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PAXIL PREGNANCY

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(Exhibits Filed Under Seal)

Attention: Donna Candelora, Esq.
The Honorable Sandra Mazer Moss
JUDGE, Philadelphia County Court of Common Peas
Complex Litigation Center
City Hall – Room 622
Philadelphia, PA 19107

Re: ***Cause No. 3220; In re: Paxil Pregnancy Cases; In Philadelphia Court of Common Pleas; September Term 2007.***

Case No. 070903247; *Roy Ayala and Kelly Capito, Individually and as Parents and Natural Guardian of Gabrielle R. Ayala, a Minor v. SmithKline Beecham Corporation d/b/a GlaxoSmithKline;* In Philadelphia Court of Common Pleas; September Term 2007.

Cause No.070903266; *Amy Davis, Individually and as Parent and Natural Guardian of Joey L. Davis, a Minor v. SmithKline Beecham Corporation d/b/a GlaxoSmithKline, Inc. and PAR Pharmaceuticals, Inc.*; In the Philadelphia Court of Common Pleas; September Term 2007.

Cause No.070903296; *Melanie Lacambra, Individually and as Parent and Natural Guardian of Kai A. Lacambra, a Minor v. SmithKline Beecham Corporation d/b/a GlaxoSmithKline, Inc.*; In the Philadelphia Court of Common Pleas; September Term 2007.

GLOBAL MOTION REGARDING THE ADMISSIBILITY OF EVIDENCE ON CHANGES TO PAXIL'S LABELING AND OTHER POST-INJURY CONDUCT

EXECUTIVE SUMMARY

Defendant SmithKline Beecham Corporation d/b/a GlaxoSmithKline ("GSK") does not want a jury to learn about the changes to Paxil's warning label in late 2005. Nor does it want a jury to see evidence of an FDA warning letter from 2008 or some of GSK's own internal documents from 2006. In earlier Paxil Pregnancy cases, GSK filed motions *in limine* to keep that evidence out.

Whether that evidence is admissible is not appropriate for case-specific motions *in limine*. The admissibility of that evidence has been—and will continue to be—an issue in every failure-to-warn claim where a pregnant woman took Paxil before the label was changed. Inconsistent rulings have already been made, and this Court should decide the issues on a global basis.

GSK's reasons for excluding this evidence are not persuasive.

The labeling change is not a subsequent remedial measure under Pennsylvania Rule of Evidence 407. Rule 407 applies only to changes that were made voluntarily by the party; it does not apply to measures that were required by a governmental authority. In this case, the labeling changes were made at the insistence of the FDA. Furthermore, evidence of the labeling change would not be unfairly prejudicial under Rule 403.

GSK's post-injury conduct is admissible if it contains evidence of GSK's knowledge prior to that time. Two internal GSK presentations from 2006 reflect information that predates the Plaintiffs' injuries. The warning letter from the FDA in 2008 also highlights GSK's withholding of important safety information. The FDA reprimanded GSK for the same type of violation committed by GSK in failing to provide earlier reports of congenital abnormalities to the FDA.

IN RE: PAXIL PREGNANCY CASES	§	**COURT OF COMMON PLEAS** **TRIAL DIVISION** **PHILADELPHIA COUNTY** **DOCKET NO. 3220**
ROY G. AYALA And KELLY M. CAPITO, Individually and as Parents and Natural Guardians of GABRIELLE R. AYALA, A Minor Plaintiffs, **vs.** **SMITHKLINEBEECHAM CORPORATION D/B/A GLAXOSMITHKLINE, INC.** Defendant.	§	**COURT OF COMMON PLEAS** **TRIAL DIVISION** **PHILADELPHIA COUNTY** **DOCKET NO. 070903247** **PAXIL PREGNANCY**
AMY L. DAVIS, Individually, and as Next Friend of JOEY L. DAVIS, A Minor **Plaintiffs,** **vs.** **SMITHKLINEBEECHAM CORPORATION D/B/A GLAXOSMITHKLINE, INC. and PAR PHARMACEUTICALS, INC.** **Defendants.**	§	**COURT OF COMMON PLEAS** **TRIAL DIVISION** **PHILADELPHIA COUNTY** **DOCKET NO. 070903266** **PAXIL PREGNANCY**

MELANIE L. LACAMBRA, Individually and as Parent and Natural Guardian of KAI A. LACAMBRA, A Minor	§	**COURT OF COMMON PLEAS**
	§	**TRIAL DIVISION**
	§	**PHILADELPHIA COUNTY**
	§	
Plaintiffs,	§	
	§	**DOCKET NO. 070903296**
vs.	§	
	§	
SMITHKLINEBEECHAM CORPORATION D/B/A GLAXOSMITHKLINE, INC.	§	
	§	
	§	
Defendant.	§	**PAXIL PREGNANCY**
	§	

ORDER

AND NOW, this _____ day of _____, 2011, this cause came on for consideration on *Plaintiffs' Global Motion Regarding the Admissibility of Evidence on Changes to Paxil's Labeling and Other Post-Injury Conduct*. The Court having considered same, having heard the arguments of counsel and being otherwise fully advised in the premises, it is thereupon

ORDERED, ADJUDGED AND DECREED that *Plaintiffs' Global Motion Regarding the Admissibility of Evidence on Changes to Paxil's Labeling and Other Post-Injury Conduct* be and hereby is GRANTED in all respects.

