . . . being treated with antidepressants should be observed similarly for clinical worsening and suicidality, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.").

Exposure time aside, Dr. Healy admitted that he interpreted these figures differently than GSK, and he explained the basis for that difference. Dr. Healy explained that when GSK provided the data to the FDA, GSK reported suicidal acts committed by three individuals during the run-in/wash-out period and one in the follow-up period as suicidal acts by participants in the placebo group, when suicidal acts by those individuals should have been excluded.[5] Dkt. 83, Ex. 12 at

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[5]In its review of this data, the EWG found no evidence that events occurring during placebo run-in or washout phases were inappropriately counted against (continued...)

16-17 (Figures 1, 2). In other words, Dr. Healy asserts that GSK artificially inflated the suicidal acts attributable to the placebo group, improperly skewing the results of the trial. The FDA and GSK now both concur that adverse events occurring during the run-in period cannot be included when calculating adverse event ratios. Dkt. 103, Ex. 32 at 361-62 (Temple Dep.) ("Do you see where it says two of the five placebo suicides occurred during run in?" "Yeah. You shouldn't count those as part of the placebo rate."); Ex. 33 at 210 (Brecher Dep.) ("Is it scientifically legitimate to count a suicidal act occurring during wash-out and run-in to the placebo count?" "No, because everybody got placebo."); see also Dkt. 103, Ex. 34-36.

GSK also suggests that Dr. Healy's entire opinion is flawed because, in relaying correctly the findings of FDA investigators set forth in a report entitled *Incidence of Suicide in Randomized Trials of Patients with Major Depressive Disorder*, which found that the suicide rate ratio for SSRIs compared to a placebo was 1.50, Dr. Healy did not further explain that once the investigators attempted to account for possible confounding factors such as age, gender, and study setting and location, the investigators found that there was no increase in the suicide rate ratios for patients taking SSRIs as compared to those taking a placebo. Dkt. 83, Ex. 17 (Hammad, T., et al, *Incidence of Suicide in Randomized Controlled Trials of Patients with Major Depressive Disorder*, Pharmacoepidemiology and Drug Safety

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[5](...continued)
placebos as if they had occurred during the randomized phase in its review of all of the then-available paroxetine studies. Dkt. 83, Ex. 10 at 82.

12, S156 (2003)). Similarly, GSK criticizes Dr. Healy's description of the Jick study. Dr. Healy wrote that Jick's analysis of the British General Practice Research Database (the "GPRD") pointed to a clear excess of suicidal acts in patients taking Paxil compared with the other antidepressants included in the study, and that the later presentation of the Jick data demonstrated a risk of 1.55 for suicidal acts on Paxil compared to amitriptyline, an older non-SSRI antidepressant. Dkt. 83, Ex. 12 at 27 (Healy Report), citing Jick, H. S., et al., *Antidepressants and the Risk of Suicidal Behaviors,* Journal of the American Medical Association 292, 338-43 (2004), and the presentation of Jick's data by Diane Woolfson at Meeting of the Psychopharmacologic Drugs Advisory Committee on September 13-14, 2004. GSK retorts that Dr. Healy's assertions are not supported by the GPRD investigators and that the authors of the Jick study wrote:

> The magnitude of the relative risk . . . is low enough that such a finding could easily be due to uncontrolled confounding by severity of depression. For example, if patients with more severe depression were more likely to be treated with the most recently marketed antidepressant among those studied (*i.e.*, paroxetine), this in itself would lead to a higher risk of suicidal behavior among those starting this drug compared with those starting an older drug (*i.e.*, dothiepin, the reference exposure in our study).

Dkt. 83 at 20, quoting Ex. 18 at 342 (Jick study). Dr. Healy reported Jick's findings without providing this additional detail. He also did not disclose that the CSM Expert Working Group did not view the Jick data as signaling an increased risk of suicidality for Paxil. Dkt. 83 at 21.[6]

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[6]The EWG found, "overall there is no strong evidence of an increased risk of suicidal events of adult patients with depression exposed to paroxetine (continued...)

