IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

MARION L. KNIPE, Individually and as Administratrix and Administratrix Ad Prosequendum of the Estate of HAROLD STANLEY JAKE GARRISON, Deceased, and HAROLD L. GARRISON, JR., Individually;	)	**Civil Action No.: 2:06-CV-3024 RB**
Plaintiffs,	)	
v.	)	
SMITHKLINE BEECHAM CORPORATION d/b/a GLAXOSMITHKLINE, a Pennsylvania Corporation;	)	
Defendant.	)	

PLAINTIFFS' OPPOSITION TO
SMITHKLINE BEECHAM CORPORATION D/B/A GLAXOSMITHKLINE'S
MOTION FOR SUMMARY JUDGMENT (Federal Preemption)

TABLE OF CONTENTS

TABLE OF AUTHORITIES

FEDERAL CASES

STATE CASES

CONSTITUTIONAL AND STATUTORY PROVISIONS

REGULATIONS

OTHER AUTHORITY

I. SUMMARY OF FACTS AND LEGAL ARGUMENTS

Plaintiffs Marion Knipe and Harold Garrison (collectively "Plaintiffs") are the parents of Jake Garrison ("Jake"), who committed suicide in September 2002 at the age of 16 while under the influence of the antidepressant, Paxil.[1] Unbeknownst to Jake's treating physician, his parents or Jake himself, Paxil was (and is) causally associated with suicidality and acts of self-harm in children and adolescents -- something GSK realized as early as1998 from its first adolescent clinical trials. GSK also knew that clinical trials of Paxil failed to demonstrate efficacy in this population. Despite this knowledge, GSK not only failed to disclose this information (until 2004/2005 when it was forced to do so), but GSK concealed this information and, instead, actively promoted Paxil as safe and effective for children and adolescents. Meanwhile, GSK reaped enormous economic benefits from its sale of Paxil to unsuspecting parents for their children and adolescents (in the amount of approximately $500,000,000 between 1993-2005). GSK was finally required, in 2005, to add a Black Box warning to its label alerting physicians and their patients that Paxil increases the risk of suicidality in children and adolescents. (Exh. 76).

Despite these facts, GSK seeks complete immunity from liability in this case by asserting the "conflict preemption defense" and claiming that, under the Federal Food, Drug, and Cosmetic Act ("FDCA"), it was *prohibited* from warning or disclosing to the public *truthful information* about the suicidality risks associated with Paxil in children and adolescents. In so arguing, GSK attempts to abrogate its duty to the millions of consumers of its multi-billion-dollar income-producing drug and has placed profits over safety. In essence, GSK argues that, because the FDA did not "make" GSK warn about the suicidality risk in pediatric patients until 2005, it could not have warned or disclosed the risks any sooner. GSK is wrong.

---

[1] Jake was fifteen when he was initially prescribed Paxil and he was sixteen when he committed suicide.

The FDCA and accompanying FDA regulations do not prohibit a manufacturer from issuing a warning regarding "off-label" pediatric use[2]. In fact, to date, no appellate court – federal or state – has ever held that the FDA's drug approval authority or its authority over drug labeling preempts a state-law tort suit premised on the manufacturer's failure to issue a warning related to "*off label*"[3] uses. GSK's conflict preemption defense is baseless because no actual conflict exists, nor does any state law that Plaintiffs seek to assert stand as an obstacle to the achievements of federal objectives.

The basic analysis of the preemption argument in this case can be summarized as follows:

- There is a "basic presumption against preemption" because preemption upsets the balance of power between the federal government and states as independent sovereigns. *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 449 (2005). The Third Circuit has similarly held that the presumption against preemption is applicable in a failure to warn claim. *Colacicco v. Apotex, Inc*., __F.3d ___. 2008 WL 927848, *9 (3rd Cir. 2008).

- The instant action involves an off-label use of Paxil (i.e., Paxil has never been approved by the FDA for use in the child/adolescent population) and, prior to Jake's suicide, the FDA never deemed Paxil to be safe for pediatric patients nor had the FDA ever rejected a warning regarding pediatric suicidality. In light of the fact that the FDA has never approved Paxil for use in the adolescent population, it defies logic to suggest that the FDCA (or FDA regulations) would prohibit issuing a *warning* regarding off-label use.

- There is no actual conflict in this case since the FDA currently requires GSK to include a "black box" warning in its label regarding the increased risk of suicidal behavior, and the clinical trial data the FDA relied upon to justify the current "black box"warning were the same data that GSK had in its possession *prior* to Jake's suicide.

- The New Jersey Supreme Court has found that such failure to warn cases are not preempted by the FDCA. *Feldman v. Lederle Labs., Inc.*, 592 A.2d 1176 (N.J., 1991).

---

[2] Pediatric patients are defined as those under the age of 18. (*See also* GSK Motion at p. 4, n.2.)

[3] "Off-label" refers to the use, prescription or marketing of an FDA-approved drug for an unapproved use, such as, in an unapproved population (i.e., children), or for a condition other than for what it has been approved. See e.g., *Perry v. Novartis Pharma. Corp.*, 456 F.Supp.2d 678, 681, n.6 (E.D.Pa.2006). Paxil has never been approved for use in children under 18 years old for any indication, however, physicians are legally permitted to prescribe drugs "off-label."

- GSK's reliance upon *Colacicco* is misplaced, since the Court in *Colacicco* was very clear that its ruling was limited to "adult suicidality" and this case deals with *pediatric* suicidality. *Colacicco v. Apotex, Inc*., __F.3d ___. 2008 WL 927848, *9 (3rd Cir. 2008).

- It can hardly be an obstacle to the accomplishment and execution of the full purposes and objectives of Congress to hold a drug manufacturer liable under state law for not adding or strengthening a warning when appropriate to do so – especially when the FDA now mandates the warning.

- GSK has a First Amendment right to issue truthful statements/warnings and the public has a First Amendment right to receive such information, consequently, neither the FDCA (nor its accompanying regulations) can restrict (a) GSK's right to issue a warning that is supported by the clinical trials; or (b) GSK's right to publish the results of its clinical trials.

- Under the Fifth Amendment of the Constitution, patients have a fundamental right to receive information regarding the possible risks associated with their medical treatment so that they can meaningfully exercise their Constitutional right as to whether to accept or reject the medication.

Applying these principles to this case, GSK's preemption arguments must fail.

II. FEDERAL REGULATORY FRAMEWORK FOR PRESCRIPTION DRUGS

All prescription drugs marketed in this country must first be approved by the FDA. To obtain permission to market a new product, a drug company must first submit a "new drug application" ("NDA") for the FDA's review and approval. 21 U.S.C. § 355(a)(b). An NDA must include information about the clinical trials that demonstrate the safety and effectiveness of the product, proposed labeling, and other information. 21 U.S.C. § 355(b)(d). The drug manufacturer drafts and submits a proposed initial label to the FDA for approval as part of the NDA process. 21 C.F.R. § 314.50(c)(2)(I); 314.50(d)(5)(viii). FDA approval includes approval of the labeling, which must, *inter alia*, identify contraindications, warnings, precautions, and adverse reactions. 21 C.F.R. §§ 201.56, 201.57. Subsequently, FDA approval is required before the manufacturer can make certain labeling changes, but the manufacturer may make other labeling changes without prior approval. 21 C.F.R. § 314.70(b)(c). Among the changes in the latter category are changes "[t]o add or strengthen a contra-indication, warning, precaution, or adverse reaction." 21 C.F.R.§

314.70(c)(2)(I).[4] Thus, the label is not fixed as of the date of FDA approval. Rather, a company's obligation to provide physicians and patients with up-to-date warnings and precautions continues as long as the product is on the market.

Because the FDA has limited knowledge of a new drug's safety at the time of approval, the FDA has acknowledged that the label is not a static document, but a fluid one that evolves over time. The FDA Commissioner has stated that "drug labeling does not always contain the most current information and opinion available to physicians about a drug because advances in medical knowledge and practice inevitably precede formal submission of proposed new labeling by the manufacturer and approval by the FDA." 44 Fed. Reg 37434, 37435 (1979). Likewise, when a drug is approved for a particular use, or indication, the FDA does not have adequate data about the drug when it is prescribed for other "off-label" uses. A drug's label constantly changes as the manufacturer learns more about the drug once it is on the market. The formal labeling of drugs lags behind the current state of knowledge. Because a manufacturer has the resources and most-thorough and up-to-date knowledge about its drug products, federal regulations place an affirmative duty on a manufacturer to continuously assess the safety of its drugs and to warn of safety hazards as these harms come to light: "[T]he labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug: a causal relationship need not have been proved." 21 C.F.R. § 201.80(e) (2008); 21 C.F.R. § 201.57(e) (2002).[5] The FDA thought

---

[4] In 2006, the FDA amended section 314.70 and, among other things, renumbered some of the regulations. For example, 314.70(c)(2)(I) (discussed *supra*) has now been relocated to 314.70(c)(6)(iii)(A). See e.g., *Colacicco*, 2008 WL 927848, *3, n.4. However, since the relevant time period for this case is 2002, the applicable provisions are the regulations as they existed in 2002. *Colacicco,* 2008 WL 927848, *3, n. 2. For the convenience of the Court, when relevant, Plaintiffs will cite to both the regulations as they existed in 2002 as well as provide parallel citations to the current regulations.

[5] 21 C.F.R §201.57(e) was the statute that was applicable in 2002 when Jake Garrison was prescribed Paxil. In 2006, that statute was relocated (without any significant change) to 21 C.F.R.§201.80(e) and it continues to govern manufacturers of older drugs such as Paxil. *See e.g., Colacicco*, 2008 WL 927848 at 3, n.2, n.3 & n.4. As previously noted, since the events of this case

it so important to put safety first that it dispensed with the normal procedure requiring FDA approval prior to a label change.[6] 50 Fed. Reg. at 7452-01, 7470. Instead, a company can "add or strengthen a contraindication, warning, precaution, or adverse reaction" for its drug at any time, without the agency's prior approval. 21 C.F.R. § 314.70(c)(6)(iii)(A) (2008); 21 C.F.R. § 314.70(c)(2)(I) (2002). Thus, despite any assertion by GSK to the contrary, it cannot avoid its duties to ensure that the labeling contains adequate directions for the drug's "intended uses,"[7] 21 U.S.C. § 352, and GSK was required to revise the labeling to include a warning "as soon as there is reasonable evidence of an association of a serious hazard with a drug." 21 C.F.R. § 201.80(e) (2008); 21 C.F.R. § 201.57(e) (2002).

In addition to modifying its label, the FDA allows GSK to communicate warnings and potential side effects to doctors and the medical community via "Dear Doctor" letters and continuing education. GSK could have warned Jake Garrison's doctor through any or all of these means. In fact, in 2004, GSK subsequently used "Dear Doctor" letters to warn doctors about Paxil's association with suicidality. See, e.g., Plaintiffs' Statement of Additional Undisputed Facts (hereinafter referred to "PSUF") No. 62, Exh. 64.[8] As a Court in this District recently noted:

---

took place in 2002, this case will be governed by the statutes applicable in 2002. *Id.*

[6] Prior to 1965, FDA regulations prohibited drug companies from strengthening their warnings without prior regulatory approval. *See Caraker v. Sandoz Pharm. Corp.*, 172 F. Supp. 2d 1018, 1034-35 (S.D. Ill 2001) (citing 25 Fed. Reg. 12,592, 12,595 (Dec 9, 1960)).

[7] The term "intended use" has a broad meaning under FDA regulations. Specifically, a manufacturer's promotion of a drug to a specific population (e.g., children) demonstrates that the manufacturer had the objective intent that the product be used by children. See 21 C.F.R. § 201.128. Thus, as demonstrated *infra*, GSK's marketing of Paxil for adolescent use indicates that GSK had an objective intent that Paxil be prescribed to the adolescent population. Furthermore, the same regulation goes on to provide: "*if a manufacturer knows, or has knowledge of facts that would give him notice, that a drug introduced into interstate commerce by him is to be used for conditions, purposes, or uses other than the ones for which he offers it, he is required to provide adequate labeling for such a drug which accords with such other uses to which the article is to be put*." *Id* (emphasis added).

[8] All exhibits referenced herein are attached to the Declaration if Bijan Esfandiari.

> even where FDA regulations or other federal law prevent a manufacturer from modifying the approved labeling, a modification of the label is not the only form that a warning could take. If, for example, a plaintiff claimed that a manufacturer was negligent in not sending a letter to prescribing physicians or other health care professionals, that might present a different case, even if modification of the approved labeling were prohibited. Because plaintiffs are not specific in the complaint as to the nature of the warning that Novartis should have provided, even if we were to find that Novartis could not have modified the FDA-approved labeling of Elidel to include a warning about pediatric cancers, we would still be obliged to deny defendants' motion if a warning of some other type would have been permissible under the regulations. The FDA has made clear that warnings other than labeling changes, such as letters to health care professionals, are permissible and the labeling regulations do not bar them.

Perry v. Novartis Pharma. Corp., 456 F.Supp.2d 678, 686 (E.D.Pa.2006).

III. PAXIL IS NOT APPROVED FOR PEDIATRIC USE

The regulatory history as to the limited indications for which Paxil has been approved by the FDA is not disputed: On December 29, 1992, Paxil was approved by the FDA for the treatment of major depressive disorder in *adults*. In the years that followed, until Jake' suicide in September 2002, Paxil was approved for other indications, such as generalized anxiety disorder, panic disorder and post traumatic stress disorder. However, each approval was limited to the *adult* population.

The first time GSK sought approval for a pediatric indication was on April 11, 2002, when GSK submitted an Application to the FDA "proposing the use of Paxil to treat children and adolescents with major depressive disorder and obsessive compulsive disorder." PSUF 9, Exh. 18-19. GSK's pediatric application was never approved by the FDA – and, to date, the FDA has never approved Paxil for pediatric use.[9]

[9] In fact, as discussed in more detail in section IV(c), *infra*, after reviewing the pediatric data submitted by GSK, the FDA noted that GSK had manipulated the coding of adverse reports and, thus, requested additional data and analysis from GSK. Following multiple requests for additional data, the FDA received the unmanipulated data and, based on that data, concluded that Paxil posed a grave risk to pediatric patients. Thereafter, in October 2004, instead of approving Paxil for pediatric use, the FDA actually ordered GSK to issue a "black box" warning to warn the public and medical community about the association between Paxil and the increased risk of suicidality in children and adolescents.