BY THE COURT:

_____
SANDRA MAZER MOSS, J.

Dear Judge Moss:

The Plaintiffs in the above-cited cases file this motion regarding the admissibility of certain evidence that the Plaintiffs will offer. Plaintiffs urge the Court to treat this motion as a global motion and to rule that evidence of changes to Paxil's warning label in 2005, of an FDA warning letter issued in 2008, and of two GSK slide presentations prepared in 2006 are all admissible.

I. INTRODUCTION

The Plaintiffs contend that Defendant GlaxoSmithKline LLC, formerly SmithKline Beecham Corporation, d/b/a/ GlaxoSmithKline ("GSK") negligently failed to warn women of Paxil's risks. Specifically, the Plaintiffs contend that Paxil's warning label did not accurately reflect the true level of risk for birth defects.

Paxil's label was changed in late 2005, shortly after the Plaintiffs took Paxil during their pregnancies. The Plaintiffs' position is that the label-change, which was instigated by the Food and Drug Administration, was based on information that GSK either was already aware of or would have obtained much sooner if it had followed up on prior research. The new warnings would have appeared earlier—long before the Plaintiffs took the drug—if GSK had taken the appropriate steps when it should have. The label-change is highly relevant to the failure-to-warn claim.

In prior cases, GSK has filed motions *in limine* to exclude this evidence under Rules 407 and 403 of the Pennsylvania Rules of Evidence. The Plaintiffs expect that an identical motion will be filed in their cases, too.

GSK has also filed motions *in limine* to exclude evidence of "post-injury conduct." GSK's motions have focused on three pieces of evidence: the 2008 FDA warning letter regarding Avandia, slides from a "pregnancy follow-up working group," and a 2006 slide presentation entitled "pregnancy registries: GSK experience and recent data."

The Plaintiffs urge the Court to do the following:

First, the Court should treat this motion as a global motion to be applied to all Paxil Pregnancy cases. There is nothing case-specific about these evidentiary issues. Trial courts have reached different conclusions in earlier cases, and the risk of inconsistent rulings is simply too high.

Second, the Court should rule that all of the evidence is admissible. Contrary to GSK's position, an FDA-mandated label change is not a "subsequent remedial measure." Rule 407

applies only to changes made voluntarily, not to changes made at the behest of a regulatory agency. Courts have been virtually unanimous on that point, and Pennsylvania law is even more favorable to the Plaintiffs' position. Rule 403 poses no obstacle to admitting the evidence of the labeling change. The FDA warning letter is relevant to Plaintiffs' argument that GSK failed to disclose knowledge of Paxil's teratogenic effects to the FDA in 2000. And the slide presentations, even assuming they were made in 2006, contain information that was in GSK's possession before the injuries occurred.

II. ARGUMENT

A. This motion should be treated as a global motion because the evidence referred to above is an integral part of every Paxil Plaintiff's case.

As the Court is aware, this motion can be designated as a global motion while leaving all truly case-specific evidentiary rulings to the trial judge. As the Civil Trial Manual explains, "All Mass Tort motions, except case-specific Motion[s] *In Limine*, are assigned to the Coordinating Judge for disposition. Case-specific Motions *In Limine* are assigned to the trial judge for disposition. The Coordinating Judge may designate any motion a 'global motion' to be applied to all cases in a particular Mass Tort program."[1]

The problem with treating the labeling change and post-injury conducts as somehow "case-specific" is that some Plaintiffs will be able to present critical evidence on the failure-to-warn theory, while other Plaintiffs may not. That risk of inconsistent rulings undermines the whole purpose of having a uniform set of procedures for Paxil Pregnancy cases.

The risk of inconsistency is not speculative. It has already occurred. In earlier cases, GSK filed motions *in limine* with respect to changes made to Paxil's warnings and labeling in the fall of 2005. GSK argued, first, that the labeling change was a subsequent remedial measure under Pennsylvania Rule of Evidence 407 and could not be admitted; and, second, that any evidence of the labeling change would be unfairly prejudicial under Pennsylvania Rule of Evidence 403. The trial judge in *Kilker* denied the motion *in limine*, but he trial judge in *Blyth* granted an identical motion, though he did so without prejudice to consider specific offers of proof at trial.