Dr. Healy's omissions of the explanatory statements found in the Hammad and Jick reports do not render his opinions inadmissible. Selection and editing are inevitable, and choices of this sort are appropriate fodder for cross-examination. GSK does not attack the validity of the underlying data and does not claim that Dr. Healy incorrectly reported the data itself. GSK argues only that Dr. Healy does not present some of the studies on which his opinion is based in full, "selectively parsing out data that support his position, while failing to account for data that do not." Dkt. 83 at 22. To the extent that GSK wishes to present the full findings of Hammad and Jick, it should have opportunity to do so at trial.

Dr. Healy's opinions regarding Paxil and suicidality are certainly controversial. However, those opinions have repeatedly been subject to professional debate and review through the peer-review and publication process. See Dkt. 83, Ex. 12 (Curriculum Vitae of Dr. David Healy). Additionally, Dr. Healy relied on other peer-reviewed articles and studies addressing Paxil and suicidality. While that research may not meet all of GSK's demands (for statistical significance, Paxil-specific rather than any other SSRI, suicide rather than suicidality, and adults in Father Tucker's age group), it has been subjected to peer review and published for professional scientific evaluation. There is not universal acceptance of the proposition that Paxil can induce suicide in adults – far from it

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[6](...continued)
compared to placebo, although the point estimates and confidence intervals are consistent with a possible increase in risk." GSK Ex. 10 at 82.

– and as GSK argues, there is a vigorous line of peer-reviewed, published research drawing the opposite result.

Nevertheless, Rule 702 permits testimony that is the product of competing principles or methods in the same field of expertise. Fed. R. Evid. R. 702, Committee Notes (2000). Rule 702 does not exclude all minority views from the relevant scientific or expert community. For now, the court's focus must be solely on the principles and methodology used, not on the conclusions generated. See *Daubert*, 509 U.S. at 595. The court has sufficient assurance that Dr. Healy will testify with the same level of intellectual rigor that he would employ outside the courtroom. See *Kumho Tire*, 526 U. S. at 152. Although not without controversy or arguable flaws, Dr. Healy's opinion is sufficiently reliable to pass muster under *Daubert*. GSK's arguments in opposition to the validity of Dr. Healy's opinion are most appropriately left to "[v]igorous cross examination, presentation of contrary evidence, and careful instruction on the burden of proof." *Daubert*, 509 U.S. at 596.

3. *Statistical Significance*

GSK also attacks the admissibility of Dr. Healy's opinion regarding general causation on the ground that Dr. Healy himself acknowledged that there is no published, peer-reviewed, placebo-controlled study in the worldwide scientific literature that demonstrates a statistically significant increased incidence in

suicide or suicidal events with Paxil. Dkt. 83, Ex. 11 at 77, 82, 239-41, 259-60 (Healy Dep.). At one point in his deposition, Dr. Healy memorably stated that he was "not awfully concerned about things being statistically significant." *Id.* at 203.

Briefly, epidemiology is the study of disease patterns and risks in human populations. "Epidemiology focuses on the question of general causation (*i.e.*, is the agent capable of causing the disease?) rather than that of specific causation (*i.e.*, did it cause disease in a particular individual?)." *Reference Manual on Scientific Evidence* 335 (Fed. Judicial Ctr. 2000). In a typical epidemiologic study, an epidemiologist compares the health of people exposed to a substance to that of persons not so exposed to determine whether the exposure to the substance is associated with an increased rate of disease. There are essentially three types of study designs used by epidemiologists in attempting to determine whether there is an association between exposure to an agent and development of a disease: (1) randomized trial or randomized clinical trial, (2) cohort studies, and (3) case-control studies. The first of these, epidemiologically speaking, is the "gold standard." *Id.* at 338. To say that a result is "statistically significant" is to say that the observed results are unlikely (most often, less than a five percent chance) to be the result of random error. *Id.* at 354. Setting the level for what is or is not statistically significant "entails a somewhat arbitrary determination," and it is a common error to equate the level of statistical significance with the legal burden of proof. *Id.* at 354, 357-58, n.67. For purposes of GSK's motion, "*Daubert* did

not set a threshold level of statistical significance either for admissibility or for sufficiency of scientific evidence." See *id.* at 359-60, n.73, quoting *Developments in the Law – Confronting the New Challenges of Scientific Evidence*, 108 Harv. L. Rev. 1481, 1535-36 (1995).