IV. GSK KNEW THERE WERE RISKS ASSOCIATED WITH OFF LABEL PEDIATRIC USE OF PAXIL, THEREFORE, GSK HAD A DUTY TO WARN OF THOSE RISKS

A. GSK's Data Shows that Paxil Is Not Safe and Is Ineffective for The Pediatric Population

Prior to Jake Garrison's suicide, GSK conducted at least three placebo-controlled Paxil pediatric clinical trials dealing with depression: Study 329, 377, and 701. *See* PSUF 5-8, 12 and 18, Exh. 15, 21 and 30. Study 329, completed in February of 1998, showed that Paxil was not only ineffective for the treatment of depression in adolescents, but, more importantly, that Paxil was associated with an at-least six times increase in the risk of a suicide event for an adolescent taking Paxil as compared to placebo. PSUF 8, Exh. 15. Despite this, GSK concluded that "[t]his study supports that paroxetine is beneficial in treating adolescents with major depression although the support is derived mainly from secondary measures."[10] *Id.* Study 377, completed in May of 1998, and Study 701, completed in January of 2001, both concluded that Paxil was ineffective. ("No clinically or statistically significant differences were detected between paroxetine and placebo in either of the primary efficacy variables.") ("Analysis of the primary endpoint *provided no evidence* that paroxetine was more efficacious than placebo in the treatment of MDD in the pediatric population."). PSUF 12, Exhs. 21, 24. All three studies found Paxil ineffective in treating pediatric psychiatric disorders like depression and found that Paxil was associated with a nearly four times greater risk of suicidal events. PSUF 8, Exh. 17.[11]

---

[10] Primary outcome measures constitute the measures by which the overall success or failure of the treatment being studied is assessed. There are other measures, known as secondary outcome measures, which support or amplify the information from the primary measure or answer secondary questions.

[11] In 2006, GSK published the results of a re-analysis of pediatric clinical trial data (*id.)*, which confirmed the increased risk of suicidality in the depression trials, noting an almost four times increase in Paxil-associated suicidal events as compared to placebo. *See also* PSUF 79, Exhs. 17 and 29.

GSK reacted to the results of Studies 329 and 377 by hiding the data from the public. In October of 1998, a GSK manager wrote that:

> "the results of the [pediatric] studies were disappointing in that we did not reach statistical significance on the primary endpoints and the data do not support a label claim for the treatment of Adolescent Depression" **and that dissemination of this information to the public "would be unacceptable commercially**."

See PSUF 9-10, Exh. 19 (emphasis added). Internal memoranda show that GSK outlined a course of action "to effectively manage the dissemination of these data in order to minimize any potential negative commercial impact." This included publishing the sparse amount of positive data it could pull out of Study 329. PSUF 9-10, Exh. 18.

Not until 2004 did GSK admit that Paxil was associated with an increased risk of suicidality with pediatric patients and did not demonstrate efficacy for the treatment of adolescent depression. *See* PSUF 73, Exh. 75. GSK finally published its analysis of the suicidality risk associated with the pediatric use of Paxil in 2006, stating that "the incidence of suicide-related events was significantly greater in the paroxetine group compared to placebo." PSUF 79, Exh. 17.

B. GSK Falsely Promoted Paxil as Safe and Effective in Adolescents

Despite their dismal Paxil pediatric clinical trial results, GSK promoted Paxil for treating pediatric conditions, such as depression, claiming that Paxil was safe and effective. These marketing efforts utilized subtle but pervasive methods designed to create a false impression regarding Paxil's benefits and risks. GSK marketed Paxil through indirect channels such as seminars and journal publications, intending its "promotional" program to reflect an "educational" tone. *See* PSUF 15, 16 and 19.

For instance, GSK ghostwrote a misleadingly positive report about study 329. Although the study results were negative, as set forth above, GSK nevertheless transformed the "negative" trial into a "positive" trial and published it in July 2001 in the journal for the American Academy of Child and Adolescent Psychiatry. PSUF 19, Exh. 31. GSK touted Paxil as "generally well-tolerated in this

adolescent population, and most adverse events were not serious." *Id.* Soon after this article was published, GSK ordered reprints and began distributing the article at conventions through its sales force. GSK wrote to its sales representatives that: "**Paxil demonstrates REMARKABLE Efficacy and Safety in the treatment of adolescent depression**." PSUF 21, Exh. 33 (emphasis original). But nowhere in these materials did GSK tell its sales representatives that GSK itself had paid for the research, paid for the manuscript, and heavily contributed to the manuscript, or that the article made unsupported conclusions and assertions. When doctors contacted GSK about pediatric use of Paxil, GSK sent the ghostwritten article and asserted that Paxil "was superior to placebo by several assessment methods." PSUF 20, Exh. 32.

GSK's false pediatric promotional activities eventually caused the State of New York to file a Complaint against GSK for the fraudulent promotion of Paxil. See PSUF 64, Exh. 66. In its Complaint, the State of New York alleged that "GSK has misrepresented information concerning the safety and efficacy of [Paxil] for treating [major depressive disorder] in children and adolescents. GSK has allowed positive information about pediatric use of [Paxil] to be disclosed publicly, but has withheld and concealed negative information concerning the safety and effectiveness of the drug..." *Id.* at ¶ 4. GSK eventually reached a multi-million dollar settlement with the State of New York and, as part of the settlement, was required to publish truthful summaries of its pediatric clinical trials.[12] See PSUF 64, Exh. 67.

C. GSK Had A Duty to Warn of Any Known Risks And Side Effects Regarding Pediatric Use

New Jersey law, Pennsylvania law, and FDA regulations require drug manufacturers such as GSK to warn (either the prescribing doctor or the patient) about any known risks and side effects associated with their products; thus, GSK had an affirmative duty to warn of known risks associated

[12] The fact that, as a result of a *State* settlement, GSK published the truthful pediatric data – proves that GSK was not preempted (or prohibited) by federal law from publishing the truthful clinical trial data.

with the off-label pediatric use of Paxil. *Feldman v. Lederle Laboratories*, 479 A.2d 374, 388 (N.J. 1984) (*Feldman I*) (under New Jersey law, a manufacturer has a duty to warn of all potential side effects); N.J.S.A. 2A:58C-4 (same); *Perez v. Wyeth Labs., Inc*., 734 A.2d 1245 (N.J. 1999) (under New Jersey law, if manufacturer engages in direct to consumer advertisement, then manufacturer has a duty to warn the patient directly); *Incollingo v. Ewing*, 282 A.2d 206, 220 (Pa. 1971) (under Pennsylvania law drug manufacturer has duty to warn); and 21 C.F.R § 201.57(e) (2002); 21 C.F.R. § 201.80(e) (2008) (manufacturer has duty to warn whenever there is reasonable evidence of an association); *see also McNeil v. Wyeth*, 462 F.3d 364, 371 (5th Cir. 2006) (drug manufacturer has duty to warn regarding off label uses); *Perry v. Novartis Pharmaceutical*, 456 F. Supp. 2d 678, 681, n.6 & 687 (E.D. Pa. 2006) (same).

Under New Jersey law, compliance with legislative enactments and administrative regulations (such as the FDA's regulations) are not conclusive as to absence of defect or negligence.[13] *Feldman v. Lederle Labs., Inc.*, 592 A.2d 1176, 1197 (N.J., 1991) (*Feldman II*); *see also Rowe v. Hoffman-La Roche, Inc.*, 917 A.2d 767, 769 (N.J.,2007) ("New Jersey law, however, considers the FDA approval to have created only a rebuttable presumption of adequacy"); *Perez v. Wyeth Labs., Inc*., 734 A.2d 1245, 1259 (1999) (FDA approval is not conclusive as to absence of defective warning). Furthermore, New Jersey law provides that manufacturers have a *post-sale* duty to warn – that is, when a manufacturer fails to include a warning on a product, but subsequently learns, or should have learned, of the dangers associated with the product (or if the product contains an inadequate warning to address the later-discovered danger), the manufacturer owes a duty to warn of the dangers as soon as reasonably feasible. N.J. Stat.Ann. § 2A:58C-4; *Feldman I*, 479 A.2d 374, 388-389; *see also Dixon v. Jacobsen*, 637 A.2d 915, 922 (N.J. 1994). In the present case, Plaintiffs are claiming that GSK had a duty to warn the medical community regarding the life threatening risks

[13] In its companion motion for summary judgment (Docket No. 63), GSK advocates that this case should be governed by New Jersey law. See Docket No. 63 at p. 4.

associated with the "off label" pediatric/adolescent use of Paxil. The following facts are relevant to the inquiry:

- When the FDA first approved Paxil in 1992, it only approved Paxil for adult use (Plaintiff's Statement of Additional Undisputed Facts, "PSUF" 92)[14];
- Each Paxil indication approved by the FDA was for the adult population only (PSUF No. 91);
- As early as 1994, GSK became aware that Paxil was being prescribed to children and adolescents (PSUF 4);
- As outlined by Plaintiffs expert, Joel W. Hay, Ph.D, Paxil pediatric/adolescent sales accounted for a significant portion of GSK's sales of Paxil and totaled approximately 500 million dollars (See Hay Decl. at ¶ p. 4;
- Beginning in 1994, GSK began to conduct its first pediatric clinical trials (Study 329) for Paxil in an attempt to obtain pediatric approval, extended patent protection and greater market share (PSUF No. 5);
- Study 329 (pediatric study) was completed in 1998 and its results revealed that Paxil was not safe or effective (PSUF No. 8-10);
- Additional pediatric clinical trials conducted by GSK prior to Jake's suicide, demonstrated and confirmed that Paxil was not safe or effective for the pediatric population (PSUF No. 12, 18);
- GSK failed to disclose the findings of these studies to the medical community and failed to issue a warning;
- In lieu of disclosing the risks, GSK actively promoted Paxil for off-label pediatric use (PSUF No. 14-16), and;
- It was not until 2004 – almost two years after Jake's suicide – that GSK finally issued a warning (PSUF No. 62).

The foregoing factual synopsis reveals that, prior to Jake's suicide, GSK had knowledge of the pediatric risks and knew that Paxil was being prescribed to pediatric patients, yet failed to issue any warnings. GSK, therefore, breached its duties under New Jersey and Pennsylvania law. GSK's sole defense to its dereliction is conflict preemption – i.e., that it was purportedly prohibited from

[14] Plaintiffs' Undisputed Statement of Facts are filed concurrently herewith as a separate document.

issuing a pediatric warning because the "FDA had not concluded that Plaintiffs' proposed warning was scientifically supported." (GSK Motion at 23). Thus, GSK's contention is that (even though it knew or reasonably should have known that its data demonstrated that Paxil posed a risk to pediatric patients – which was subsequently confirmed by the FDA), it could not issue a warning until the FDA had substantiated the risk. Such a proposition flies in the face of more than a century of common law jurisprudence which has consistently held that the duty to warn lies with the manufacturer – not the FDA.

V. PLAINTIFFS FAILURE TO WARN CLAIMS ARE NOT PREEMPTED BY FEDERAL LAW

In its moving papers, GSK asks this Court to sweep aside decades of case law, ignore Congress's intent, and deprive injured citizens of legal recourse against pharmaceutical wrongdoers. In essence, GSK is asserting that it and other drug companies are immunized from tort liability common law claims for failure to warn under the FDCA. However, nothing within the FDCA would preempt a manufacturer from warning regarding risks associated with "off-label" pediatric use. The displacement of the state law protecting the health and safety of its citizens is not favored, and a party seeking preemption of state law bears a heavy burden of proof. GSK has not met its burden here. For the reasons detailed in Plaintiffs' Introduction, *supra*, and as set forth below, Defendants' motion should be denied.

A. There Is a Strong Presumption Against Preemption

The Supreme Court has identified three types of preemption: express preemption, field (or implied) preemption, and conflict preemption. *English v. General Elec. Co.,* 496 U.S. 72, 78-79 (1990). Express preemption exists when Congress clearly states its intent to preempt state law. *Id.* at 78. Field preemption arises where Congress has intended the federal government to occupy an entire field of regulation exclusively, leaving no room for states to supplement federal law. *Id.* at 79. To find field preemption, the Supreme Court "has looked for a specific [legislative] statement

of pre-emptive intent where it is claimed that the mere 'volume and complexity' of agency regulations demonstrate an implicit intent to displace all state law in a particular area." *Geier v. American Honda Motor Co.* 529 U.S. 861, 884 (2000). Conflict preemption may exist where " [1] it is impossible for a private party to comply with both state and federal requirements, or [2] where state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Sprietsma v. Mercury Marine*, 537 U.S. 51, 64 (2002) (internal quotations and citations omitted). As Defendants basically concede in their moving papers, express and field preemption do not apply here because Congress did not explicitly intend for the FDCA to displace state tort law; nor has Congress expressed any intent for the FDCA to govern drug safety exclusively. Therefore, conflict preemption is GSK's sole basis for alleging preemption in this case. (GSK's Motion at at pp. 1, 21).

There is a "basic presumption against pre-emption" because preemption upsets the balance of power between the federal government and the states as independent sovereigns. *Bates v. Dow Agrosciences LLC,* 544 U.S. at 439. The Supreme Court has emphasized: "[I]n areas of traditional state regulation, we assume that a federal statute has not supplanted state law unless Congress has made such an intention 'clear and manifest." *Id.* (citations omitted). An analysis of preemption begins with the purpose of Congress and "starts with the basic assumption that Congress did not intend to displace state law." *Maryland v. Louisiana,* 451 U.S. 725, 746 (1981). When a claim of preemption is asserted, the claim must overcome this presumption. *Rice v. Santa Fe Elev. Corp.,* 331 U.S. 218 (1947). It must be assumed that Congress did not intend to preempt state law addressing traditional areas of state concern, such as public health and safety. *Id.* at 230. The Third Circuit has similarly concluded that the there is a presumption against preemption. *Colacicco*, 521 F.3d 253, 2008 WL 927848 at * 8.

The presumption against preemption is especially strong if preemption would effectively deny plaintiff a remedy. The Supreme Court has stressed that a preemptive federal regulatory

scheme that would leave injured citizens without any federal or state recourse runs counter to the fundamental principles of justice. *Sprietsma v. Mercury Marine,* 537 U.S. 51, 64 (2002) (noting that it would be irrational for Congress to preempt common law claims that provide an important remedy for compensating accident victims); *Silkwood v. Kerr-McGee Corp.,* 464 U.S. 238, 251 (1984) (same). As the Supreme Court recently noted:

> The long history of tort litigation against manufacturers of poisonous substances adds force to the basic presumption against preemption. If Congress had intended to deprive injured parties of a long available form of compensation, it surely would have expressed that intent more clearly.

Bates v. Dow Agrosciences, LLC, 554 U.S. at 449. Because displacement of state law protecting the health and safety of their citizens is not favored, a party seeking preemption of state law bears a heavy burden of proof. In the context of FDA preemption, one court noted, "Congress knows how to enact FDA legislation that contains a preemption clause. Thus, the absence of any such clause with respect to prescription drugs demonstrates an implied intent not to preempt cases, such as this." *Cartwright v. Pfizer, Inc.*, 369 F. Supp. 2d 876, 885 (E.D. Tex. 2005). Recently, the Supreme Court similarly emphasized in their decision in *Riegel v. Medtronic, Inc.*, that unlike the express preemption provision enacted by Congress concerning medical devices, there is no similar provision in regard to prescription drugs. 552 U.S. ___, 128 S. Ct. 999 (2008). Justice Scalia commented upon this sharp distinction in addressing Justice Ginsberg's dissent:

> If, as the dissent believes, the preemption clause permits tort lawsuits for medical devices just as they are (by hypothesis) permitted for drugs and additives; and if, as the dissent believes, Congress wanted the two regimes to be alike; Congress could have applied the pre-emption clause to the entire FDCA. It did not do so, but instead wrote a pre-emption clause that applies only to medical devices.