Whether this evidence is admissible is not appropriate for a case-specific motion *in limine*. It will be a recurring issue in every failure-to-warn claim where the injury occurred before the label was changed. A uniform decision is needed.

[1] *Civil Trial Manual, Complex Litigation Center* at 3, at http://courts.phila.gov/pdf/manuals/civil-trial/complex-litigation-center.pdf. The revised mass tort motion procedures (dated October 29, 2008) do not address motions *in limine*. *See* http://www.courts.phila.gov/pdf/manuals/civil-trial/Mass-Tort-Motion-Procedures-Rev-2008.pdf .

B. Evidence regarding changes to Paxil's label is admissible under the Pennsylvania Rules of Evidence.

1. *Evidence of Paxil's labeling change is relevant to the causation issues in every Plaintiff's case.*

Under the learned intermediary doctrine, GSK's duty to provide adequate warnings of Paxil's risks was directed to the prescribing physician, not to the patient who is prescribed the drug. Thus, on the issue of causation, the parties will have to elicit testimony on whether "a proper warning would have changed the decision of the treating physician, i.e., that but for the inadequate warning, the treating physician would have not used or prescribed the product." *Ackermann v. Wyeth Pharm.*, 526 F.3d 203, 208 (5th Cir. 2008) (applying Texas law) (internal quotation marks and citations omitted); *see also Eck v. Parke, Davis & Co.*, 256 F.3d 1013, 1018 (10th Cir. 2001) (applying Oklahoma law, which presumes a physician would "read and heed" an adequate warning offered by the manufacturer). (A Plaintiff could also show that she would have rejected the drug if the drug company's warning had been adequate and the doctor had then adequately informed the plaintiff of the risks. *See McNeil v. Wyeth*, 462 F.3d 364, 373 (5th Cir. 2006).)

The prescribing physicians in *Ayala*, *Davis*, and *Lacambra* testified in their depositions that they would *not* have prescribed Paxil if the warning had been adequate. They all testified unequivocally that they changed their prescribing habits when Paxil's label was changed from Pregnancy Category C to Category D.

The difference between a Category C drug and a Category D drug is striking. With a Category C drug, doctors are advised that animal reproduction studies have shown an adverse effect on fetuses, but there are no adequate, well-controlled studies in humans, and the potential benefits may warrant use of the drug in pregnant women despite potential risks. The warning given for a Category D drug is much stronger: "There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks." 21 C.F.R. § 201.57(c)(9)(i)(A)(4), (3).

When Paxil was changed from Category C to Category D in December 2005, physicians had to change their risk-benefit analysis when prescribing Paxil. The physicians in the *Ayala*, *Davis*, and *Lacambra* cases did so. They all testified in their depositions that

- they understood the FDA Pregnancy Category system,
- they relied on the Category C classification when prescribing Paxil to the Plaintiffs,
- they would not have prescribed Paxil to the Plaintiffs if it had been a Category D drug,
- they currently do not prescribe Paxil to potentially pregnant women because Paxil is a Category D drug, and

- they would not prescribe Paxil to these Plaintiffs if they presented the same symptoms today.

(The physicians' deposition testimony was quoted at length in response to GSK's motions for summary judgment in *Ayala*, *Davis*, and *Lacambra*.)

The physicians in those three cases did, in fact, change their prescribing habits based on the 2005 labeling change. If the label had been changed years earlier—as the Plaintiffs contend should have been done—the physicians never would have prescribed Paxil to these Plaintiffs.

The belated labeling change from Category C to Category D is highly relevant to the issue of causation in every Paxil Pregnancy case. To prove causation under the learned intermediary doctrine, a plaintiff must be able to present evidence of the label change and ask the prescribing physician how such a change affects their prescribing decisions.

2. *Because the change was dictated by the FDA, GSK cannot argue that the labeling change was a subsequent remedial measure under Rule 407.*

a. The label changes

GSK made two changes to Paxil's label in late 2005. In September 2005, it added a precaution about the risk of heart defects. Then in December 2005, at the insistence of the FDA, GSK strengthened the warning and changed the pregnancy category from C to D. (The Category D labeling is required by federal regulation whenever there is "positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans." 21 C.F.R. § 201.57(i)(A)(1)-(5). The regulation further requires a warning that Paxil "can cause fetal harm when administered to a pregnant woman. . . . If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.")

b. Rule 407

The first sentence of Pennsylvania Rule of Evidence 407 provides as follows:

> When, after an injury or harm allegedly caused by an event, measures are taken which, if taken previously, would have made the injury or harm less likely to occur, evidence of the subsequent measures is not admissible to prove that the party who took the measures was negligent or engaged in culpable conduct, or produced, sold, designed, or manufactured a product with a defect or a need for a warning or instruction.

The second sentence of Rule 407 then explains that evidence of subsequent remedial measures may be admissible with a proper limiting instruction: "This rule does not require the exclusion of evidence of subsequent measures when offered for impeachment, or to prove other

matters, if controverted, such as ownership, control, or feasibility of precautionary measures." Pa. R. Evid. 407.