The study of suicide is rife with both ethical and practical difficulties. Meaningful studies require large numbers of participants. Thankfully, suicide is a rare act. Not only that, but to conduct a placebo-controlled study, some patient-participants already at risk necessarily would be treated with a placebo. For practical and ethical reasons, "suicidality itself has rarely if ever been studied in large, randomised placebo-controlled double-blind epidemiological studies . . . . the trials upon which the FDA based its 2006 meta-analysis 'were not designed to specifically detect suicidality.'" *Giles v. Wyeth, Inc.*, 500 F. Supp. 2d 1048, 1058 (S.D. Ill. 2007) (admitting testimony of Dr. Glenmullen on general causation in Effexor suicide case), quoting Marc Stone & M. Lisa Jones, *Clinical Review: Relationship Between Antidepressant Drugs and Suicidality in Adults*, 43 (Nov. 17, 2006).

The plaintiff argues that where there have been no studies to test a particular outcome, the question of "statistical significance" does not arise, and suicidality has not been the subject of any placebo-controlled clinical trial of Paxil. Dkt. 103 at 22, citing Healy Dec. ¶ 17. The plaintiff reasons that Dr. Healy's statement is technically correct – a statistically significant association between

Paxil and suicidality has not been found in any such clinical trial – but that failure does not mean that the research surrounding suicidality that has been conducted should be ignored or disregarded.

Essentially, the plaintiff argues that the onus is on GSK to disprove Dr. Healy's opinion with a placebo-controlled clinical trial, and until it does so, Dr. Healy is free to come to his own conclusions regarding Paxil's association with suicidality in spite of lack of statistical significance to any of the studies on which he relies. This approach would improperly shift the burden to GSK to disprove Dr. Healy's theories, and the court is not convinced that the concept of statistical significance can be entirely separated from scientific reliability until an unknown future point in time when the "perfect" study using all conceivable controls is conducted.

More convincing, however, is GSK's own acknowledgment that the 2006 analysis of the GSK clinical trials database revealed a statistically significant increase in suicidal behavior in adult patients with major depressive disorder being treated with Paxil compared to those administered a placebo. Dkt. 83 at 11, n.11, citing Ex. 8 (GSK Dear Healthcare Professional Letter, dated May 2006); Ex. 9 (FDA May 12, 2006 Safety Alert). In response to this information, GSK also voluntarily (though temporarily) amended Paxil's label to carry the following warning:

> ***In adults with MDD (all ages), there was a statistically significant increase in the frequency of suicidal behavior in patients treated with paroxetine compared with placebo (11/3,455 [0.32%] versus 1/1,978 [0.05%]); all of the events were suicide attempts.*** **However, the majority of these attempts for paroxetine (8 of 11) were in younger adults aged 18-30 years. These MDD data suggest that the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24.**

Dkt. No. 99, Ex. 3 at 12 (emphasis added). Paxil's May 2006 "Dear Doctor" letter and amendments to Paxil's label plainly stated that GSK had found a statistically significant increase in the frequency of suicidal behavior in adult patients treated with Paxil compared to a placebo. GSK downplays this finding. The Dear Doctor letter states that because the absolute number of events was very small, a causal relationship cannot be inferred and the data should be "interpreted with caution." But GSK's acknowledgment that it had uncovered a statistically significant increase in suicidality among adult patients cuts directly against its argument that Dr. Healy's expert opinion – an opinion that was drafted without benefit of the data that led to GSK's Dear Doctor letter and revised label – finding a "robust" increased risk of suicidality in adult patients taking Paxil should be deemed inadmissible. The weight of Dr. Healy's opinion will be left to a jury. In light of all the evidence supporting his opinion, the absence of a "gold standard" published, peer-reviewed, placebo-controlled study demonstrating a statistically significant increased incidence in suicide or suicidal events with Paxil, does not render Dr. Healy's opinion inadmissible.