Riegel v. Medtronic, Inc, 128 S. Ct. at 1009. This presumption against preemption (which applies to pharmaceutical product liability claims) is further enhanced in the context of a case that involves an "off-label" pediatric use. As outlined in greater detail below, this Court should deny GSK's motion, because there is no evidence that Congress intended to preempt failure to warn causes of

action regarding "off label" uses involving children. To the contrary, the FDCA was initially enacted primarily to protect children and to co-exist with common law rights of action. GSK cannot and does not overcome this strong presumption against preemption.

B. Prior to Jake Garison's Suicide, The FDA Never Considered Or Rejected A Paxil Suicide Warning Regarding Pediatric Suicidality

GSK's entire preemption argument rests on its *false* premise that "Plaintiffs here assert claims based on warnings which FDA has considered and rejected during the relevant time period." (Motion 25-26).[15] However, GSK fails to cite a single document that establishes that, prior to September 2002 (the "relevant time period"), the FDA "considered and rejected" a *pediatric* suicidality warning for Paxil. The fact is that, prior to this time, GSK never submitted a proposed pediatric warning to the FDA, thus, there was no warning for the FDA to consider or reject. In its memorandum of law (as well as the voluminous exhibits), GSK equally fails to reference a single document that demonstrates that, prior to Jake's suicide, the FDA actually reviewed and considered populations other than adults for the approved indications.

The reason GSK is unable to cite to a single piece of evidence is because, for each instance in which GSK sought approval for an indication for Paxil, it was adults, never children or adolescents. Accordingly, the FDA *never* received (and thus never reviewed) any significant Paxil safety and efficacy data regarding pediatric or adolescent use. When the FDA first approved Paxil in 1992, as well as with respect to the approval for all of the subsequent indications, the FDA limited its review and consideration solely to the safety and efficacy of Paxil for the *adult* population (i.e., the limited indication/population being sought for approval). GSK has not established that it submitted any safety or efficacy data pertaining to off-label pediatric uses when it sought approval for adult indications. There is not one single pre-September 2002 formal FDA document or written communication between the FDA and GSK that reflects that the FDA reviewed and considered a

[15] GSK admits that the "relevant time period" is "prior to September 2002." (Motion at 2.)

safety issue regarding any off-label indication as part of its approval of Paxil. Nor is there a document or written communication between the FDA and GSK that reflects that the FDA ever rejected a warning about an association between Paxil and suicide or suicidality within the pediatric/adolescent population.[16]

In its motion, GSK boldly claims that "Plaintiffs claim that GSK was required to warn of an association between Paxil and suicidality *even though FDA had reached the opposite conclusion*" (Motion at 29) (emphasis added). Yet GSK does not cite to a single document to support its proposition that, at any point in history, the FDA had reached a formal conclusion that Paxil is not associated with *pediatric* suicidality – the fact is that the FDA has never approved Paxil as being safe or effective for the *pediatric* population. The only formal conclusion the FDA has reached regarding the pediatric population is in agreement with Plaintiffs' contentions – that Paxil increases the risk of suicidality.[17] The FDA's refusal to require or prohibit a warning of this association prior to 2004, brings this case squarely within the Supreme Court's unanimous decision in *Sprietsma*, in which the Supreme Court held that the Coast Guard's decision not to impose propeller guards did not preempt plaintiffs' common law tort claims arising out of failure to install propeller guards on a boat engine. *Sprietsma v. Mercury Marine*, 537 U.S. 51 (2002).

---

[16] *See e.g., In re Zyprexa Products Liability Litigation*, 489 F.Supp.2d 230, 277 (E.D.N.Y.,2007) (denying preemption since the defendant manufacturer had never proposed and the FDA never rejected statements for inclusion in labeling relating to the increased risks of hyperglycemia and diabetes associated with the antipsychotic drug Zyprexa); *Perry v. Novartis Pharmaceutical*, 456 F. Supp. 2d 678 (E.D. Pa. 2006) (denying preemption since the FDA had never made a formal finding regarding a link between the use of the drug and increased cancer risks in children).

[17] Following its analysis of the GSK data, the FDA confirmed what GSK already knew (and should have known prior to Jake's suicide) – that Paxil increases suicidal thinking and behavior in children and adolescents. See PSUF 55-72.

C. The FDA Found That Paxil Was Not Safe or Effective for Pediatric Use And Therefore Never Approved GSK's Application for Pediatric Use

Curiously, GSK's Motion (as well as the accompanying Declaration of Barbara Arning , its director of U.S. Regulatory Affairs), recites all of the adult indication approvals Paxil has received, however, GSK neglects to mention that its one and only attempt at seeking approval for *pediatric use* was *never approved* by the FDA. It is thus necessary for Plaintiffs to correct the record and fill in the void that GSK has left on this issue.

The first time GSK sought approval for a pediatric indication was on April 11, 2002[18], when GSK submitted an Application to the FDA "proposing the use of Paxil to treat children and adolescents with major depressive disorder and obsessive compulsive disorder." See PSUF 9, Exh. 36. Prior to this time, GSK had *never* submitted any pediatric clinical trials data to the FDA for approval of pediatric indications. The pediatric Application included the three pediatric clinical trial studies dealing with depression -- Study 329, 377 and 701. As previously noted, all three of these Studies were completed (and analyzed) by GSK *years prior* to their April 2002 submission to the FDA.[19] Further, since the studies had been completed and analyzed prior to Jake's suicide, GSK knew (or should have known) that the studies demonstrated that Paxil was not effective and that it increased suicidality in the pediatric population.

Once the FDA received GSK's Pediatric Application, it began to conduct a review of the clinical trials GSK had submitted. Within a few months of receiving the data, in October 2002, the FDA noted (what GSK had already known) that these studies *failed to show efficacy*. See PSUF 28,

---

[18] Jake was originally prescribed Paxil on January 10, 2002, 10 mg for 15 days. He renewed his prescription on Jan 27, 2002, 20 mg for 30 days, after which he stopped taking Paxil. On April 8, 2002, he filled another prescription for Paxil, 20 mg for 30 days and thereafter quit taking Paxil again. On Sept. 11, 2002, Jake refilled his Paxil prescription, 20 mg, and consumed Paxil over an approximately 3-day period before committing suicide on September 14, 2002 (See PSUF 26-27).

[19] Study 329 and 377 had been completed in **1998**; and Study 701 was completed in January 2001.

Exh. 39 at pg. 2-3 (note, exhibit does not contain page numbers). With respect to safety, the FDA could not determine safety since GSK had manipulated and confounded the reporting of its adverse events. See PSUF 29, Exh. 39 at pg. 6 ("As previously noted, the sponsor's method of coding these events was potentially confusing, and thus additional information will be helpful for the purpose of definitively assessing the potential behavioral toxicity of paroxetine treatment in pediatric patients.") The FDA thus asked GSK for additional safety information. *Id.* GSK delayed 7 months and finally, in May of 2003, GSK submitted a "partial response" to the FDA's request for additional information.[20] *See* PSUF 39, Exh. 47 (June 3, 2003 Mosholder e-mail). Upon reviewing the supplemental information GSK had provided, FDA senior reviewer, Russell Katz, noted that, in its original pediatric Application, GSK had hidden the suicide adverse events "by various inappropriate coding maneuvers." *See* Exh. 47 (June 2, 2003 Katz e-mail). To hide the pediatric suicide adverse events, GSK had subsumed them under the vague heading of "emotional lability." *See* PSUF 30, and 39-43, Exh. 40 and 47. In his e-mail, Dr. Katz noted that the unmanipulated data shows that "almost all of these events [coded as "emotional lability"] related to suicidality." PSUF 41, Exh. 47. He further noted that "[GSK] has not proposed labeling changes, and makes a feeble attempt to dismiss the finding." *Id.* Thus, despite being caught with chocolate on its face and hands in the cookie jar, GSK continued to deny that a suicidal risk existed and refused to provide labeling changes or issue warnings. Not surprisingly, GSK's pediatric Application was never approved by the FDA – and, to date, the FDA has never approved Paxil for pediatric use. Rather, shortly after receiving GSK's unmanipulated data, the FDA issued a Public Health Advisory on June 19, 2003 stating:

[20] GSK's 7 month delay in producing the data to the FDA is curious given the fact that, on October 25, 2002 (within four days of receiving the FDA's request for additional information), GSK employee John Davies, issued a report in which he concluded that, based on his analysis of the pediatric data (which were available years prior to Jake's suicide), there was a statistically significant increased risk of suicidality in patients that were taking Paxil versus placebo. See PSUF 31, Exh. 41.

> The Food and Drug Administration (FDA) said today it is reviewing reports of a possible increased risk of suicidal thinking and suicide attempts in children and adolescents under the age of 18 treated with the drug Paxil for major depressive disorder (MDD). Although the FDA has not completed its evaluation of the new safety data, *FDA is recommending that Paxil not be used in children and adolescents for the treatment of MDD*. There is currently no evidence that Paxil is effective in children or adolescents with MDD, and Paxil is not currently approved for use in children and adolescents.

PSUF 48, Exh. 51 (emphasis added). Thereafter, the FDA eventually ordered GSK to place a black box warning in the Paxil label regarding pediatric suicidality. PSUF 74, Exh. 76. Within four months of receiving GSK's pediatric data, the FDA was able to conclude that Paxil was not effective in pediatric population; and within a month of receiving the safety data, the FDA was able to deduce that there was a potential problem and possible risk of pediatric suicidality which caused the FDA to issue the health advisory alert. GSK had this information years earlier (i.e., the 329 Study was completed in 1998) and had an obligation to issue warnings or at least forward the information to the FDA in a more timely fashion.

D. GSK Did Not Need to Seek the FDA's Permission Prior to Issuing A Warning

In its motion, GSK essentially contends that the duty to warn falls on the FDA and that, because the FDA had not made a finding regarding Paxil and pediatric suicidality, GSK did not have a duty (and was prohibited) from issuing any such warning. (GSK Motion at 23.) However, GSK's theory regarding its lack of duty is not supported by the FDA regulations. GSK, not the FDA, had the affirmative obligation to (a) conduct pharmacovigilance to detect new risks, (b) to inform the FDA when such risks are discovered, and (c) to issue appropriate warnings.

Contrary to GSK's contentions, the FDCA does not prevent pharmaceutical manufacturers from strengthening warnings on their products, nor does GSK need to obtain the FDA's permission or blessing before it is required to issue a truthful and scientifically valid warning. Importantly, FDA regulations expressly permit manufacturers to make certain labeling changes to increase safety *without prior approval*, simply by notifying the agency of the changes. 21 C.F.R. § 314.70(c).

Specifically, manufacturers may use the Changes Being Effected ("CBE") supplement process "to add or strengthen a contraindication, warning, precaution or adverse reaction." 21 C.F.R. § 314.70(c)(6)(iii)(A) (2008); 21 C.F.R. § 314.70(c)(2) (2002).[21]

Numerous courts have noted that FDA regulations regarding prescription drugs set forth "minimum standards" and have cited the CBE procedure for strengthening warnings as a basis for concluding that failure-to-warn claims are not preempted.[22] Indeed, as one court has observed:

> [t]o argue that, once the FDA approves a package insert, the defendant has no further duty to give an adequate warning creates an incentive for pharmaceutical companies to oppose all efforts by the FDA to secure clearer package inserts. If that were the case, drug manufacturers could avoid liability simply by resting on the formerly approved package insert (regardless of how long ago the approval occurred and how much information about the drug had changed) and resist all efforts to change it.

Globetti v. Sandoz Pharms. Corp., 2001 U.S. Dist. LEXIS 2391 at *29 (N.D. Ala. 2001).

The FDA itself has recognized repeatedly that "drug labeling does not always contain the most current information and opinion available to physicians about a drug because advances in medical knowledge and practice inevitably precede formal submission of proposed new labeling by

---

[21] In 2002 (the relevant time period), the regulations provided that a drug manufacturer can strengthen a warning prior to informing the FDA. 21 C.F.R. § 314.70(c)(2) (2002). The new regulation still allows the manufacturer to strengthen a warning but requires that the manufacturer *inform* the FDA 30 days prior to distributing the new warning. 21 C.F.R. § 314.70(c)(6)(iii)(A) (2008); see also *Colacicco*, 521 F.3d 253, 2008 WL 927848 at *3, n.4. Importantly, neither regulation requires a manufacturer to obtain the FDA's permission or approval prior to issuing the new warning.

[22] *See, e.g.*, *Tobin v. Astra Pharmaceutical Prods., Inc.*, 993 F.2d 528, 537-538 (6th Cir. 1993); *Hill v. Searle Labs.*, 884 F.2d 1064, 1068 (8th Cir. 1989); *In re Vioxx Prods. Liability Litigation*, 501 F.Supp.2d 776, 788-789 (E.D.La.2007); *In re Zyprexa Prods. Liability Litigation*, 489 F.Supp.2d 230, 275-278 (E.D.N.Y.2007); *Perry v. Novartis Pharma. Corp.*, 456 F.Supp.2d 678, 685-687 (E.D.Pa.2006); *Jackson v. Pfizer, Inc.*, 432 F.Supp.2d 964, 968 (D.Neb.2006); *Laisure-Radke v. Par Pharmaceutical, Inc.*, 426 F.Supp.2d 1163, 1169 (W.D.Wash.2006); *Witczak v. Pfizer, Inc.*, 377 F.Supp.2d 726, 732 (D.Minn.2005); *Zikis v. Pfizer, Inc.*, No. 04 C 8104, 2005 WL 1126909, *3 (N.D.Ill., May 9, 2005); *Cartwright v. Pfizer, Inc.*, 369 F.Supp.2d 876, 885-886 (E.D.Tex.2005); *Eve v. Sandoz Pharmaceutical Corp.*, No. IP 98-1429-C-Y/S, 2002 WL 181972, *1 (S.D.Ind., Jan.28, 2002); *Caraker v. Sandoz Pharmaceuticals Corp.*, 172 F.Supp.2d 1018, 1044 (S.D.Ill.2001); *Motus v. Pfizer, Inc.*, 127 F.Supp.2d 1085, 1087 (C.D.Cal.2000); *Collins v. SmithKline Beecham Corp.*, Case No. 0762, slip op., (Phil. Ct. Com. Pleas., March 11, 2008) (a copy of the *Collins* opinion is attached as Exh. 157).

the manufacturer and approval by the FDA." 44 Fed. Reg. 37434, 37435 (June 26, 1979). Therefore, FDA regulations place the burden on drug manufacturers to strengthen label warnings as soon as possible: "[T]he labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been established." 21 C.F.R. § 201.57(e) (2002); 21 C.F.R. § 201.80(e) (2008).