The official comment observes that Pennsylvania Rule 407 "is substantially the same" as Federal Rule 407. Comment to Pa. R. Evid. 407. One difference is that the Pennsylvania rule is expressly limited to "the party who took the measures." Though the federal rule does not contain that express limitation, federal courts "have generally held that the federal rule does not apply when one other than the alleged tortfeasor takes the action because the reason for the rule (to encourage remedial measures) is not then implicated." Comment to Pa. R. Evid. 407. The drafters of the Pennsylvania rule did not want to leave the intended construction to chance, so they wrote the limitation into the rule itself. *Id.* (noting that the wording of the Pennsylvania rule "has been modified in order to clarify two ambiguities in the federal formulation," the first of which is the federal rule's silence on who instigated the changes).

Pennsylvania Rule 407 thus makes it clear that "the rule of exclusion favors only the party who took the subsequent remedial measures." *Id.*

c. The policy behind Rule 407

Rule 407 exists to protect the "'prudent and well-meaning defendant who guards against the recurrence of an accident he had no reason to anticipate, or who out of a considerate regard for the safety of others exercises a higher degree of care than the law requires.'" *Duchess v. Langston Corp.*, 564 Pa. 529, 769 A.2d 1131, 1137-38 n.7 (2001) (quoting *Baron v. Reading Iron Co.*, 202 Pa. 274, 284, 51 A. 979, 980 (1902)). The rule encourages manufacturers to improve the safety features of their products. *Id.* at 1137; *see also* Fed. R. Evid. 407 Advisory Committee's Note (referring to the "social policy of encouraging people to take, or at least not discouraging them from taking, steps in furtherance of added safety"); *Stecyk v. Bell Helicopter Textron, Inc.*, 295 F.3d 408, 415 (3d Cir. 2002) ("Rule 407 rests on the strong public policy of encouraging manufacturers to 'make improvements for greater safety.'").

Because of those policy concerns, federal courts have held that a subsequent remedial measure is not covered by Rule 407 if it is taken by a third party. For example, the Third Circuit held that a mechanic's re-design of a road grader was admissible in a negligent-design action because the mechanic was a non-party. *Diehl v. Blaw-Knox*, 360 F.3d 426, 428-30 (3d Cir. 2004) ("Rule 407 does not apply to evidence of subsequent remedial measures taken by a non-party. . . .").

For precisely the same policy concerns, federal and state courts have also held that Rule 407 does not apply to subsequent remedial measures mandated by government agencies. This issue is one of first impression in Pennsylvania.

d. Decisions on government-mandated changes

As the Third Circuit recently pointed out, other courts have held that Rule 407 does not apply to

> remedial action mandated by superior governmental authority, such as a regulatory agency, because the policy goal of encouraging *voluntary* improvements for greater public safety would not necessarily be furthered by the exclusion of such evidence.

Pineda v. Ford Motor Co., 520 F.3d 237, 246 n.13 (3d Cir. 2008). The Third Circuit did not reach that question in *Pineda*, which involved Ford's issuance of a safety recall instruction ("SRI") after the plaintiff had been injured. The Court specifically stated that "the record before us gives no indication of what prompted Ford to issue the SRI in 2004." *Id.*

Federal courts have applied this "superior governmental authority" exception to cases involving directives from federal regulatory agencies:

- In a case involving an airplane crash, a trial court erred when it excluded a series of post-crash FAA Airworthiness Directives under Rule 407: "Where a superior authority requires a tortfeasor to make post-accident repairs, the policy of encouraging voluntary repairs which underlies Rule 407 has no force—a tortfeasor cannot be discouraged from voluntarily making repairs if he must make repairs in any case." *Herndon v. Seven Bar Flying Serv., Inc.*, 716 F.2d 1322, 1331 (10th Cir. 1983).

- A trial court erred when it excluded under Rule 407 a "trend cost estimate" that was required by the National Highway Safety Administration. That remedial measure was required by a "superior authority" instead of being implemented voluntarily "out of a sense of social responsibility." In light of the policy underlying Rule 407, excluding the evidence would be "particularly inappropriate." *Rozier v. Ford Motor Co.*, 573 F.2d 1332, 1343 (5th Cir. 1978).

- A trial court could not rely on Rule 407 to exclude evidence that, following an accident that injured the plaintiff, a state inspector required mine operators to give added support to the power cable that had fallen. *Lolie v. Ohio Brass Co.*, 502 F.2d 741, 744 (7th Cir. 1974).