4. *Influence of Litigation*

Finally, GSK argues that Dr. Healy's opinion regarding general causation was developed exclusively for purposes of litigation, and that prior to becoming a paid expert, Dr. Healy eschewed the conclusions he since has drawn. Dkt. 83 at 22-26. GSK suggests that when writing in scientific publications, Dr. Healy is "circumspect" in his conclusions, but that in litigation his circumspection becomes certainty. *Id.* at 23. The court is not persuaded. As early as 1991 Dr. Healy opined that suicidal thoughts "may in some instances be produced by the antidepressants." Dkt. 103, Ex. 7 at 3 (Creaney, W., Murray I., and Healy D., *Antidepressant Induced Suicidal Ideation*, Human Psychopharmacology 6, 329, 331 (1991)). And as Dr. Healy explained, scientific authors rarely express their opinions in scientific literature in absolute terms. Dkt. 105, Healy Dec. ¶ 12. Again, for purposes of GSK's *Daubert* motion, the court is interested not in absolute truths but in reliability. Dr. Healy's opinions have been reasonably consistent and seemingly unaffected by his participation in litigation as an expert witness. To the extent that Dr. Healy may have wavered in his language or his convictions regarding SSRIs and suicide, GSK will be free to raise those issues in cross-examination. Also, no one should be too surprised by the prospect that a scientist's views may evolve as more data become available and the question receives more study. GSK's motion *in limine* to exclude the testimony of Dr. David Healy is denied.

E. *Opinion of Dr. Glenmullen*

1. *General Causation*

As an initial matter, GSK criticizes Dr. Glenmullen's opinion regarding general causation by accusing him of basing his opinion entirely on news reports, case reports, and distorted FDA statements. Dkt. 83 at 28. Dr. Glenmullen's report citations show otherwise. He researched the medical literature on SSRIs and suicide and drew on his extensive knowledge of suicidality as a side effect of treatment with SSRIs. He cited numerous medical journal articles in the endnotes of his report, and he cited numerous medical journal articles in Appendix A of his report. Dkt. 83, Ex. 27 at 4, 26-28, Appx. A.

GSK also criticizes Dr. Glenmullen's reliance on case reports. Case reports are published reports of a physician's clinical observations in the treatment of a single patient or a series of patients. Dkt. 83 at 4, n. 5. The FJC's *Reference Manual on Scientific Evidence* cautions that "case reports lack controls and thus do not provide as much information as controlled epidemiological studies do," so "causal attribution based on case studies must be regarded with caution." *Reference Manual* at 475. However, "such studies may be carefully considered in light of other information available." *Id.*; see also *Cella v. United States*, 998 F.2d 418, 426 (7th Cir. 1993) (affirming admission of expert medical testimony that was based in part on case reports). Just so here. Given Dr. Glenmullen's uncontested expertise, his "review of experimental, statistical or other scientific data gathered by others may suffice as a reasonable methodology upon which to base an

opinion." *Walker v. Consolidated Rail Corp.*, 111 F. Supp. 2d 1016, 1017 (N.D. Ind. 2000), citing *Clark v. Takata Corp.*, 192 F.3d 750, 758 (7th Cir. 1999); *Cummins v. Lyle Indus.*, 93 F.3d 362, 369 (7th Cir. 1996).

Dr. Glenmullen also relied on GSK's 2006 analysis of the Paxil adult clinical trials database submitted to the FDA. GSK argues that this analysis showed a higher frequency of suicidal behavior – but not suicide – in patients under the age of 30 with major depression disorder – but not other conditions – so that GSK's own analysis is not a reliable source. Dkt. 83 at 27. GSK also argues that its analysis had the potential for "confounding," the absolute number of events was low, and the analysis was retrospective. *Id.* GSK's explanatory backpedaling may have merit, but it certainly is not beyond reasonable dispute. Dr. Glenmullen appropriately relied on GSK's voluntary issuance of a "Dear Doctor" letter, in which GSK stated: "in the analysis of adults with MDD (all ages), the frequency of suicidal behavior was higher in patients treated with paroxetine compared with placebo (11/3455 [0.32%] versus 1/1978 [0.05%]). This difference was statistically significant." Dkt. 83, Ex. 27 at 6, referencing Dkt. 83, Ex. 8 (GSK May 2006 "Dear Doctor" letter). As Dr. Glenmullen explained, "the revised label . . . says that there [was a] statistically significant six-fold increase in suicidal behavior in adults with major depressive disorder. I read that as statistically – that's achieved a statistical definition of causality." Dkt. 83, Ex. 26 at 105.