Finally, according to Dr. Richard Kapit, who was a safety reviewer at the FDA for 16 years and specialized in SSRI antidepressants, prior to September 2002, there was "reasonable evidence of an association between Paxil and suicidality in pediatric patients" and thus, GSK had an obligation to warn the medical community about this pediatric risk. See Kapit Decl. at ¶16. Further, as noted by Dr. Kapit, had GSK issued a pediatric suicidality warning in 2002, the FDA would not have, nor could it have, deemed the drug misbranded. *Id.* at ¶17.

E. GSK Had A Duty, At The Very Least, To Request FDA Approval For Additional Warnings

Notwithstanding the fact that, under FDA regulations, GSK could have voluntarily strengthened its warning without prior FDA approval (see e.g., 21 C.F.R. § 314.70(c)(6)(iii)(A) (2008); 21 C.F.R. § 314.70(c)(2) (2002)), Court's have held that, even if the manufacturer does not voluntarily enhance its warning, the manufacturer can additionally be found liable if it does not "at least request FDA approval of an additional warning" where appropriate. *Caraker v. Sandoz*, 172 F. Supp. 2d 1018, 1034-35 (S.D. Ill. 2001); *Perry v. Novartis Pharmaceutical*, 456 F. Supp. 2d 678 (E.D. Pa. 2006). As the *Caraker* Court noted:

> Until 1965, the FDA regulations applicable to drugs prohibited companies from adding warnings or other information without prior approval. These regulations were amended in 1965, allowing labeling changes related to safety to be "placed into effect at the earliest possible time," the goal of which was for drug manufacturers "to enable prompt adoption of such changes." 30 Fed. Reg. 993 (1965). Liability, irrespective of the Food, Drug, and Cosmetic Act ("FDCA"), may attach if drug manufacturers *do not at least request FDA approval of an additional warning as soon as* new hazards or elevated risk associations are discovered. These options for conveying additional risk information are not prohibited but encouraged. Because there is no indication that Congress and the FDA have attempted to impede what the FDA has

> referred to as the "sophisticat[ed] and complex [ ] private tort litigation in the United States," this Court is right to interpret the FDA standards as minimum ones and to find that drug manufacturers still have a duty to timely disclose new known risks to learned intermediaries, especially because any other interpretation would run contrary to what appears to be an intent to preserve these tort remedies.

Caraker v. Sandoz, 172 F. Supp. 2d 1018, 1034-35 (S.D. Ill. 2001) (emphasis added). In this case, Plaintiffs seek redress from a Defendant who was well aware of "reasonable evidence of an association" between a serious hazard, i.e. suicidality, posed to the pediatric and adolescent population ingesting Paxil, yet GSK failed to provide any warnings of this serious risk.

This case is similar to *Perry v. Novartis Pharmaceutical*, 456 F. Supp. 2d 678 (E.D. Pa. 2006). Both concern manufacturers who illegally promoted their drug for off-label indications, despite knowledge that the drug posed significant risks. In *Perry*, following the FDA's 2001 approval of Elidel (a prescription drug to treat atopic dermatitis for short-term or intermittent long-term use in non-immunocompromised patients at least two years of age), it was discovered that the drug was being used off-label by patients under the age of two. *Id.* at 681. The plaintiff, *Perry*, had been diagnosed with lymphoma after he was prescribed and treated with the drug Elidel. *Id.* at 679, 680. At the time Perry was prescribed Elidel, the FDA had "made no finding regarding a link between use of the drug and increased cancer in children and no statute or regulation prevented [the manufacturer] from adding the warning." *Id.* at 687. The District Court denied preemption, finding that "state law may require a manufacturer to at least seek FDA approval for the addition of a new warning where there has been no determination by the agency whether there is a link between the adverse health effect to be warned against and the use of the drug." *Id.* at 685

Here, like the manufacturer in *Perry*, GSK failed in its duty to seek to strengthen the warning for Paxil regarding the risks of pediatric suicidality. Accordingly, similar to *Perry* and *Caraker*, preemption is not warranted in the instant case.

F. The FDCA Does Not Preempt Failure to Warn Claims Regarding Off-Label Pediatric Uses

To date, no appellate court – federal or state – has ever held that the FDA's drug approval authority or its authority over drug labeling preempts a state-law tort suit premised on the manufacturer's failure to issue a warning related to "*off label*" uses. As previously discussed, in approving a drug application, the FDA does not analyze off-label uses, such as pediatric use – and the FDA is not given any pediatric clinical trial data to review in those approved drug applications. In light of the fact that this is an off-label use, it is difficult to imagine how the FDCA could possibly prohibit a manufacturer from issuing truthful warnings or precautions regarding off-label use. Tellingly, pharmaceutical manufacturers rarely raise preemption in an off-label failure to warn case. Counsel's research has uncovered only a few cases in which a pharmaceutical manufacturer sought preemption in an off-label failure to warn case. The only Court to issue a *published* decision on this specific issue found that off-label use is not preempted. *See e.g.*, *Utah v. Eli Lilly and Co.*, 509 F.Supp.2d 1016, 1025 (D.Utah, 2007) (FDCA does not preempt claims based on off-label sales).

In fact, Plaintiffs are only aware of one district court that has ever found preemption in an off-label use case, and that court's unpublished holding was limited to the facts of the case. *O'Neal v. SmithKline Beecham Corp.,* 2008 WL 275782 (E.D.Cal., Jan. 30, 2008).[23] The case is currently on appeal before the Ninth Circuit. *O'Neal* was a Paxil case in which an adolescent committed suicide in February 1997. The Eastern District of California, in an *unpublished* decision, held that plaintiffs' claims were preempted since GSK had not completed its pediatric clinical trial (Study 329) until 1998 – and, thus, prior to the completion of the pediatric clinical trial, GSK did not have a duty to warn. *O'Neal,* 2008 WL 275782 at *12. In this case, however, Jake Garrison committed suicide in 2002 and, by that time, GSK had completed *three* pediatric clinical trials which

[23] Tellingly, other than the *O'Neal* case, GSK does not cite to any other cases in which a court has found preemption in an off-label failure to warn case.

demonstrated that Paxil was neither safe nor effective. Thus, GSK had reasonable evidence to support a pediatric warning prior to September 2002. Accordingly, the facts of this case are distinguishable from the *O'Neal* case.[24]

Finally, the FDCA was initially enacted primarily to protect the health and safety of children. (See discussion infra in Section V.(I.)). The FDCA regulation specifies that a drug shall be deemed misbranded if its labeling does not bear "adequate warnings against use...*by children* where its use may be dangerous to health." 21 U.S.C § 352(f). Thus, contrary to GSK's assertion, it is the lack of pediatric warning that causes the drug to be misbranded -- not the inclusion of a pediatric warning. Accordingly, as mandated by 21 U.S.C. § 352(f), GSK should have included a warning regarding pediatric suicidality – especially since GSK had reasonable evidence of an association between Paxil and pediatric suicidality. Kapit Decl., at ¶16; see also PSUF 9-10.

G. The New Jersey Supreme Court Has Found That Such Cases Are Not Preempted

In its accompanying motion for summary judgment (Docket No. 63), GSK has advocated that this case should be governed by New Jersey law. Curiously, though, nowhere in its preemption motion does GSK advise the Court that the New Jersey Supreme Court has found that failure to warn

---

[24] Aside from being distinguishable, the *O'Neal* Court also committed a number of legal errors, which are the subject of an appeal. See Plaintiffs' Notice of Appeal, Exh. 159. Significantly, contrary to established legal precedent, the Court held that a pharmaceutical company does not have a duty to warn until it receives the "final results" of its post market clinical trials, and that adverse event reports showing serious side effects cannot create a duty to warn. *O'Neal,* 2008 WL 275782 at * 12. This conflicts with a number of previous opinions which have uniformly held that adverse event reports trigger a duty to warn. *See e.g.*, *McNeil v. Wyeth,* 462 F.3d 364, 370-71 (5th Cir. 2006)(in the context of off-label uses, manufacturers are permitted and required to "change their labels and warn physicians of side effects *based on simple case reports*, not actual studies showing causation."); *Benedi v. McNeil-P.P.C., Inc*., 66 F.3d 1378, 1387 (4th Cir. 1995) (adverse case reports can give rise to a duty to warn); *see also Hoffman v. Sterling Drugs, Inc.*, 485 F.2d 132, 146 (3rd Cir. 1973) (adverse event reports reported in journal articles and obtained from physician letters should have prompted the manufacturer to issue a warning); *Golod v. Hoffman La Roche*, 964 F.Supp. 841, 855-856 (S.D.N.Y. 1997) (adverse event reports give rise to duty to warn); *Feldman v. Lederle Laboratories*, 479 A.2d 374, 387 (N.J. 1984) (manufacturer has duty to warn based on adverse event reports reported to manufacturer).

claims are not preempted by the FDCA. *Feldman v. Lederle Labs., Inc.*, 592 A.2d 1176, 1197 (N.J., 1991) (*Feldman II*).[25]

In *Feldman II*, a pediatric patient suffered tooth discoloration of both her baby teeth and permanent teeth after taking an antibiotic for three years.[26] Plaintiffs filed a failure to warn claim alleging that the manufacturer knew or should have known of the discoloration risk, but failed to warn. The manufacturer argued that the claims were preempted by the FDCA. Specifically, the manufacturer asserted that, at the relevant time period, it had sent a letter to the FDA proposing to issue a warning regarding tooth discoloration. *Feldman II,* 592 A.2d at 1180. The FDA initially responded to the request by stating that the FDA had not reached a formal decision on the issue. *Id.* The FDA thereafter required the warning for some antibiotics, but specifically excluded the defendant's drug, Declomycin. *Id.* Through various correspondence between the FDA and the manufacturer, the FDA continued to pass on the proposed warning. *Id.* Approximately a year after the initial proposed warning request (and after the plaintiff had ceased using the product), the FDA authorized the warning. *Feldman II,* 592 A.2d at 1181. Based upon these facts, the manufacturer argued that the plaintiffs failure to warn claim was preempted because, during the relevant time period, the FDA had specifically not authorized the proposed warning. The Supreme Court of New Jersey disagreed and concluded that the correspondence between the manufacturer and the FDA did not support a finding of preemption. *Feldman II,* 592 A.2d at 1192. The Court went on to conclude that the FDA's "determination" in the correspondence "was really a non-decision-namely, that the evidence was not yet unequivocal or 'substantial' as defined by the FDCA. It does not reflect a

---

[25] The Pennsylvania Supreme Court has yet to address the issue of preemption in this context, however, just recently, a lower court in Pennsylvania found that a Paxil failure to warn claim would not be preempted. *Collins v. SmithKline Beecham Corp*., Case No. 0762, slip op., (Phil. Ct. Com. Pleas., March 11, 2008) (a copy of the *Collins* opinion is attached to the Declaration of Bijan Esfandiari as Exhibit 157).

[26] The patient took the antibiotic from infancy until the age of three. *Feldman II*, 592 A.2d at 1179.

carefully considered risk-benefit analysis of Declomycin's utility such that it should shield [the manufacturer] from plaintiff's claims for the harm caused by Declomycin." *Feldman II,* 592 A.2d at 1196. The New Jersey Supreme Court thus held that the plaintiffs' claims were not preempted.[27]

Contrary to the manufacturer in *Feldman,* who was actively communicating with the FDA regarding the risks and had actually proposed a warning, GSK in this case never even proposed a warning to the FDA and did not submit its clinical trials data to the FDA until four years after it was completed (i.e., Study 329). GSK, in fact, engaged in the opposite – it promoted the commercially positive data from the pediatric clinical trials while managing "dissemination of these data in order to minimize any potential negative commercial impact..." PSUF 9, Exh. 18. Thus, given that no preemption was found under the facts of *Feldman* (which involved a much more diligent manufacturer), there certainly should be no preemption in the present case. Similar to the facts of *Feldman*, during the relevant time period, the FDA had not yet made a decision regarding the pediatric risks associated with Paxil, nor had the FDA completed a pediatric risk-benefit analysis to warrant a finding of immunity – thus, like the *Feldman* case, this Court should similarly conclude that the Plaintiff's claims are not preempted.[28]

H. The Authorities Cited By GSK In Support of Its Preemption Defense Are Not Applicable To the Facts of This Case

To support its preemption argument, GSK relies particularly on three recent developments: (1) the Third Circuit's recent opinion in *Colacicco*; and (2) certain pronouncements made by FDA lawyers in *amicus* briefs in unrelated cases, in particular the *amicus* brief filed in the *Kallas* case;

---

[27] Recently, a New Jersey Appellate Court reconfirmed the holding of *Feldman* and held that "[e]xisting New Jersey precedent clearly supports the conclusion that the FDCA does not preempt state tort remedies under theories of express conflict or implied preemption in this duty-to-warn context." *McDarby v. Merck & Co.*, A.2d, 2008 WL 2199871, * 21 (N.J. App. Div., May, 29, 2008) (relying upon *Feldman II*, 592 A.2d at 1197).

[28] Notably, the *Feldman* Court also opined that, even if the FDA had not permitted a substantiated warning, a responsible manufacturer should cease production or marketing of the drug or press the FDA for additional warnings. *See Feldman*, *supra*, 592 A.2d at 1195-1196.

and (3) the FDA's 2006 "Preamble," as well as a 2008 Proposed New Rule by the FDA. However, none of these authorities or developments warrant a finding of preemption under the facts of this case.

i. The *Colacicco* Opinion Was Limited to *Adult* Suicidality Cases

GSK boldly (yet erroneously) claims that "[t]he Third Circuit's recent decision in *Colacicco v. Apotex, Inc*., is dispositive of Plaintiffs' claims." (Motion at 22.) The Court in *Colacicco* was clear to note that, when it comes to preemption, "[o]ne size does not fit all." *Colacicco*, 521 F.3d 253, 2008 WL 927848 at *1. Despite this limitation, GSK attempts to fit a pediatric "off label" use case within the limited confines of *Colaccico*.

The *Colacicco* decision clearly is not dispositive of this case since *Colacicco* limited its ruling to adult suicidality and did not address pediatric off-label use. In fact, throughout the opinion, the Third Circuit is cautious to note that its decision concerns the association between SSRIs (such as Paxil) and *adult* suicidality. *Colacicco v. Apotex Inc*., 521 F.3d 253, 2008 WL 927848, * 13-15 (3rd Cir. 2008). The Court also noted that, in June 2003 and October 2003 (upon receipt and analysis of GSK's pediatric data), the "FDA issued a Public Health Advisory regarding increased suicidality in pediatric users of antidepressants." However, the FDA did not issue any health advisory warnings regarding adults at that time. *Colacicco*, 521 F.3d 253, 2008 WL 927848 at * 13.[29] The Court concluded that, since (a) Paxil had been approved for adult use; (b) the FDA had approved multiple indications for adult use; (c) that the FDA, after reviewing the applicable studies, had purportedly stated that Paxil was not associated with adult suicidality, and (d) the FDA had never required (and had purportedly rejected) an adult suicide warning, therefore, plaintiffs adult failure to warn claim conflicted with the FDA's regulatory actions. *Colacicco*, 521 F.3d 253, 2008 WL 927848 at * 13-

[29] The June 19, 2003 and October 27, 2003 FDA Public Health Advisory regarding the increased risk of pediatric suicidality are attached to the Declaration of Bijan Esfandiari as Exhs. 51, 58 and 151.