This same rationale articulated in *Rozier*, *Herndon*, and other cases also applies to post-event warnings required by the FDA.

e. Decisions involving FDA-mandated changes

One of the leading cases on Rule 407 and FDA warnings is *Kociemba v. G.D. Searle & Co.*, 683 F. Supp. 1579 (D. Minn. 1988). Shortly after the plaintiff obtained an IUD, the manufacturer issued additional safety warnings at the FDA's behest. *Id.* at 1580. At trial, the manufacturer sought to exclude evidence of the changed warning, arguing that it was a subsequent remedial measure under Rule 407. *Id.* Quoting from *Herndon*, the court reiterated that "'where a superior authority requires a tortfeasor to make post-accident repairs, the policy of encouraging voluntary repairs which underlies Rule 407 has no force—a tortfeasor cannot be discouraged from voluntarily making repairs if he must make repairs in any case.'" *Id.* at 1581 (quoting *Hearndon*, 716 F.2d at 1331). Rule 407 thus "[did] not bar admission of the November warning . . . [because] the defendant changed the warning only after the federal government *required* it to do so." *Id.*

The holding of *Kociemba* was reaffirmed last year in a case involving an anti-epilepsy drug. *See Smith v. Pfizer Inc.*, No. 3:05-0444, 2010 U.S. Dist. LEXIS 42481 at *8-*12 (M.D. Tenn. April 30, 2010). The critical facts were stated by the court as follows:

> In 2008, the FDA conducted a meta-analysis of studies on anti-epileptic drugs, including Neurontin, and concluded that these drugs might increase patients' risk of committing suicide. As a result of this study, in 2009, the FDA required the manufacturers to add warning labels stating that the drugs might increase the risk of suicidal behavior and ideation. Pfizer complied by adding these warnings to its Neurontin labeling and Neurontin patient guide.

Id. at *8. At trial, Pfizer argued that the new warning label and patient guide were inadmissible under Rule 407, but the court disagreed. "Here, the FDA mandated that Pfizer add the warnings. The policy behind Rule 407 is not implicated, so it does not bar admission of the 2009 label and patient guide." *Id.* at *11.

In its prior motions *in limine*, GSK has cited a few cases where drug companies were acting as "model citizens" and took it upon themselves to change labels, warnings, package inserts, or product designs. *Cf. Stahl v. Novartis Pharmaceuticals Corp.*, 283 F.3d 254, 270 n.10 (5th Cir. 2002) (involving an apparently voluntary change to package insert); *DeLuryea v. Winthrop Labs*, 697 F.2d 222, 228 (8th Cir. 1983) (same). But those changes were made by companies acting independently and voluntarily, without the FDA telling them what to do. As explained below, it was the FDA—not GSK—that is responsible for the changes to Paxil's label in 2005.

In short, Rule 407 covers only those subsequent remedial measures that are made voluntarily by a defendant. Remedial measures that are brought about by the FDA or other agencies cannot be excluded under Rule 407. Pennsylvania courts have not resolved this precise issue, but federal courts have consistently and firmly rejected arguments similar to GSK's.

f. Pennsylvania law

There is no reason to think that Pennsylvania law requires a different result. The text is virtually the same—in fact, the Pennsylvania rule arguably places more emphasis on the defendant's role in taking the remedial measures. The underlying policy is clearly the same. *See Duchess*, 769 A.2d at 1138 n.7 (emphasizing that Pennsylvania Rule 407 protects the "prudent and well-meaning defendant . . . who out of a considerate regard for the safety of others exercises a higher degree of care than the law requires"). If a remedial measure was caused by governmental authority, then evidence of that remedial measure is admissible under Rule 407 for all purposes. *See also* OHLBAUM ON THE PENNSYLVANIA RULES OF EVIDENCE § 407.08 at 229 (LexisNexis 2007-08) (agreeing that Pennsylvania law should follow federal law on this issue).

g. The role of the FDA in this case

In the fall of 2005, GSK changed the warnings for Paxil at the FDA's behest. The changes were not made voluntarily.

There is no question that the FDA requires accurate warnings as part of medication labels to provide consumers with notice of potential adverse effects. *See* 21 U.S.C. § 355(e); *Lindsay v. Ortho Pharmaceutical Corp*., 637 F.2d 87, 94 (2d Cir. 1980) ("[I]n view of the control over label terminology exercisable by the FDA . . . we question whether a change in language should be construed as a voluntary admission by the manufacturer.") (citations omitted).

The events leading up to the labeling change were summarized by one of the Plaintiffs' expert witnesses, Dr. Suzanne Parisian. In late 2002, a GSK employee recommended a "large database study of pregnancy outcomes . . . to ascertain the frequency and types of major birth defects in women with prescriptions for bupropion [Wellbutrin] during the first trimester." Parisian Report [Ex. A, October 19, 2010 Expert Report of Dr. Suzanne Parisian] at 107.[2] (This study has been referred to as the "Bupropion Study" or "Ingenix Study." *Id.* at 108.) The FDA reviewed the findings and requested that GSK conduct additional analysis. Id. As a GSK employee explained, the Ingenix study had used a control group consisting of women who used other antidepressants in the first trimester, and "[t]he group of other antidepressants includes primarily Zoloft, Paxil and Prozac." *Id.* at 108-09. What the FDA needed to know was "the frequency of cardiac malformations with each of the 'other antidepressants.'" *Id.* at 109.