Particularly in light of the fact that the court will also permit Dr. Healy to testify regarding general causation, the court finds Dr. Glenmullen's opinion on general causation to be sufficiently reliable and relevant to pass muster under *Daubert*. GSK will be entitled to cross-examine Dr. Glenmullen vigorously, but the ultimate issue of general causation will be left to the jury.

2. *Specific Causation*

Dr. Glenmullen's opinion supports the plaintiff's claim on specific causation – that is, not only the general proposition that Paxil can induce adults to commit suicide, but also that Paxil induced Father Tucker to commit suicide. To reach his opinion, he relied on the familiar process of differential diagnosis, which provides a framework under which all reasonable hypotheses are ruled in as possible causes of a medical problem and then some of these possible causes are ruled out to the extent reliable evidence makes it appropriate to do so. See *Gayton v. McCoy*, 593 F.3d 610, 618-19 (7th Cir. 2010) (reversing grant of summary judgment; district court erroneously excluded doctor's opinion on causation based on differential diagnosis and review of medical history and other relevant background); *Ervin v. Johnson & Johnson*, 492 F.3d 901, 903 (7th Cir. 2007) (affirming exclusion of doctor's opinion about causation and explaining that determining reliability of differential diagnosis requires case-by-case determination). In general, a differential diagnosis satisfies a *Daubert* analysis if

the expert uses reliable, scientifically valid methods in both ruling in and ruling out potential causes. *Id.* at 904.

GSK first argues that Dr. Glenmullen improperly ruled in Paxil as a possible cause of Father Tucker's suicide. Generally, GSK argues that Dr. Glenmullen's conclusion that Paxil can cause suicide at all is unreliable. Those arguments were addressed above. Looking more specifically to Father Tucker, GSK argues that Dr. Glenmullen ruled in Paxil based on GSK's expressly limited finding of a potential increased risk of suicidality in patients being treated with Paxil for *major depressive disorder*, but Dr. Glenmullen believed that Father Tucker had been prescribed Paxil for *anxiety*. Dkt. 83 at 30. This alone does not condemn Dr. Glenmullen's opinion. After all, GSK's own expert Dr. Rothschild opined "to a reasonable degree of medical and scientific certainty, that Father Tucker was suffering from an episode of Major Depression based on DSM-IV diagnostic criteria before he took Paxil." Dkt. 83, Ex. 2 at 33. At least one study has found an increased risk of suicidality amongst non-MDD patients taking SSRIs over a placebo. Dr. Dean Fergusson reviewed 702 clinical trials involving 87,650 patients, 59% of which were conducted in patients with a diagnosis other than major depression, and documented an association between suicide attempts and the use of SSRIs. Dkt. 103, Ex. 17 (Fergusson D., et al., *Association Between Suicide Attempts and Selective Serotonin Reuptake Inhibitors: Systematic Review of Randomised Controlled Trials*, British Medical Journal 330(7488), 396 (2005)); see also Erratum in: British Medical Journal 330(7492), 653 (2005) (correcting odds

ratio of fatal suicide attempts for SSRIs compared with tricyclic antidepressants but leaving main conclusions and main message of the article intact). Overall, Dr. Fergusson found "A significant increase in the odds of suicide attempts (odds ratio 2.28, 95% confidence 1.14 to 4.55 ...; P=.02) for patients receiving SSRIs compared with placebo." Dkt. 103, Ex. 17 at 4.[7] Although unable to narrow the confidence interval to support conclusions drawn for particular subgroups, Dr. Fergusson wrote: "Estimates for patients with major depression favoured a decrease in suicides with SSRIs, whereas patients with depression and other clinical indications may have as much as an eightfold increase in the rates of suicide." *Id.* at 5. Dr. Glenmullen's opinion is sufficiently reliable to be admissible regardless of whether Father Tucker was suffering from MDD or just anxiety when he was prescribed Paxil, three weeks before his suicide.

GSK also faults Dr. Glenmullen for his opinion that Father Tucker suffered from Paxil-induced akathisia and that this state was so unbearable to Father Tucker that he killed himself. Dkt. 83 at 30; see generally Ex. 27. Dr. Glenmullen testified that akathisia is a dose-dependent side effect of Paxil but that he knew of no peer-reviewed scientific article in the literature reporting that a patient had developed akathisia while taking only 10 milligrams per day of Paxil, the amount Father Tucker had been prescribed. GSK argues that Dr. Glenmullen's conclusion that someone on a dose of Paxil as low as 10 milligrams could develop akathisia

[7]Contrary to the plaintiff's assertion, it does not appear that Dr. Glenmullen relied directly on the Fergusson study in reaching his opinion. Dkt. 103 at 37.

cannot be said to have been derived from a reliable application of the differential diagnosis process.