14.

However, contrary to the facts of *Colacicco*, in this case, Paxil has never been approved for pediatric use; and, unlike adult cases, the FDA has never rejected a pediatric suicide warning and has, in fact, found that Paxil *is associated* with pediatric suicidality. Further, the *Collacico* Court based its finding of preemption on the grounds that "[t]he FDA clearly and publicly stated its position *prior to* the prescriptions and deaths at issue here." *Colacicco*, 521 F.3d 253, 2008 WL 927848 at 14 (emphasis added). However, in this case, prior to September 2002 (Jake's prescription and death), the FDA had *never* publicly stated its position on the issue of pediatric suicidality. Thus, the holding in *Colacicco* is not applicable to a pediatric off label use case. Finally, to abolish all doubts about the limitations of its ruling, the *Colacicco* Court noted:

> Therefore, we need not decide whether preemption would be appropriate under different facts-such as where the FDA had not rejected the substance of the warning sought or where the FDA only stated its position after a lawsuit had been initiated-or under the broader theories of preemption argued by the parties. Thus, we do not decide whether the FDA's mere approval of drug labeling is sufficient to preempt state-law claims alleging that the labeling failed to warn of a given danger, whether FDA approval of drug labeling constitutes minimum standards in the absence of the FDA's express rejection of a specific warning..

.
Colacicco, 521 F.3d 253, 2008 WL 927848 at 14.

The facts of the present case (off-label pediatric use) come within the parameters of the "different facts" under which the *Colacicco* Court stated preemption would not apply. Therefore, GSK's reliance upon *Colacicco* is misguided.[30]

[30] It is important to note that, when *Colacicco* was decided, the Paxil case came to the Third Circuit on a motion to dismiss -- thus, the Third Circuit did not have before it the internal GSK data and documents that establish that, even with respect to adult patients, the unmanipulated GSK data showed that adult patients were eight times more likely to commit suicide. See PSUF 112; see also *Colacicco*, 521 F.3d 253, 2008 WL 927848 at *12 n.13. On a developed record, the outcome of the *Colacicco* case may have been quite different. *See also*, Plaintiffs' PSUF 140-166, Exhs. 60-61, 95, 101, 106 and 122-138.

ii. The FDA *Amicus* Briefs Are Inadmissible, Irrelevant And Do Not Relate To Pediatric Paxil Suicidality

As discussed in greater detail in Plaintiffs' accompanying Motion to Strike, the *Kallas* brief (and other FDA *amicus* briefs) are inadmissible for a host of reasons, including but not limited to (a) hearsay and (b) relevance. While the Court may take judicial notice of the fact that the briefs were filed in other cases, the "facts" contained therein cannot be accepted as true. *Kramer v. Time Warner, Inc.*, 937 F.2d 767, 774 (2d Cir.1991) (even if the Court could take judicial notice of the fact that the briefs were filed in other cases, the "facts" contained therein cannot be accepted as true).[31] Thus, the statements of FDA counsel contained in the *amicus briefs* all constitute hearsay, since they are out of court statements offered for the truth asserted therein.[32] As to relevance, the *Motus* and *Colacicco amicus* briefs concerned adult use of an SSRI, thus, they do not apply to this case. The only *amicus* brief that discussed off-label pediatric use was the *Kallas* brief. However, the *Kallas* brief did not relate to Paxil, but rather concerned the drug Zoloft. This fact is important since, as the FDA notes in the brief, prior to the time the patient in the *Kallas* case committed suicide, the FDA had reviewed the Zoloft pediatric data and had purportedly made a determination that there were no issues/risks with suicidality. (*Kallas Amicus* Brief at 18-19.) On the other hand, prior to Jake Garrison's suicide, the FDA had not completed its review of the Paxil suicide data and *had not made any* determinations as to Paxil's safety. To the contrary, a month after Jake's suicide, the FDA

---

[31] GSK has not attached any certified copies of the briefs but merely has provided an unauthenticated copy of the brief the FDA filed in the Third Circuit *Colacicco* case (See Exh. 2 to Howard Decl); and, GSK has provided Westlaw cites to the other three FDA amicus briefs: FDA *Kallas Amicus* Brief, 2005 WL 2559710 (D.Utah 2005); FDA *Motus* Brief, 2002 WL 32303084 (9th Cir. 2002); and FDA *Colacicco* Brief (filed in District Court), 2006 WL 1724170 (E.D.Pa. 2006). While Westlaw citations are appropriate for judicial opinions, it is not clear if Westlaw citations are sufficient to authenticate third-party briefs filed in other cases. Thus, this raises some concerns regarding the authenticity of the briefs. See e.g., Fed.R.Evid., Rule 902(1), (2) & (4) (requiring public records to bear a seal or be properly certified by a custodian of record).

[32] Further, the FDA has not filed any briefs in this case. In contrast, in the *Colacicco* case, the FDA filed an *amicus* brief both in the District Court as well as the Third Circuit.

informed GSK that it could not make a safety assessment since GSK had manipulated the coding of the adverse event reports (causing the FDA to ask for additional information from GSK) – thus, unlike the *Kallas* case, prior to Jake's suicide, the FDA had not made a determination that Paxil was safe and free of suicide risks. *See Kallas Amicus* Br. at 9 & 19. Further, as noted in the *Kallas Amicus* brief, the trigger that alerted the FDA to the potential risk of pediatric suicidality was the "FDA's concerns regarding the coding of the Paxil data in the New Drug Application supplement for pediatric Major Depressive Disorder for that drug [Paxil]," which "triggered a series of events that led the agency to conclude that there is reasonable evidence of an association between SSRIs and suicidality in children and adolescents." *Kallas Amicus* Br. at 19. Therefore, as the FDA brief acknowledges, the data from Paxil was what triggered the alarm regarding pediatric suicidality risks – and as previously noted, GSK was in possession of this data years prior to Jake's suicide, yet failed to timely release the information to the public or the FDA.

Even if the *amicus* briefs are deemed relevant, they should not be considered by this Court since there is no ambiguity in either the FDCA or FDA's regulations which require interpretation by the FDA. Here, the statutes and regulations which are being interpreted by the FDA in these briefs are 21 U.S.C. § 355 (prohibiting false and misleading statements in product labeling); 21 C.F.R. § 201.80(e) (requiring stronger warning when there is reasonable evidence of an association between a drug and a serious hazard); and 21 C.F.R. § 314.70(c)(6)(iii) (allowing manufacturers to strengthen a drug's label without prior FDA approval). The FDA does not assert, nor does GSK argue, that any of these statutes or regulations are ambiguous. In fact, they are not.

Earlier this year, the Supreme Court refused to give *any* deference to the *amicus* briefs the FDA had filed in a case on the grounds that the statutes at issue were not ambiguous and, thus, it was not necessary to rely upon the FDA's views. *Riegel v. Medtronic*, 128 S.Ct. 999, 1009 (2008); see also *Levine v. Wyeth*, __ A.2d __, 2006 WL 3041078, ¶31-34 (Vt. Oct. 27, 2006). Accordingly, the

FDA's statement is neither an authoritative interpretation of an ambiguous statutory provision entitled to deference, nor a persuasive policy statement entitled to much respect. *Id.*

Finally, even if the *amicus* briefs are considered by this Court, they should not be afforded much deference since they merely represent the litigation position of the agency. In fact, the Third Circuit, in analyzing the amount of deference to give to the brief filed in that case, only gave the briefs *Skidmore* deference[33] – which is the weakest deference available. *Colacicco*, 521 F.3d 253, 2008 WL 927848 at 17, n. 21.

iii. Even Under the Recent FDA Preamble, Plaintiffs' Claims Would Not Be Preempted Because GSK Had Knowledge of A Substantiated Reasonable Risk And The FDA Never Rejected A Pediatric Suicidality Warning Prior to Jake Garrison's Death

Throughout its Motion, GSK liberally relies upon the 2006 FDA Preamble 71 Fed.Reg. 3935 (Jan. 24, 2006) ("Preemble") and a recent FDA *proposed* rule 73 Fed. Reg. 2848 (Jan. 16, 2008) ("Proposed Rule"). Plaintiffs will not go into detail on all of the issues related to the controversial Preamble, which, for the first time in 70 years, purports that the FDCA establishes both a "floor and a ceiling." 71 Fed.Reg. 3935 (GSK Motion at 26). But, suffice it to say, the Preamble, which is not binding (see 21 C.F.R. § 10.85(d)(1))[34] is the polar opposite of policy conclusions the FDA recently reached, in which the FDA stated:

> FDA does not believe that the evolution of state tort law will cause the development of standards that would be at odds with the agency's regulations. FDA's regulations *establish the minimal standards* necessary, but were not intended to preclude the states form imposing additional labeling requirements."

63 Fed.Reg. 66378, 66384 (1998). Ironically, even in the 2006 Preamble (and the portion quoted by GSK in its motion), the FDA concedes that *only* those additional warnings that "are

---

[33] *Skidmore* deference refers to U.S. Supreme Court case in which the Supreme Court held that agency interpretations contained in statements that "lack the force of law" are "entitled to respect" only to the extent they have the" power to persuade". *Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944); *see also Colacicco*, 521 F.3d 253, 2008 WL 927848 at 17, n. 21.

[34] *See also Perry*, 456 F.Supp.2d at 683 (noting that the Preamble is not binding).

unsubstantiated or otherwise false or misleading" will subject a manufacturer to liability under the FDCA. 71 Fed.Reg. at 3935 (GSK Motion at 26). In other words, the Preamble does not impose a "ceiling" or restrictions on *truthful*, substantiated risk information – precisely the type of warnings Plaintiffs advocate in the instant action. Finally, and most importantly, the Preamble deals mainly with "specific warnings that FDA had specifically considered and rejected as scientifically unsubstantiated." 71 Fed.Reg. at 3934; *see also Perry*, 456 F.Supp.2d at 683. In this case, it is undisputed that GSK never proposed a pediatric warning to the FDA and the FDA never rejected a pediatric warning prior to Jake's suicide.

The Supreme Court, in the upcoming case of *Wyeth v. Levine*[35] will have an opportunity to address what effect to give to the Preamble.[36] However, as outlined above, even if the Preamble is given any weight, it will not change the outcome of this case because, under the facts of this case, prior to Jake's suicide, GSK knew, through its pediatric clinical trials, that there was a substantiated "reasonable evidence of an association of a serious hazard." Thus, even under the reasoning of the Preamble, GSK had a duty to warn of the substantiated risks. 71 Fed.Reg. at 3935; 21 C.F.R. § 201.57(e); 21 C.F.R. § 201.80(e) (2008); 21 C.F.R. 314.70(c)(6)(iii)(A) (2008); *see also Levine v. Wyeth*, ___ A.2d. __, 2006 WL 3041078 at ¶30-32 (noting that, even under the 2006 Preamble, there would be no direct and positive conflict between state and federal law), *cert granted*, 2008 WL 161474 (Jan. 18, 2008); *Perry*, 456 F.Supp.2d at 683-684.

---

[35] *Wyeth v. Levine*, No. 06-1249, __ U.S. __, 2008 WL 161474 (Jan. 18, 2008)

[36] In *Levine*, the Supreme Court of Vermont noted that there is tension as to whether the Preamble should be entitled to any deference but skirted the issue by firmly concluding that the plaintiffs' failure to warn claim "did not pose a direct and positive conflict with federal law".*Levine v. Wyeth*, ___ A.2d. __, 2006 WL 3041078 at ¶28. The Second Circuit has rejected The Preamble, and held that "an agency cannot supply, on Congress's behalf, the clear legislative statement of intent required to overcome the presumption against preemption." *Desiano v. Warner-Lambert & Co.*, 467 F. 3d 85, 97, n.9 (2d Cir. Oct. 5, 2006) (citing *Alexander v. Sandoval*, 532 U.S. 275, 291 (2001) ("Agencies may play the sorcerer's apprentice but not the sorcerer himself.")). The Third Circuit in *Colacicco* gave the Preamble only limited *Skidmore* deference – the weakest deference available. *Colacicco*, 521 F.3d 253, 2008 WL 927848 at 17, n. 21.

With respect to the FDA Proposed Rule (73 Fed.Reg. at 2849), which seeks to amend 21 C.F.R. 314.70(c), the Proposed Rule *has not been approved* and thus has no bearing on this case.[37] Further, members of Congress have written letters to Andrew C. von Eschenbach, Commissioner of the FDA, voicing concerns over the proposed rule, which the House letter stated "seeks to substantively amend current regulations."[38] See PSUF 99-100, Exh. 88-89. Finally, even if the proposed rule is passed, it cannot impact this litigation, since GSK's conduct must be measured by the regulations applicable at the time relevant to this litigation (i.e., September 2002). *See Colacicco*, 521 F.3d 253, 2008 WL 927848 at * 3, n. 2 (noting that manufacturers' conduct must be measured by the regulations applicable "[a]t the times relevant to this litigation"); *Perry*, 456 F.Supp.2d at 684 ("The FDA cannot retroactively absolve [a manufacturer] of a duty it may have owed the [plaintiff] in 2003").

I. Plaintiffs' Claims Would Not Interfere With the FDA's and Congress' Objectives of Providing Safe and Effective Drugs to American Consumers.

GSK contends that Plaintiffs' claims would interfere with the purposes of FDA regulations (Motion at 29) and that their claims stand as an obstacle to Congress' intent (Motion at 31).

---

[37] The proposed rule would set a higher standard as to when a manufacturer is required to issue a warning. The current regulation states that a manufacturer must issue new warnings as soon as there is "*reasonable evidence of an association*"of a risk. 21 C.F.R. § 201.80(e), emphasis added. The proposed rule would modify this requirement by requiring new warnings only when there is a evidence of a "*causal association*" – thus setting a higher threshold before warnings are required. 73 Fed.Reg. at 2850, emphasis added.

[38] The House of Representatives' letter noted their intention that state law claims remain viable: "We included language in the FDAA to preserve the status quo, allowing the FDA and state remedies to remain complementary and necessary safeguards to protect American families. However, we believe the FDA's proposed rule directly contradicts this language by reversing a drug manufacturer's obligation to warn of new risks and hazards and, instead, allowing these companies to claim immunity from liability because they had no duty to warn. This is contrary to congressional intent and to the FDA's mission to protect the public health." PSUF 99, Exh. 88. The other Congressional letter questioned the motivation behind the proposed rule, stating: "[The] proposal has no purpose other than to shore up the industry's legal arguments for avoiding liability. Indeed, the proposal fails to identify a single problem associated with these regulations that would warrant a modification much less a public health threat of such magnitude as to put issuing the proposal at the top of the FDA's priority list." PSUF 100, Exh. 89.