Within days of submitting the new data to the FDA, GSK sent a Dear Health Care Professional Letter regarding Paxil. *Id.* The letter added a precaution about the risk of birth defects, but GSK reiterated that Paxil was classified as a Category C drug: "Paroxetine currently carries a Category C pregnancy precaution, indicating that there are no adequate and well-controlled studies in humans to determine the effect of paroxetine on the fetus." *Id.* Dr. Parisian offered her opinion that the letter "still continued to fail to adequately warn physicians about the

[2] To prevent accumulative Exhibits, Plaintiffs have only attached the Expert Report of Dr. Suzanne Parisian in *Ayala* v. GSK, and have not attached Dr. Parisian's Expert Reports in *Davis* v. GSK or *Lacambra* v. GSK.

increased reports of risk of congenital abnormalities for children of women taking paroxetine during the first trimester." *Id.*

Then in December 2005, at the FDA's insistence, Paxil was changed from a Category C drug to a Category D drug. The reclassification reflects "positive evidence" in humans of a teratogenic association. 21 C.F.R. § 201.57(i)(A)(1)-(5).

The FDA's correspondence with GSK indicates that the FDA was responsible for the change. In a letter to GSK, FDA officials wrote that the agency found "it necessary to request that the decreased survival of rat pups" in the animal studies "receive more emphasis in labeling" and recommended that additional animal studies be done. [Ex. B, October 12, 1995 FDA Letter.] One of GSK's own epidemiologists testified that the FDA took the lead in changing the Paxil label in late 2005:

Q. Whether it was a mandate or a request, it wasn't something GSK voluntarily did?
A. But GSK did do it.
Q. After the FDA mandate/request, right?
A. The FDA did request it, and GSK did do it.

[Ex. C, Excerpts from the Deposition of Sara Ephross at 102:5-108.]

In sum, GSK did not voluntarily change the Paxil warning labels. It was the FDA who directed GSK to conduct further analyses and to change the label based on the findings.

h. Limiting instructions

The label-change evidence is also admissible for other, more limited purposes. The second sentence of Rule 407 provides that evidence of subsequent remedial measures can be admitted "when offered for impeachment, or to prove other matters, if controverted, such as . . . feasibility of precautionary measures." Pa. R. Evid. 407.

In the *Duchess* case, the Supreme Court held that the plaintiff's evidence of subsequent remedial measures was *admissible* for the limited purposes of demonstrating feasibility and impeaching the defendant's expert's testimony. 769 A.2d at 1145-50. In the context of Rule 407, "feasibility" is defined "broadly . . . to encompass not only technological possibility, but also considerations of cost and practicality and technological possibility." *Id.* at 1146; *see also Smalls v. Pittsburgh-Corning Corp.*, 843 A.2d 410, 413 (Pa. Super. 2004) (affirming a trial court's admission of a post-exposure warning about asbestos for the purpose of impeaching company witnesses).

GSK has suggested in pleadings, motions, and at trials that it was not feasible to perform additional studies to examine Paxil's teratogenicity. The company has designated corporate witnesses to discuss GSK's compliance with federal regulations, its review of scientific data on

the association between Paxil and birth defects, and safety and pharmacovigilance practices. If GSK continues to make those arguments, it will open the door to evidence regarding subsequent remedial measures.

Courts have held that the introduction of evidence relating to subsequent remedial measures must be admitted when the defendant contests the feasibility of protective measures:

- *See Adams v. City of Chicago*, 469 F.3d 609 (7th Cir. 2006) (Rule 407 explicitly does not require the exclusion of evidence of subsequent remedial measures when offered to prove the feasibility of precautionary measures)

- *Robbins v. Farmers Union Grain Terminal Association*, 552 F.2d 778, 794, 794 n.5 (8th Cir. 1977) (subsequent remedial measures were relevant to show that a different design or warning would have prevented the harm and that it was feasible to include this design or warning before the product was sold)

- *Dixon v. International Harvester Co.*, 754 F.2d 573, 584 (5th Cir. 1985) (when defendant testified that the installation of protective devices was not feasible, evidence showing their subsequent installation was admissible).

- *Kenny v. Southeastern Pennsylvania Transp.*, 581 F.2d 351, 356 (3d Cir. 1978) ("defendant opens up the issue by claiming that all reasonable care was being exercised at the time, then the plaintiff may attack that contention by showing later repairs which are inconsistent with it").