Akathisia is a recognized side effect of Paxil. Under "precautions," GSK's 2007 prescribing information for Paxil states: "The use of paroxetine or other SSRIs has been associated with the development of akathisia, which is characterized by an inner sense of restlessness and psychomotor agitation such as an inability to sit or stand still usually associated with subjective distress. This is most likely to occur within the first few weeks of treatment." Dkt. 83, Ex. 28 at 16. Dr. Fergusson offered a possible explanation for up to an eightfold increase in suicide in patients with depression and other clinical indications (rather than major depression): "If the mechanism of action thought responsible for inducing suicidality is true, the agitation and akathasia known to occur with this class of agents may have affected non-depressed and depressed patients differently, *inducing more distress in patients with less severe clinical conditions than in those with severe depression.*" Dkt. 103, Ex. 17 at 5 (emphasis added). GSK does not dispute that akathisia is a recognized side effect of Paxil. Nor does it dispute Dr. Fergusson's findings, which suggest that there may be an inverse relationship between severity of clinical condition and severity of akathisia. Nor does it raise any evidence that akathisia can occur only in patients taking more than 10 milligrams of Paxil daily. GSK's experts will be free to offer their own professional opinions as to whether a dose as low as 10 milligrams can cause akathisia in

adult patients taking Paxil, but this issue does not undermine the admissibility of Dr. Glenmullen's opinion under *Daubert*.

GSK takes issue with Dr. Glenmullen's assertion that the FDA's review of the data regarding suicidality in pediatric patients being treated with antidepressants produced a 'list of side effects that the FDA warns may lead to anti-depressant induced suicidality." Dkt. 83 at 31, quoting Ex. 27 at 6. GSK argues that "in fact, the FDA did not suggest that any of these listed symptoms can induce suicidality; the agency actually concluded just the opposite." The warning in Paxil's prescribing information required by the FDA states that "although a causal link between the emergence of [anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania and mania in adult and pediatric patients] and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality." Dkt. 83 at 31, citing Ex. 28 at 12 (Paxil Prescribing Information). The FDA's warning, contrary to GSK's assertion, does not indicate that the FDA has reached a firm conclusion regarding Paxil and akathisia. This issue, as well, will be fertile ground for cross-examination, but it does not make unreliable Dr. Glenmullen's decision to rule in as a possible cause Paxil-induced akathisia.

Likewise, the parties' experts' varied interpretations of Father Tucker's diary are best suited for cross-examination, not for exclusion of either side's opinions. GSK contends that Dr. Glenmullen, in considering Father Tucker's diary, ignored statements found in passages written in 1995 and 1997 that could indicate akathisia-like symptoms. Dkt. 83 at 32. The plaintiff argues in response that GSK has taken these entries out of context and without the benefit of eyewitness descriptions. Dkt. 103 at 35-36. GSK also argues that Dr. Glenmullen did not give credence to the statements of witnesses describing Father Tucker as "slow and deliberate" and "zombie-like" in the time immediately preceding his suicide. Dkt. 83 at 32. The plaintiff counters that these descriptions are not inconsistent with the theory that Father Tucker was suffering from akathisia. Dkt. 105 at 36. Regardless of which theory is correct, the contrary interpretations of this evidence offered by the parties do not show that Dr. Glenmullen's specific causation opinion is unreliable or irrelevant. A jury may choose to disagree with that opinion, but at a minimum Dr. Glenmullen's decision to rule in Paxil as a possible explanation for Father Tucker's suicide meets the requirements of *Daubert*.