However, in making this argument, GSK completely ignores the FDA's *primary* objective -- which is to protect consumers, and in particular children. See e.g., *United States v. Dotterweich*, 320 U.S. 277, 282 (1943); see also *62 Cases, More or Less, Each Containing Six Jars of Jam v. United States,* 340 U.S. 593, 596 (1951) (stating that Congress intended the FDCA to protect consumers who are unable to protect themselves). As set forth more fully below, Plaintiffs' claims actually serve to further the FDA's and Congress's interests and objectives by promoting drug safety for children.

i. The FDCA Was Enacted To Ensure the Health and Safety of Children

The history of the FDCA as well as its predecessor, the Pure Food and Drugs Act of 1906, demonstrate that Congress' primary motivations for enacting the statute was to protect the health and safety of the public and in particular *children*.

When a series of deadly reactions to a diphtheria vaccine in 1902 killed children in Camden, New Jersey, Congress combined the concerns about adulterated foods and unsafe drugs to pass the Biologics Controls Act of 1902, ch. 1378, 32 Stat. 728 (1902). Congress followed with the Pure Food and Drugs Act of 1906, which prohibited the manufacture of any drug that was "adulterated or misbranded."[39] *See* The Pure Food and Drugs Act of 1906, ch. 3915, 34 Stat. 768 (1906); *see also* Sue McGrath, *Only A Matter Of Time: Lessons Unlearned at the Food and Drug Administration Keep Americans at Risk*, 60 Food & Drug L.J. 603, 604 (2005).

In 1938, when reports revealed that the "miracle" drug Elixir Sulfanilamide (used to combat streptococcal sore throat) had caused hundreds of children to be poisoned and had killed more than 100 people, mostly children, Congress took action and finally enacted the Food, Drug, and Cosmetic Act of 1938, ch. 675, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. § 301 et seq.). *See*

[39] The 1906 Act authorized regulations to ensure that pharmaceutical manufacturers did not adulterate or mislabel their products but did not deal with the safety or effectiveness of drugs.

also McGrath, *supra,* at 609. The Act required that drug manufacturers provide proof that their products were safe before they could be marketed.[40] *See id.*

In 1955, some children vaccinated with polio vaccine contracted paralytic polio causing fifty-one cases of paralysis and ten deaths. The problem was traced to one manufacturer who apparently did not properly inactivate the virus used to make the vaccine. This incident and others like it led to increased factory inspections and testing of the safety of products before their release to the public. Gary E. Gamerman, *Regulation of Biologics Manufacturing: Questioning the Premise*, 49 Food & Drug L.J. 213, 213 (1994). Finally, the thalidomide incident (a sleeping pill that caused world wide birth defects) in the early 1960s led to the passage of the Kefauver-Harris Amendments, which required that drugs be proven to be safe and effective before release. See Drug Amendments of 1962, Pub.L. No. 87-781, § 102, 76 Stat. 780, 781 (1962) (codified as amended at 21 U.S.C. § 355 (2002)); see also McGrath, *supra,* at 609. It is thus evident that, from its inception, the FDCA and similar Acts of Congress were enacted to protect the health and safety of the public, and in particular children and adolescents. In fact, as illustrated *supra*, the major revisions and amendments to the FDCA (i.e., inclusion of more stringent regulations) were a direct reaction to a health and safety crisis affecting the children of our nation. It is for this reason the FDCA specifically provides that all drugs should have "adequate warnings against use...*by children* where its use may be dangerous to health." 21 U.S.C. § 352(f) (emphasis added).

Despite this robust history, GSK stands before this court and proclaims that it would interfere with the goals and objectives of Congress for GSK to issue truthful warnings regarding the life threatening risks associated with children's "off-label" use of Paxil.

---

[40] Importantly, at the time Congress enacted the Food, Drug, and Cosmetic Act of 1938, it was well aware of the ongoing state tort actions over drug products, yet purposely decided not to include a private right of action for damages in the FDCA on the grounds that it was "unnecessary," because a "common-law right of action exists." *See* Robert S. Adler & Richard A. Mann, Preemption and Medical Devices: *The Court Run Amok*, 59 Mo. L. Rev. 895, 924 & n.130 (1995).

ii. Plaintiffs' Claims Would Complement The FDA's Goal of Promoting Health and Safety

A number of Courts have rejected the argument that lawsuits stand as an obstacle to the goals and objectives of Congress. As the New Jersey Supreme Court has noted :

> The suggestion that [the manufacturer] was in some way compelled to continue distributing a drug without warning of the strong likelihood of serious side effects for some child users and that Congress and the FDA intended that it would be immune from liability for doing so cannot be reconciled with the primary purpose of the FDA to promote and protect the health of the citizens of the United States.

Feldman II, 592 A.2d at 1195-1196. Similarly another Court noted:

> FDA and GSK's position vitiates, rather than advances, the FDCA's purpose of protecting the public. That is, FDA and GSK invite the Court to find that in enacting the FDCA for the purposes of protecting public health, Congress not only declined to provide for a private cause of action, but also eliminated the availability of common law state claims. This position contravenes common sense.

In re Paxil Lit., Case No. 01-07937, 2002 WL 31375497 at *1 (C.D.Cal. 2002). Further, a number of courts have held that state lawsuits complement the goals and objectives of the FDCA. For example, one district court held:

> [T]he Court notes that permitting plaintiff's state law "failure to warn" claims may complement the congressional purposes of FDA regulations. . . . Indeed, state suits may complement the regulatory methods of promoting safety by directly flushing out more information about the risks of drugs and indirectly encouraging manufacturers to make complete risk disclosures to the FDA. [citations]

Motus v. Pfizer, Inc., 127 F. Supp. 2d 1085, 1099-1100 (C.D. Cal. 2000); see also *Witczak v. Pfizer, Inc*., 377 F.Supp.2d 726, 732(D.Minn. 2005) ("State consumer-protection law compliments rather than frustrates, the FDA's protective regime."); *Cartwright*, 369 F.Supp.2d at 886-887 (same); *Mazur v. Merck & Co.*, 742 F.Supp. 239, 247 (E.D.Pa. 1990) (same).

Finally, even the FDA has noted the importance of state product liability action. 59 Fed. Reg. 3944, 3948 (1994) ("FDA recognizes that product liability plays an important role in consumer protection."); 44 Fed. Reg 37434, 37437 (1979) ("It is not the intent of FDA to influence the civil tort liability of the manufacturer..."); 65 Fed. Reg. 81082, 81103 (Dec. 22, 2000) (setting forth

FDA's intent to revise its regulations pertaining to prescription drug labeling, and announcing that *"this proposed rule does not preempt State law"* and "FDA has determined that this proposed rule does not contain policies that have federalism implications or that preempt State law.") Furthermore, Former Chief Counsel of the FDA, Margaret Jane Porter, wrote, "FDA product approval and state tort liability usually operate independently, each providing a significant, yet distinct, layer of consumer protection." Margaret J. Porter, *The Lohr Decision: FDA Perspective and Position,* 52 Food & Drug. L.J. 7, 11 (1997). In fact, in the context of SSRIs, the FDA, in denying a 1990 Citizen's Petition that sought to remove Prozac (an SSRI) from the market due to suicide risk, stated:

> On the other hand, *an actual court finding* of a causal relationship between Prozac and violent behavior would be relevant. In that event, the agency would be able to evaluate the scientific basis for the court's conclusion and consider whether court's conclusion warranted a modification of its own position.

PSUF 163, Exh. 138, at 15[41]. Thus, even in denying the Citizen's petition, the FDA admitted that litigation is relevant because the outcome of the litigation would allow the FDA the opportunity to reexamine its previous positions based on the evidence submitted in Court. Accordingly, Plaintiffs' claims (i.e., that GSK should have disclosed pediatric clinical trial data and should have issued truthful warnings) do not stand as an obstacle to the accomplishments of the FDA and Congress's objectives. Rather, they complement those objectives by promoting drug safety for children. This is especially true in light of the fact that the FDA now mandates the very warning that is advocated by Plaintiffs.

iii. The Medical Community Has Acknowledged the Positive Role of Litigation in Uncovering Drug Risks and Ensuring Consumer Safety

An article titled "The Role of Litigation in Defining Drug Risks," published in *Journal of the American Medication Association* by Jerry Avorn, M.D., Professor of Medicine at Harvard Medical School and Aaron S. Kesselheim, J.D., M.D., explains that lawsuits have "help[ed] uncover

[41] A copy of the FDA's response to the Citizen's petition was also attached as an exhibit by GSK as Exhibit 8 to the Declaration of Heather Howard.

previously unavailable data on adverse effects, questionable practices by manufacturers, and flaws in drug regulatory systems." JAMA, January 17, 2007 – Vol. 297, No. 3, p. 308[42]. The authors point out that the sources available to doctors for drug information "provide a limited perspective on a drug's benefits and risks" and "lawsuits have helped uncover important and previously unavailable data about major adverse events." *Id*., p. 308. "Litigation has also helped the medical community reassess drugs by bringing to light new information about adverse effects." *Id.* Litigation, the authors write, has also uncovered companies that have "downplayed and kept secret research." *Id*. 309. Lawsuits have also "exposed important limitations in the FDA information collection and dissemination procedures." *Id.* Avorn and Kesselhem state that, of the drug safety issues highlighted in the article, "the legal system played an important role in spurring change in regulatory or corporate procedures, as well as extending knowledge about drug risks by adding to the evidence available for evaluation by physicians, patients and regulators." *Id.* The authors point out that "limiting legal involvement in the prescription drug arena is likely to increase the nation's problem of poorly defined and inadequately presented drug risk information." *Id.* p., 311. Moreover, they explain: "Clinical trials and routine regulatory oversight as currently practiced often fail to uncover important adverse effects for widely marketed products." *Id.*

The importance of the role of litigation is critical when one considers that the FDA is far from infallible. A recent article published in the *New England Journal of Medicine* highlights the FDA's shortcomings in terms of funding, organization, and a lack of dedication to creating a culture of safety. *See* Exh. 158, Smith, "Sidelining Safety - The FDA's Inadequate Response to the IOM," *N. Engl. J. Med*. 2007;357: 960-962. The article discusses a recent report published by the Institute of Medicine concerning the FDA's performance and identified "weaknesses in laws, regulations, resources, and practice of ensuring drug safety." *Id.* at 960.

---

[42] A copy of the JAMA article is attached to the Declaration of Bijan Esfandiari as Exh. 163.

The Institute of Medicine's findings are consistent with FDA epidemiologist, Dr. David Graham's congressional testimony wherein he stated that, not only is the FDA "broken," but Americans are "virtually defenseless" as a result of FDA's current operating scheme. PSUF 95, Exh. 85, Testimony of David Graham. His testimony illustrates why FDA approval and subsequent post-marketing acquiescence should have no preemptive effect, absent precise congressional language or strict literal application of the "impossibility rule" in the area of conflict preemption. *See also McDarby v. Merck & Co.*, ___ A.2d ___, 2008 WL 2199871, * 21 (N.J. App. Div., May, 29, 2008) (noting the FDA's shortcomings and lack of power with respect to post-market labeling).

VI. PLAINTIFFS' CLAIMS ARE NOT PREEMPTED BECAUSE GSK HAS A FIRST AMENDMENT RIGHT TO ISSUE TRUTHFUL WARNINGS

To establish conflict preemption in this case, GSK would have to prove that: (a) it would have been illegal for GSK to communicate a *truthful* warning regarding the pediatric suicide risks associated with Paxil; and (b) it would have been illegal for GSK to publish the *truthful* data from its pediatric clinical trials. However, GSK cannot establish either contention, since (as GSK has admitted), GSK has a First Amendment right to engage in truthful speech and, furthermore, the public has a first amendment right to receive such information. *Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc*., 425 U.S. 748, 756 (1976). GSK acknowledges this very fact through its Eighth Affirmative Defense in which GSK states:

> the commercial speech of GSK relating to Paxil is not false or misleading and is protected under the First Amendment to the United States Constitution.[43]

Thus even GSK acknowledges that it has a First Amendment right to issue *truthful* statements.

[43] *In lieu* of making truthful statements about Paxil (which would be protected by the First Amendment), GSK instead made false statements regarding the safety and efficacy of Paxil within the pediatric population.

Like all other federal laws and regulations, the FDCA and the FDA regulations must comply with the Free Speech Clause of the First Amendment. *See Thompson v. Western States Medical Center*, 535 U.S. 357, 365, 122 S. Ct. 1497 (2002). As a Court recently held, "Scientific and academic speech resides at the core of [the] First Amendment." *Washington Legal Foundation v. Friedman*, 13 F.Supp.2d 51, 62 (D.D.C. 1998) ("*WLF I*"), vacated as moot by, *Washington Legal Foundation v. Henney*, 202 F.3d 331, 337, n.7 (D.C.Cir. Feb 11, 2000) (*WLF III*); see also *Board of Trustees of Leland Stanford Junior University v. Sullivan*, 773 F.Supp. 472, 474 (D.D.C.1991) ("It is equally settled, however, though less commonly the subject of litigation, that the First Amendment protects scientific expression and debate just as it protects political and artistic expression.").

In this case, Plaintiffs are merely claiming that GSK should have issued truthful warnings regarding the pediatric safety risks associated with Paxil and that GSK should have published the results from its pediatric clinical trials, instead of hiding it, so as to inform the medical community. The dissemination of such truthful factual information containing "factual material of clear 'public interest'" is entitled to First Amendment protection. *Bigelow v. Virginia*, 421 U.S. 809, 822 (1975). The degree of protection is determined by whether a warning or the publication of clinical trial data are deemed pure speech (which is afforded the highest level of protection) or if it is "commercial speech" (in which case it is entitled to a lower level of protection). However, as illustrated below, irrespective of whether the warnings and publications of clinical trials are deemed to be "pure speech" or "commercial speech," the First Amendment would nonetheless protect GSK's right to issue warnings and to publish its pediatric clinical trial data.

A. Issuing Truthful Warnings and Publishing Truthful Pediatric Clinical Trial Data Constitutes Pure Speech Which Deserves the Highest Degree of First Amendment Protection

It is Plaintiffs' contention that a warning regarding off-label use of a prescription drug or the publication of pediatric clinical trials (that demonstrate lack of efficacy and safety risks) does not

constitute commercial speech. As the Supreme Court has noted, whether or not a given communication constitutes commercial speech is predicated upon "the commonsense distinction between speech proposing a commercial transaction...and other varieties of speech." *Bolger v. Youngs Drug Products Corp.*, 463 U.S. 60, 64 (1983). The Court identified three factors in determining whether a form of speech constitutes "commercial speech." The factors are: (1) whether the speech is concededly an advertisement; (2) whether the speech refers to a specific product; and (3) whether the speaker has an economic motivation for disseminating the speech. *Bolger,* 463 U.S. at 66. If *all three factors are present* the speech may properly be characterized as commercial speech. *Id. see also WLF I*, 13 F.Supp.2d at 64.