In this case, the events leading up to the labeling change establish that adequate testing was feasible. GSK knew that the testing was *feasible* but not *desirable* due to the possibility that any unfavorable safety data would impact Paxil's commercial success and the content of its label. Thus, the evidence of the 2005 label change is relevant to show that the label could have been changed years earlier (as GSK clearly recognized) if GSK had only conducted adequate research.

i. Causation

Finally, it bears repeating that evidence of the labeling change and the events leading up to it (especially the additional analysis of the Ingenix Study results) are relevant to the fundamental issue of causation. A study showing that Paxil causes birth defects is relevant to show that Paxil caused birth defects in a particular Plaintiff. The timing of the study does not affect the relevance of that evidence on the issue of causation.

3. *Evidence of the labeling change is not unfairly prejudicial under Rule 403.*

In its motions *in limine* regarding the labeling change, GSK has relied primarily on Rule 407 but has also cited Rule 403 as a fallback argument. There is nothing unfairly prejudicial about this evidence.

Rule 403 is concerned only with evidence that is unfairly or unduly prejudicial:

> Since all effective evidence is prejudicial in the sense that it damages the party against whom it is offered, prejudice that calls for exclusion requires a more specialized meaning. The prejudice must be *unfair*. The evidence must possess an undue tendency to suggest a decision on an improper basis, commonly an emotional one, such as bias, sympathy, hatred, contempt, retribution, or horror.

OHLBAUM ON THE PENNSYLVANIA RULES OF EVIDENCE § 403.09 at 127. The change in labeling does not rise to that level. GSK cannot come close to proving that evidence of the labeling change would create "an undue tendency to suggest a decision on an improper basis." *Mahan v. Am-Gard, Inc.*, 841 A.2d 1052, 1057 (2003) (citing *Leahy v. McClain*, 732 A.2d 619, 625 (Pa. Super. 1999)) (adding that "unfair prejudice" does not mean "detrimental to a party's case"); *see also Espeaignette v. Gene Tierney Co., Inc.*, 43 F.3d 1, 7 (1st Cir. 1994) (evidence of subsequent remedial measures taken by a non-party was not misleading or unfairly prejudicial).

Moreover, when determining whether evidence is unfairly prejudicial, courts take into account the importance of the evidence to the offering party's case. Evidence is less likely to be deemed prejudicial if it is central to a party's theory of the case. *See Mahan*, 841 A.2d at 1057 (holding that the plaintiff was entitled to introduce evidence regarding defendant's alleged violation of the Private Detective Act because that evidence was central to the exposition of plaintiff's theory of liability, i.e., negligence *per se*). The probative value of this evidence far outweighs any alleged prejudice because this evidence is particularly relevant to a number of central issues in this case, including causation, knowledge of the risks associated with Paxil use during pregnancy, the adequacy of warnings, and the sufficiency of GSK's research upon becoming aware of Paxil's teratogenic potential.

C. Evidence of certain post-injury conduct is admissible because it is relevant to GSK's earlier knowledge that Paxil causes congenital malformations.

This motion is limited to three pieces of evidence that GSK has sought to exclude in previous trials: a FDA warning letter issued in 2008, a set of slides from a "pregnancy follow-up working group" (which appear to have been created in 2000 but were used in 2006), and another slide presentation entitled "pregnancy registries: GSK experience and recent data" that was created in 2006. Regardless of their creation dates, however, all three documents are relevant because they are probative to fact issues in the present case.

1. *The FDA warning letter*

GSK has repeatedly withheld from the FDA the results of tests required by foreign regulatory agencies. In 2000, GSK failed to provide the FDA with Paxil results required by the Japanese government. Later, GSK engaged in the same behavior with its Avandia drug, and the FDA issued a stinging rebuke in a 2008 warning letter. The reprimand addressed the same safety practices at issue here.

GSK admits that it failed to provide the FDA with a government-mandated report on congenital abnormalities associated with Paxil. GSK's Director of the Neurosciences Safety Evaluation and Risk Management Group testified that a report requested by the Japanese government was never submitted to the FDA.

> Q. …the FDA never, ever got an opportunity to evaluate what they thought of the cumulative data, right?
> A. This document was not – you're right or correct that this document, in its entirety, was not submitted to the FDA.

[See Ex. D, Excerpts from the Deposition of Dr. Stephen Hughes, at 170-72, 175-78].

Dr. Hughes went on to testify that the cumulative data was not given to the FDA because the FDA had not specifically requested it:

> Q. So you have a regulatory body, a Japanese regulatory agency, requested that you prepare a position piece on congenital abnormalities, and you prepared one, right?
> A. Yes.
>
> * * *
>
> Q. Right. Why not submit it to the FDA at the same time?
> A. Because the FDA had not requested a specific review of reports of congenital abnormalities.

Id.