On the other side of the differential diagnosis process coin, GSK argues that Dr. Glenmullen improperly ruled out other potential causes of Father Tucker's suicide. GSK argues that Dr. Glenmullen inappropriately discounted the fact that there were a number of stressful events in Father Tucker's life that were coming to a head at the time he took his own life. Dkt. 83 at 33. For instance, Father Tucker's sister's allegations of sexual abuse against the diocese were about to be

made public, and he feared that an audit of parish books was about to reveal that he had embezzled funds from the parish. GSK argues that Dr. Glenmullen dismissed these factors based only on his conclusion that Father Tucker's mental health plummeted right when he started taking Paxil, and Dr. Glenmullen's opinion therefore is unreliable because temporal proximity is not enough to establish causation. See, *e.g.*, *McClain v. Metabolife Intern. Inc.*, 401 F.3d 1233, 1243 (11th Cir. 2005) ("proving a *temporal* relationship between taking [a drug] and the onset of symptoms does not establish a *causal* relationship" and "leads to the blunder of the *post hoc ergo propter hoc* fallacy") (emphasis in original).

Dr. Glenmullen fully discussed the potential impacts of both Father Tucker's sister's allegations of sexual abuse and the upcoming church audit in his opinion. He explained why he believes that Paxil was the more likely cause of Father Tucker's suicide. The plaintiff's sexual abuse case had been part of Father Tucker's life for many years, and there was no evidence in either the diary or the witness statements on which Dr. Glenmullen relied to suggest that the news that the church would not settle her case prompted Father Tucker's deterioration. Dkt. 83, Ex. 27 at 21-22. Also, Dr. Glenmullen explained in some detail why he did not believe the audit was the cause of Father Tucker's suicide. The church conducted audits on a routine basis, but the witnesses Dr. Glenmullen interviewed stated that before his suicide, Father Tucker seemed unusually anxious and paranoid, particularly because the informal audit by Boyd (and, presumably, the formal audit conducted by the church) did not uncover any

irregularities in Father Tucker's bookkeeping. Dkt. 83, Ex. 27 at 21-22. Dr. Glenmullen's report makes clear that he considered and ruled out these other possible causes for Father Tucker's descent. He has provided facially reasonable explanations for doing so. GSK is entitled to challenge those explanations, but those challenges do not render Dr. Glenmullen's causation opinion inadmissible.

Accordingly, GSK's motion *in limine* to exclude the testimony of Dr. Glenmullen is also denied. Having found that the plaintiff has come forward with admissible evidence from which a reasonable jury could find that Paxil can increase the risk of suicidality in adult patients and that it did so in the case of Father Tucker, the court turns to GSK's remaining arguments on summary judgment.

III. *Breach of Duty to Warn*

Under Indiana law, pharmaceutical manufacturers fulfill their duty to warn of potential adverse effects of drugs by adequately warning the prescribing physician. See *Crisostomo v. Stanley*, 857 F.2d 1146, 1152 n.17 (7th Cir. 1988) (manufacturer is "absolved of liability so long as adequate warnings of a medication's adverse side effects have been imparted to treating physicians"); *Phelps v. Sherwood Medical Industries*, 836 F.2d 296, 299 (7th Cir. 1987); *Ortho Pharm. Corp. v. Chapman*, 388 N.E.2d 541, 548 (Ind. App. 1979) ("Since such drugs are available only by prescription, a manufacturer's duty to warn extends

only to the medical profession, and not the ultimate users."). Where the manufacturer warns of the precise adverse effect of which the plaintiff complains, the warning may be deemed adequate as a matter of law. See *Ziliak v. AstraZeneca LP*, 324 F.3d 518, 521 (7th Cir. 2003); *Crisostomo*, 857 F.2d at 1153. GSK argues that the warning regarding suicidality included in the 2002 Paxil package insert was adequate and fulfilled its duty to warn as a matter of law.

In 2002, when Dr. Bright prescribed Paxil to Father Tucker, Paxil's packaging contained the following warning concerning suicide and suicidality:

> **PRECAUTIONS: Suicide**
>
> **The possibility of a suicide attempt is inherent in major depressive disorder and may persist until significant remission occurs. Close supervision of high-risk patients should accompany initial drug therapy. Prescriptions for Paxil should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose.**
>
> **Because of well-established comorbidity between major depressive disorder and other psychiatric disorders, the same precautions observed when treating patients with major depressive disorder should be observed when treating patients with other psychiatric disorders.**

Dkt. 85, Ex. A at 10. The plaintiff argues that this general warning about the risks of suicide in those with major depressive disorder was no warning at all with respect to the risk that Paxil itself would increase the risk. The plaintiff relies on the opinion of Dr. Arvin Shroff, who believes that the information provided in Paxil's 2002 prescribing information "was insufficient to adequately inform doctors and the medical community of the association between Paxil and suicidality."