Analysis of the first factor illustrates that this is not commercial speech, since a warning or the publication of *negative* clinical trial data can hardly be deemed as advertisements. After all, an *advertisement* "calls public attention to, especially by emphasizing desirable qualities so as to arouse desire to buy or patronize." *WLF I*, 13 F.Supp.2d at 64, quoting *Webster's Ninth New Collegiate Dictionary* (1990). A warning (or publication of *negative* clinical trial data) is the exact opposite of an advertisement since, rather than emphasizing desirable qualities, it discusses the negative aspects and risks associated with the product. Similarly, publication of the negative clinical trial data – calling public attention to the lack of efficacy of a product – similarly would not be classified as an advertisement. Thus, the first factor alone establishes that a warning is not commercial speech. While the analysis ceases at this point because all three factors would need to be established to be characterized as "commercial speech"(and GSK would not even be able to establish the first factor), analysis of the third factor also re-confirms that a warning/publication of clinical trial data is not commercial speech.[44]

[44] As to the second factor (specific product), in the context of this case, GSK's warning would probably be specific to Paxil.

The third factor (economic motivation) also leads to the conclusion that this is not commercial speech since the manufacturer would not have any positive economic motivation to release negative clinical trial data about its product. As one case noted, "[t]ypical commercial speech is authored and/or uttered directly by the commercial entity that wishes to financially benefit from the message." *WLF I*, 13 F.Supp.2d at 62. Since GSK would have no financial benefit from issuing or disseminating its negative clinical trial data – the dissemination of the data and the warnings that are supported by the data do not constitute "commercial speech."

Having established that the truthful off-label warnings and dissemination of clinical trial data is considered pure speech, then such speech is entitled to the highest degree of First Amendment protection. For GSK to argue that it was prohibited by the FDA from issuing non-commercial truthful factual information regarding the risks associated with Paxil in pediatric use is tantamount to content-based speech restriction, which is subject to a strict scrutiny standard. *See e.g., Sable Communications of Cal., Inc. v. FCC*, 492 U.S. 115, 126 (1989); *see also U.S. v. Playboy Entertainment Group, Inc*., 529 U.S. 803, 813-814 (2000). "If a statute regulates speech based on its content, it must be narrowly tailored to promote a compelling Government interest." *Playboy*, 529 U.S. at 813. If a less restrictive alternative would serve the Government's purpose, the legislature must use that alternative. *Reno v. ACLU*, 521 U.S. 844, 874 (1997) ("[The CDA's Internet indecency provisions'] burden on adult speech is unacceptable if less restrictive alternatives would be at least as effective in achieving the legitimate purpose that the statute was enacted to serve"). To do otherwise would be to restrict speech without an adequate justification, a course the First Amendment does not permit. *Playboy*, 529 U.S. at 813.[45]

---

[45] Similarly, in the event GSK argues that it could not publish the pediatric clinical trial data and could not issue the truthful warning without first obtaining the FDA's approval, such a contention would amount to a "prior restraint" on protected expression – which is the most serious and the least tolerable infringement on First Amendment rights. *See Organization for a Better Austin v. Keefe*, 402 U.S. 415, 419 (1971); *see also The Florida Star v. B.J.F.*, 491 U.S. 524, 533 (1989).

The purported prohibition against GSK issuing off label warnings or disseminating clinical trial data to aid physicians and the medical community is not a narrowly tailored regulation (since it would constitute a blanket prohibition against off label speech) and thus would not survive First Amendment scrutiny. Furthermore, it could hardly be argued that the government has a compelling interest in keeping people in the dark about risks associated with the drugs they are consuming.[46] In fact, this would go against the very spirit of the FDCA whose primary objective is to protect consumers. *United States v. Dotterwiech*, 320 U.S. 277, 282 (1943); *see also Cartwright*, 369 F.Supp.2d at 886; *Witczak*, *supra*, 377 F.Supp.2d at 732 ("The primary purpose of both the FDCA and FDA's regulatory scheme is to protect the public.")

Further, the facts of this case illustrate that there is no prohibition against GSK publishing its pediatric clinical trial data or issuing off label warnings. In 2001, GSK published portions of its study 329 data – of course, GSK was selective in the data and results it published to give a favorable impression of the results.[47] The fact that GSK published the clinical trial data (even though it was incomplete and misleading) demonstrates that GSK had a First Amendment right to publish its pediatric clinical trials data. It is thus disingenuous for GSK to now claim (in an effort to seek tort immunity) that it was prohibited from issuing truthful warnings or publishing its pediatric clinical trials data.[48] Finally, it would be difficult to reconcile GSK's current litigation position with GSK's

---

[46] Prior to Jake's suicide, the FDA had never analyzed the issue of pediatric suicidality – rather, the clinical trials (which demonstrated a lack of pediatric efficacy and increased risk of suicidality) were solely in the possession of GSK.

[47] As previously discussed, the true data revealed that Paxil was associated with an at-least six times increase in the risk of a suicide event for an adolescent taking Paxil as compared to placebo – of course GSK failed to disclose this portion of the clinical trial data.

[48] GSK effectively concedes that, during the relevant time period (i.e., prior to September 2002) it was not prohibited from publishing the truthful pediatric clinical trial data. Of course, GSK cannot dispute this point because, in July 2001 (without prior FDA approval) GSK published the sparse amount of positive data that it could pull from the studies. See PSUF 19, Exh. 31. GSK should have used this publication (and similar publications and newsletters) to disclose all of the truthful data – both positive and negative. None of the conclusions reached by GSK in the July 2001

own public policy statement concerning "disclosure of clinical trial information." According to GSK's own public policy position, GSK "publicly discloses the results of GSK-sponsored clinical trials that are relevant for patient care irrespective of whether the results are positive or negative for GSK prescription medicines and vaccines." PSUF 102, Exh. 91.

Perhaps more importantly, the First Amendment issue here is not only GSK's right to disseminate truthful factual information -- but just as paramount is the public's and medical community's (i.e., recipients) right to receive the information. *Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc*., 425 U.S. 748, 756 (1976) ("where a speaker exists, as is the case here, the protection afforded is to the communication, to its source and to its recipients both."); *Kleindienst v. Mandel*, 408 U.S. 753, 762-763(1972) ("it is now well established that the Constitution protects the *right to receive information and ideas*") (emphasis added). It would be a grave violation of the public's (including Plaintiffs and their prescribing physicians) First Amendment right if the Government prohibited the public from receiving truthful information regarding the safety risks associated with hazardous drugs and pharmaceutical products.

As the Supreme Court has noted, "the general proposition that freedom of expression upon public questions is secured by the First Amendment has long been settled by our decisions." *New York Times Co. v. Sullivan,* 376 U.S. 254, 269 (1964). This constitutional safeguard, "was fashioned to assure unfettered interchange of ideas for the bringing about of political and social changes desired by the people." *Roth v. United States*, 354 U.S. 476, 484 (1957). The First Amendment, said Judge Learned Hand, "presupposes that right conclusions are more likely to be gathered out of a multitude of tongues, than through any kind of authoritative selection. To many this is, and always will be, folly; but we have staked upon it our all." *United States v. Associated Press*, 52 F.Supp. 362, 372

---

article were ever approved by the FDA. Thus, it would be preposterous for GSK to argue that it is allowed to publish false promotional material (none of which had been approved or established by the FDA), yet it could not use these same venues, as well as "Dear Doctor" letters to disclose the true data regarding Paxil's risks.

(S.D.N.Y.1943). Justice Brandeis, in his concurring opinion in *Whitney v. California*, 274 U.S. 357, 375-376 (1927), noted the following:

> 'Those who won our independence believed...that public discussion is a political duty; and that this should be a fundamental principle of the American government. They recognized the risks to which all human institutions are subject. But they knew that order cannot be secured merely through fear of punishment for its infraction; that it is hazardous to discourage thought, hope and imagination; that fear breeds repression; that repression breeds hate; that hate menaces stable government; *that the path of safety lies in the opportunity to discuss freely supposed grievances and proposed remedies*; and that the fitting remedy for evil counsels is good ones. *Believing in the power of reason as applied through public discussion, they eschewed silence coerced by law-the argument of force in its worst form.* Recognizing the occasional tyrannies of governing majorities, they amended the Constitution so that free speech and assembly should be guaranteed.

Whitney, 274 U.S. at 375-376.

To hold that GSK was prohibited from issuing truthful information regarding safety risks; that the public should be kept in the dark regarding information that impacts their health and safety; and that such information cannot be disclosed until the Government (i.e., FDA) has had an opportunity to authorize or bless the message is the type of evil the First Amendment was meant to safeguard against. *Washington Legal Foundation v. Henney*, 56 F.Supp.2d 81, 85 (D.D.C.,1999) ("The First Amendment is premised upon the idea that people do not need the government's permission to engage in truthful, nonmisleading speech about lawful activity.")

B. Even If Deemed Commercial Speech, GSK Has A First Amendment Right To Issue Truthful Warnings and Publish Truthful Clinical Trial Data Regarding Off-Label Use

Even if off label warnings and publications of clinical trials is deemed "commercial speech" – GSK would have a First Amendment right to issue *truthful* warnings and to publish *truthful* facts (i.e., pediatric clinical trial data). *Western States*, 535 U.S. at 365. In *Western States*, the Supreme Court struck down a ban on advertising unapproved compounded drugs in the FDA Modernization Act of 1997 (FDAMA). The Court applied the commercial speech test of *Central Hudson Gas & Electric Corp. v. Public Serv. Comm'n*, 447 U.S. 557 (1980). Thus, the Court asked: (1) whether

the speech was untruthful or misleading, or concerned unlawful activity (characteristics that would strip the speech of First Amendment protection and end the analysis); (2) whether the Government had asserted a "substantial" interest in restricting the speech; (3) whether the Government had demonstrated that the restriction "directly advanced" such a substantial interest; and (4) whether the Government had established that the restriction was "not more extensive than is necessary to serve that interest." *Western States*, 535 U.S. at 365.[49]

i. Issuing Warnings And Publishing Pediatric Clinical Trials Regarding Off Label Use Is Neither Unlawful Nor Inherently Misleading

As discussed supra, Plaintiffs are merely claiming that GSK should issue truthful warnings pertaining to off-label use and that it should have published its pediatric clinical trial data. Furthermore, the warnings and publication of clinical trial data pertain to off-label pediatric use of Paxil – which is a lawful activity. *WLF I,* 13 F.Supp.2d at 66. Thus, the first element of *Central Hudson* is satisfied. In its Motion, GSK has argued that it could not issue such warnings and could not publish its pediatric clinical trials without first obtaining the FDA's approval (i.e., that only the FDA can determine if the warning and publication of factual clinical trial data is *truthful*). (GSK Motion at 23).[50]

Numerous cases have explicitly rejected the proposition that speech is "inherently misleading" because it does not satisfy Government requirements. In *Pearson v. Shalala*, 164 F.3d

---

[49] The Court also clarified some ambiguities in past cases concerning the "final prong" of the commercial speech analysis, holding that "if the Government could achieve its interests in a manner that does not restrict speech, or that restricts less speech, the Government must do so." Id. at 1506. The Court emphasized that "[i]f the First Amendment means anything, it means that regulating speech must be a last - - not first - - resort."Id. at 1507.

[50] Of course, this is a specious argument in light of the fact that GSK waited four years before even submitting its pediatric studies (Studies 329 and 377) to the FDA since as noted by GSK the dissemination of the data was "unacceptable commercially." PSUF 9-10. Further, even when GSK did submit the data, it hid the safety and (as noted by the FDA officials), it prevented the FDA from timely conducting a safety analysis. See PSUF 29-30, 41-42 and 44. However, the speciousness of the argument aside, as discussed *infra* GSK's contention cannot stand first amendment scrutiny.

650, 655 (D.C. Cir.), *reh'g denied*, 172 F.3d 72 (D.C. Cir. 1999), the FDA contended that the health claims appellants wished to include on dietary supplements were inherently misleading because they did not meet FDA's requirement that there be "significant scientific agreement" about such claims before they could be included in the labeling for dietary supplements. The court disagreed, finding the argument that health claims were inherently misleading unless they satisfied FDA's significant scientific agreement requirement "almost frivolous." 164 F.3d at 655. The court even concluded that the claims at issue had the potential to mislead, but that FDA failed to prove that the problem could not be cured through disclosures and therefore justified an outright ban on the claims. *Id.* at 655-60.

In the context of prescription drugs, the theory that statements lacking FDA approval were inherently misleading was considered and rejected in *WLF I.* There, FDA argued that manufacturer-funded or manufacturer-disseminated speech about off-label uses is inherently misleading because the FDCA "prescribes a specific system for determining the 'truth' of claims about drugs and devices." *WLF I,* 13 F. Supp.2d at 67. The court concluded that FDA had no power to impose a "specific system for determining truth," holding that:

> In asserting that any and all scientific claims about the safety, effectiveness, contraindications, side effects and the like regarding prescription drugs are presumptively untruthful or misleading until the FDA has had the opportunity to evaluate them, FDA exaggerates its overall place in the universe.

Id.

The *WLF I* court went on to hold that scientific conclusion are "*not untruthful or inherently misleading merely because the FDA has not yet had the opportunity to evaluate the claim*." *Id.* Cases decided outside of the FDA context have reached the same conclusions about the Government's power to dictate truth. In *Bioganic Safety Brands, Inc. v. Ament*, 174 F. Supp.2d 1168 (D. Colo. 2001), for example, the State of Colorado argued that safety claims about pesticides were inherently misleading because a Colorado statute banned such claims. The court found otherwise,

rejecting the theory that the State could properly determine that safety claims on pesticide labels were inherently misleading "as a matter of law":

> Whether speech is "inherently misleading" . . . is a determination for the court, not the legislature, to make. If a legislature could place speech outside First Amendment protection by simply declaring the speech "inherently misleading," the First Amendment . . . would be subject to de facto modification by state legislatures.