GSK's withholding of important safety information about Paxil makes the FDA Warning Letter particularly relevant in this case. The FDA reprimanded GSK for doing the very same thing with test results on Avandia. In the case of Avandia, GSK had not given the FDA the results of tests required by European regulatory authorities because the FDA had not specifically requested the results. The FDA soundly rejected GSK's position. As the FDA explained, federal regulations require GSK to report new actions taken because of adverse drug experiences, without regard to which regulatory authority requested the new action. [See Ex. E, 2008 FDA Warning Letter at 2.]

The FDA warning letter clearly addresses similar actions to those taken by GSK in 2000. The letter is relevant to the Plaintiffs' claim that GSK failed to provide the 2000 Report of Congenital Abnormalities requested by the Japanese regulatory authority to the FDA in violation of federal regulations.

2. *The "working group" slides*

In April 2000, a GSK employee prepared a PowerPoint presentation for the "Worldwide Clinical Safety International Safety Meeting." [See Ex. F, Excerpts from the Deposition of Jane Neiman at 168, 171-72.] GSK has asserted that the slides were created in 2006, even though the named author of the presentation testified in her deposition that she created them in 2000. Regardless of the date of composition, the slides are relevant and admissible.

The slide presentation, which is entitled "Pregnancy Follow-up Working Group," demonstrates GSK's abysmal record in tracking reports of abnormal pregnancy outcomes as far back as 1997. The information contained on the slides reflects that GSK failed to follow pregnancy outcomes for Paxil.

3. *The "pregnancy registries" slides*

The set of slides entitled "Pregnancy Registries: GSK Experience and Recent Data" note various recommendations for a pregnancy registry and describe GSK's experiences with them. Most, if not all, of this information was known by, or available to, GSK before the Plaintiffs were born. For example, one of the slides outlines the criteria for determining when a pregnancy registry should be established for a drug. The same criteria appear in a 1999 article written by a GSK epidemiologist assigned to Paxil. [See Ex. G, Excerpts from the Deposition of Sara Ephross at 41-44.] This slide show also contains a summary of the information available to GSK regarding Paxil.

One of Plaintiffs' contentions in this case is that GSK should have had a pregnancy registry for Paxil. GSK's knowledge about pregnancy registries, the information GSK used to justify its decision not to create a pregnancy registry for Paxil, and GSK's ability to create and maintain a pregnancy registry for Paxil are all relevant to the issues in this case. This set of slides is relevant to those issues.

III. CONCLUSION

For the reasons set forth above, urge the Court to treat this motion as a global motion and to rule that evidence of changes to Paxil's warning label in 2005, the FDA warning letter, and the slide presentations are all admissible.

Respectfully submitted,

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IN RE: PAXIL PREGNANCY CASES	§	**COURT OF COMMON PLEAS** **TRIAL DIVISION** **PHILADELPHIA COUNTY** **DOCKET NO. 3220**
ROY G. AYALA And KELLY M. CAPITO, Individually and as Parents and Natural Guardians of GABRIELLE R. AYALA, A Minor Plaintiffs, **vs.** **SMITHKLINEBEECHAM CORPORATION D/B/A GLAXOSMITHKLINE, INC.** Defendant.	§	**COURT OF COMMON PLEAS** **TRIAL DIVISION** **PHILADELPHIA COUNTY** **DOCKET NO. 070903247** **PAXIL PREGNANCY**

AMY L. DAVIS, Individually, and as Next Friend of JOEY L. DAVIS, A Minor **Plaintiffs,** **vs.** **SMITHKLINEBEECHAM CORPORATION D/B/A GLAXOSMITHKLINE, INC. and PAR PHARMACEUTICALS, INC.** **Defendants.**	§	**COURT OF COMMON PLEAS** **TRIAL DIVISION** **PHILADELPHIA COUNTY** **DOCKET NO. 070903266** **PAXIL PREGNANCY**
MELANIE L. LACAMBRA, Individually and as Parent and Natural Guardian of KAI A. LACAMBRA, A Minor **Plaintiffs,** **vs.** **SMITHKLINEBEECHAM CORPORATION D/B/A GLAXOSMITHKLINE, INC.** **Defendant.**	§	**COURT OF COMMON PLEAS** **TRIAL DIVISION** **PHILADELPHIA COUNTY** **DOCKET NO. 070903296** **PAXIL PREGNANCY**

ATTORNEY CERTIFICATION OF GOOD FAITH

I hereby certify that counsel for Plaintiff contacted opposing counsel in an effort to amicably resolve the issues and relief sought in their *Global Motion Regarding the Admissibility of Evidence on Changes to Paxil's Labeling and Other Post-Injury Conduct*, to no avail.

/s/ Jason A. Itkin

ATTORNEYFOR PLAINTIFFS

CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of the foregoing instrument will silmutaneously be served via ☒ U.S. Mail; ☐ Facsimile; ☒ Electronically; ☐ Overnight Delivery; and/or ☐ Hand Delivery, on this 23rd day of February, 2011, to the following:

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