Dkt. 99, Ex. 2 at 4. In comparison, the plaintiff points out that in 2006, GSK voluntarily strengthened the warning by explicitly linking Paxil to suicidality in adult patients. Dkt. 99 at 18-19, citing Ex. 3 at 11-12. This, the plaintiff argues, was "a more clear statement that Paxil was associated with an increased risk of suicidality." Dkt. 99 at 19.

The court agrees that from a plain reading of the 2002 warning, a reasonable jury could find that the label was inadequate to warn of Paxil's association with an increased risk of suicide. To be adequate, at least as a matter of law, the warning must warn of the precise risk of which the plaintiff complains. See *Ziliak*, 324 F.3d at 521. Paxil's 2002 label stated only the well-known fact that suicide is a risk with all patients suffering from MDD. It did not warn that taking Paxil could increase that risk. Even without comparing Paxil's 2002 label with GSK's 2006 revisions, a reasonable jury could find that the 2002 label was inadequate.

GSK also argues that summary judgment should be granted because Dr. Bright knew of Paxil's risks but prescribed the medication anyway. Dkt. 85 at 12, citing *Minisan v. Danek Medical Inc.*, 79 F. Supp. 2d 970, 978-79 (N.D. Ind. 1999) (granting summary judgment for medical device manufacturer because surgeon knew of risks, and inadequate label did not affect decision to use device). Known as the "learned intermediary doctrine," this theory applies where "a physician is alerted to the dangerous propensities of a particular drug and nonetheless decides

to prescribe it." *Ashman v. SK & F Lab. Co.*, 702 F. Supp. 1401, 1405 (N.D. Ill. 1988).

Dr. Bright had prescribed SSRIs to his patients "probably since they have been introduced." Dkt. 85, Ex. C at 27. He testified that he had read Paxil's package insert. *Id.* at 34. But Dr. Bright also testified that he was unaware that Paxil itself was or could be associated with an increased risk of suicide in adults when he prescribed Paxil to Father Tucker, and he testified that if he had been warned of such an association, he would have considered those warnings in deciding whether or not to prescribe Paxil to Father Tucker. Dkt. 99, Bright Dec. ¶¶ 4, 6. Nonetheless, he believed that he possessed the information he needed and that he advised Father Tucker to call him if he experienced any problems. Dkt. 85, Ex. C at 64-66. Father Tucker did not contact Dr. Bright with any complaints before he killed himself. *Id.*

On summary judgment, any inferences the court might draw from these facts must be construed in favor of the plaintiff as the non-moving party. On this record, a reasonable jury could find that in 2002 Dr. Bright would not have decided to prescribe Paxil to Father Tucker if there had been an explicit warning of an increased risk of suicide associated with use of the drug. Dr. Bright testified that he would have "considered" such information. He did not opine as to what his ultimate decision would have been. (Also, his choices were not limited to a binary prescribe/do not prescribe choice. He also could have prescribed under

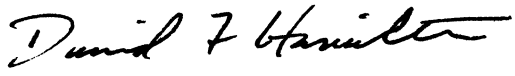
tighter supervision, for example.) Dr. Bright's statement is not definitive either way, and so, at this stage of the proceedings, it must be construed in favor of the plaintiff. Some of the threads holding this case together are thin, and a few more tugs may well unravel them. But under the summary judgment standard, they still hold. GSK's motion for summary judgment is denied.

Conclusion

For the foregoing reasons, GSK's motion for summary judgment is denied. Plaintiff's motion to designate an additional expert (Dkt. 122) is denied as untimely. Plaintiff's supplemental responses to GSK's motion *in limine* (Dkt. 131 & 137) are untimely and impermissible surreplies and are stricken. Accordingly, GSK's Amended Reply and Request to Strike (Dkt. 136) is moot. GSK's motion to depose an additional witness (Dkt. 124) is granted, and discovery is reopened for 90 days from the date of this order for that limited purpose.

So ordered.

Date: March 30, 2010



DAVID F. HAMILTON, Circuit Judge*
***Sitting by designation**

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