Id. at 1180.[51]

In short, GSK cannot sustain a position that truthful warnings regarding pediatric off-label use and publication of pediatric clinical trial data is inherently misleading unless it complies with FDA requirements. Such a position would nullify the constitutional protections accorded to commercial speech, and the cases have squarely rejected this sort of "*de facto* modification" of the First Amendment. Simply put, government-mandated systems for determining truth are not a part of our First Amendment jurisprudence.

ii. While the FDA May Have A "Substantial" Interest In Protecting The Health and Safety of Citizens, It Cannot Restrict Truthful Information Out of Fear That it May be Misused

It is not disputed that Government agencies may seek to regulate speech for certain legitimate purposes - - perhaps most importantly in the FDA context, to prevent the serious harms that can result from *untruthful* speech. Whether speech is categorized as commercial or non-commercial, a restriction designed to prevent citizens from using *truthful* information to make choices about lawful activities does not satisfy this requirement. The First Amendment "directs us to be especially

---

[51] For additional cases, *see, e.g.*, *Peel v. Attorney Reg. & Disciplinary Commission*, 496 U.S. 91, 108 (1990) ("[w]hether the inherent character of a statement places it beyond the protection of the First Amendment is a question of law over which Members of this Court should exercise de novo review"); *Nutritional Health Alliance v. Shalala, 953* F. Supp. 526, 529 (S.D.N.Y. 1997), *aff'd in part, vacated and dismissed in part on other grounds*, 144 F.3d 220 (2d Cir. 1998) ("[a]lthough the Government argues that health claims that have not been FDA approved are inherently misleading, not all potential health claims are misleading; at least some can be presented in a non-misleading fashion"); *Ass'n of Nat'l Advertisers, Inc. v. Lungren*, 809 F. Supp. 747, 756 (N.D. Cal. 1992), aff'd, 44 F.3d 726 (9th Cir. 1994) ("[i]f First Amendment scrutiny in the commercial speech arena is to have any bite at all, a legislative body cannot justify its restrictions on commercial speech simply by declaring that marketing claims are misleading").

skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good." *44 Liquormart, Inc. v. Rhode Island*, 517 U.S. 484, 503 (1996).

This principle has been recognized repeatedly in cases involving restrictions on information about drugs and devices, including the first Supreme Court decision to extend First Amendment protection to commercial speech. In that case, *Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748, 769 (1976), the State of Virginia argued that a ban on advertising prescription drug prices was justified by the fear "that if the pharmacist who wishes to provide low cost, and assertedly low quality, services is permitted to advertise, he will be taken up on his offer by too many unwitting customers." The Supreme Court disagreed, holding at 770 that:

> Virginia is free to require whatever professional standards it wishes of its pharmacists . . . . But it may not do so by keeping the public in ignorance of the entirely lawful terms that competing pharmacists are offering . . . . [T]he justifications Virginia has offered for suppressing the flow of prescription drug price information, far from persuading us that the flow is not protected by the First Amendment, have reinforced our view that it is. We so hold.

Similarly, the court in *WLF I* rejected paternalism as a valid basis for restricting the dissemination of truthful information about off-label uses of drugs and devices, holding that "[t]o the extent that the FDA is endeavoring to keep information from physicians out of concern that they will misuse that information, the regulation is wholly and completely insupportable." *WLF I*, 13 F. Supp.2d at 69. "If there is one fixed principle in the commercial speech arena," the court observed, "it is that 'a State's paternalistic assumption that the public will use truthful, nonmisleading commercial information unwisely cannot justify a decision to suppress it.'" *Id.* at 69-70 *quoting 44 Liquormart, Inc. v. Rhode Island*, 517 U.S. 484, 497 (1996).

In *Western States*, the Supreme Court rejected the theory that an interest in protecting patients from truthful information could justify its suppression. There, the Court addressed the argument that FDAMA's ban on advertising compounded drugs could be sustained by an interest in preventing patients who do not need compounded drugs from seeking them, holding that:

> Even if . . . FDAMA's speech-related restrictions were motivated by a fear that advertising compounded drugs would put people who do not need such drugs at risk by causing them to convince their doctors to prescribe the drugs anyway, that fear would fail to justify the restrictions. Aside from the fact that this concern rests on the questionable assumption that doctors would prescribe unnecessary medications . . . [it] amounts to a fear that people would make bad decisions if given truthful information about compounded drugs. . . . We have previously rejected the notion that the Government has an interest in preventing the dissemination of truthful commercial information in order to prevent members of the public from making bad decisions with the information.

Western States, 535 U.S. at 374.

Other Courts have similarly held that "[t]he First Amendment mandates that we presume that speakers, not the government, know best both what they want to say and how to say it., *Riley v. Nat'l Fed'n of Blind, Inc*., 487 U.S. 781, 790-91(1988). In fact, "[t]he very purpose of the First Amendment is to foreclose public authority from assuming a guardianship of the public mind through regulating the press, speech, and religion." *Thomas v. Collins*, 323 U.S. 516, 545 (1945) (Jackson, J., concurring). "To this end, the government, even with the purest of motives, may not substitute its judgment as to how best to speak for that of speakers and listeners; free and robust debate cannot thrive if directed by the government." *Riley*, 487 U.S. at 791. Accordingly, in light of the foregoing Supreme Court authority, the FDA could not prevent GSK from issuing truthful warnings regarding off-label/pediatric risks and publishing its pediatric clinical trial data.

iii. The Purported Restrictions on Speech Do Not Advance the Government's Substantial Interest in Protecting the Health and Safety of Consumers.

In light of the fact that the FDCA's primary objective is to protect consumers, that objective and interest would not be advanced if we were to believe GSK's contention that the FDA would prohibit a truthful pediatric warning or dissemination of truthful clinical trial data. See e.g., *United States v. Dotterwiech*, 320 U.S. 277, 282 (1943); *see also Cartwright*, 369 F.Supp.2d at 886; *Witczak*, *supra*, 377 F.Supp.2d at 732. Further, the purported FDA restriction would undermine FDA's interest in promoting physicians' access to reliable scientific and medical information and

thereby endanger the lives of patients (i.e., children and adolescents) who are prescribed medications off-label. Under the First Amendment, such prohibitions would be unlawful.

iv. A Restriction on Off Label Warning and Dissemination of Clinical Trial Data Is More Extensive than Necessary.

Finally as to the fourth factor, GSK's contention that the FDA would bar all off-label warnings (and dissemination of clinical trial data) until approved by the FDA is more extensive than necessary since it burdens substantially more speech than necessary. *U.S. v. Edge Broadcasting Co.*, 509 U.S. 418, 430 (1993). First, as already noted, such a restriction would be an unnecessary and unconstitutional prior restraint. *See e.g., WLF II*, 56 F.Supp.2d at 85. Second, as the *WLF I* court noted, in lieu of prohibiting speech, the FDA could require "full, complete, and unambiguous disclosure by the manufacturer." *WLF I,* 13 F.Supp.2d at 73. Finally, as the *WLF I* Court noted, the FDA cannot restrict the dissemination of truthful information especially when the "truthful information may be life saving information." *WLF I,* 13 F.Supp.2d at 73. Truthful warnings and publication of pediatric clinical trial data is exactly the type of life saving information that cannot be restricted and is fully protected by the First Amendment.

The FDA has long understood that completely suppressing the exchange of accurate scientific and medical information on off-label uses between physicians and the manufacturers of drugs and devices does not serve its public health objectives. For example, the FDA stated in 1994 that, "because the agency recognizes the importance of dissemination of reliable scientific information on . . . unapproved uses, it has developed a number of policies related to dissemination of such information." 59 Fed. Reg. 59820, 59822 (Nov. 18, 1994).[52] In its most recent pronouncement on

---

[52] *See also* 21 CFR 312.7(a) (providing that manufacturers may not represent in a promotional context that a drug under investigation is safe and effective for the purposes for which it is under investigation, and that "[t]his provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media"). In analyzing section 312.7, the FDA has held that manufacturer is allowed to discuss off label clinical trials with investors and to disclose such information in SEC filings. See PSUF 103, Exh 92-93, FDA Letter to WLF. Thus, it would defy logic for GSK to attempt to argue that it

this issue, the FDA confirmed that manufacturers have a right to "disseminate truthful and non misleading medical journal articles and medical or scientific reference publications on unapproved uses of approved drugs...to healthcare professionals." See PSUF 101, Exh. 90 FDA Guidance for Industry at 3. The FDA further held that, along with the dissemination of such information, the manufacture should also disclose "*any significant risks or safety concerns known to the manufacturer concerning the unapproved use...*" See Id. at 6. Thus, contrary to GSK's contention, GSK was not only permitted, but in fact encouraged to disclose any known safety risks regarding off label/unapproved uses. For this reason alone, GSK's preemption argument should be rejected.[53]

Accordingly, the foregoing establishes that GSK had a First Amendment right to issue truthful warnings and to publish and disseminate its pediatric clinical trial data to the medical community, and the public has a First Amendment right to receive information, thus Plaintiffs' claims cannot be preempted by the FDCA.

VII. PATIENTS HAVE A FIFTH AMENDMENT FUNDAMENTAL RIGHT TO RECEIVE INFORMATION REGARDING THE POSSIBLE RISKS ASSOCIATED WITH THEIR TREATMENT

The Fifth and Fourteenth Amendments of the Constitution prohibit the "depriv[ation] of life, liberty, or property." U.S. CONST. amend. V., XIV. Encompassed within this right is the right to refuse medical treatment. *Cruzan v. Director, Missouri Department of Health*, 497 U.S. 261, 269 (1990). In *Cruzan*, the Supreme Court held that patients have a fundamental right to refuse medical treatment, including a right to refuse life-sustaining medical treatment, *Cruzan*, 497 U.S. at 278

---

would be illegal for it to publish the pediatric clinical trials to the medical community, but that it is perfectly legal for the same information to appear in an SEC filing or be given to investors. Such capricious restriction as to who may receive information cannot stand First Amendment scrutiny.

[53] Like FDA, Congress has also recognized the benefits of allowing manufacturers to disseminate scientific and medical information on off-label uses to health care professionals. In enacting Section 401 of FDAMA, Congress sought to ensure "that health care practitioners can obtain important scientific information about uses that are not included in the approved labeling of drugs, biological products, and devices." H.R. Conf. Rep. No. 105-399 (Nov. 9, 1997), 1997 WL 703162 (Leg. Hist.), * 99.

(1990) ("person has a constitutionally protected liberty interest in refusing unwanted medical treatment..."). "[A] necessary corollary to the interest articulated in....*Cruzan* is the right of ...patients to information sufficient to reach an informed judgment on whether to consent to a particular treatment or to refuse it." *Clarkson v. Coughlin*, 898 F.Supp. 1019 (S.D.N.Y.,1995) citing to (*White v. Napoleon*, 897 F.2d 103, 113 (3d Cir.1990)).

As other cases have made clear, in order for a patient to exercise this fundamental right, he (or his legal guardian) must be given the medical "options available and the risks attendant upon each." *Canterbury v. Spence* 464 F.2d 772,780 (D.C. Cir. 1972). That is that the patient must be given (via his physician or otherwise) all of the potential risks associated with the medication as well as the available alternative so that the patient can make an informed decision regarding whether to accept or reject the treatment. *Id.*: *see also*, *Harnish v. Children's Hosp. Medical Center*, 439 N.E.2d 240, 242 (Mass.,1982). As the Third Circuit has noted, if a patient's decision to accept treatment is to be a knowing and intelligent one, he must be informed of the risks associated with the treatment.[54] *Dunham v. Wright*, 423 F.2d 940, 943-946 (3d Cir. 1970)(applying Pennsylvania law). *see also Cobbs v. Grant*, 8 Cal.3d 229, 242 (1972) ("[I]t is the prerogative of the patient, not the physician, to determine ... the direction in which ... his interest lie.").

Under New Jersey law, the concept of informed consent equally applies to prescription drugs. *Calabrese v. Trenton State College*, 392 A.2d 600, 605(N.J.1978). In *Calabrese* the Court held that, as part of the obligation to obtain "informed consent," a doctor has a duty to disclose "possible adverse side-effects of the drug." *Calabrese,* 392 A.2d at 605; *see also SK&F, Co. v. Premo Pharmaceutical Laboratories, Inc.*, 481 F.Supp. 1184, 1190 (D.N.J., 1979) (noting that

[54] In fact, the Third Circuit has held that even convicted prisoners have a right to know of the risks associated with their medication so that they can properly exercise their right to refuse medication or request viable alternatives. *See White v. Napoleon*, 897 F.2d 103, 113 (3d Cir.1990).

informed consent even extends to patient's right to know if he is being prescribed a brand name drug or a "generic equivalent.").

Thus, all of these cases illustrate that, in order for a patient to make a meaningful decision regarding his/her medical treatment, a doctor must disclose the possible adverse side-effects associated with the medication. Of course, for a doctor to know about the possible side-effects (especially in the context of an "off-label" use), the doctor must obtain the information from the manufacturer. GSK, however, is claiming that the FDCA prohibited it from informing the doctors and the medical community about the risks associated with pediatric use of Paxil. However, in the same way it is not the prerogative of the doctor to determine which adverse risks he chooses to disclose to the patient – it should similarly not be the prerogative of the manufacturer or the federal government to determine which adverse risks should be reported to the doctor/patient. *See e.g., Dunham,* 423 F.2d at 944-945. Simply put, a patient should be given all the necessary and material information (including possible adverse risks) so that he or she can make an informed decision regarding whether to accept or reject the medication. Allowing the manufacturer or government to hide or conceal known risks from the patient (or his doctor) would infringe upon the patient's fundamental and constitutional right and ability to make an informed decision regarding his treatment. Such an infringement would violate the liberty protected by the Due Process Clause of the Fifth Amendment as espoused by the Supreme Court in *Cruzan* and it progeny.

VIII. CONCLUSION

GSK's motion for summary judgment regarding federal preemption fails to demonstrate that Plaintiffs' claims in this case conflict with either the FDCA, FDA's regulations, or any specific actions taken by the FDA. GSK has failed to overcome the presumption against preemption. The evidence clearly shows that, prior to the relevant time period, the FDA never "considered and rejected" the warnings advocated by Plaintiffs in this case, and that, once the FDA was given the unmanipulated pediatric data, it ordered GSK to issue a "black box" warning concerning the risk of

pediatric suicidality. Nothing within the FDCA or the FDA regulations would prohibit GSK from issuing a warning regarding "off-label" pediatric use. Furthermore, GSK's preemption defense would violate the First and Fifth Amendments of the Constitution. Specifically, patients have a First Amendment and Fifth Amendment fundamental right to receive information regarding the risks associated with their medication; and GSK has a First Amendment right to issue truthful warnings and to disseminate truthful clinical trial data. Accordingly, for all of the foregoing reasons, this Court should hold that Plaintiffs' claims in this case are not preempted.

Dated: June 19, 2008

Respectfully Submitted,

s/Bijan Esfandiari

Bijan Esfandiari, *pro hac vice*
George W. Murgatroyd, III, *pro hac vice*
Kate E. Gillespie, *pro hac vice*
Frances M. Phares, *pro hac vice*
BAUM HEDLUND ARISTEI & GOLDMAN, P.C.
12100 Wilshire Blvd., Suite 950
Los Angeles, California 90025
(310) 207-3233
(310) 820-7444 (fax)

Cara J. Luther (P.S.B. #52545)
BAUM HEDLUND ARISTEI & GOLDMAN, P.C.
1250 24th Street, N.W., Suite 300
Washington, D.C. 20037-1124
(202) 466-0513
(202) 466-0527 (fax)

Attorneys for Plaintiffs