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UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF CALIFORNIA

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TERRI S. O'NEAL, individually
and as successor-in-interest
to the Estate of BENJAMIN L.
BRATT; BARRY M. BRATT,
individually,

Plaintiffs,

v.

SMITHKLINE BEECHAM CORPORATION
d/b/a GLAXOSMITHKLINE, a
Pennsylvania Corporation; and
DOES 1-50,

Defendants.

NO. CIV S-06-1063 FCD/DAD

MEMORANDUM AND ORDER

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This matter is before the court on defendant SmithKline Beecham Corporation, d/b/a GlaxoSmithKline's ("GSK") motion for summary judgment on the ground plaintiffs Terri O'Neal and Barry Bratt's ("plaintiffs") state tort claims are preempted by federal law, *i.e.*, the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 301 *et seq.*, and its implementing regulations, because they require warnings that directly conflict with federal law

1 governing the labeling and warnings for Paxil® ("Paxil").
2 Plaintiffs bring this action for the wrongful death of their son,
3 Benjamin Bratt ("Benjamin"), who attempted suicide, on February
4 14, 1997, at the age of 13, while being treated with Paxil, an
5 antidepressant medication manufactured and sold by GSK. Benjamin
6 died on February 15, 1997 from injuries sustained from his
7 suicide attempt.

8 The gravamen of plaintiffs' claims is that GSK should have
9 provided, at the time of Benjamin's death, a warning that Paxil
10 is associated with suicidality¹ in pediatric patients. GSK
11 contends, however, that plaintiffs' state tort claims directly
12 conflict with the FDA's-mandated labeling for Paxil in February
13 1997, and implementation of the warning urged by plaintiffs would
14 have rendered Paxil's prescribing information false and
15 misleading under federal law, as no reasonable evidence existed,
16 at the time, to support implementation of the warning. As such,
17 because there is a direct and actual conflict between plaintiffs'
18 state law claims and federal law, GSK asserts plaintiffs' claims
19 are preempted and must be dismissed.

20 The court heard oral argument on the motion on January 18,
21 2008. By this order, the court now renders its decision,
22 granting GSK's motion in its entirety. For the reasons set forth
23 below, the court finds that federal law preempts plaintiffs'
24 instant action against GSK.

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28 ¹ As used by the parties, the term "suicidality" refers
to suicidal thoughts and behavior.

1 BACKGROUND

2 **A. FDA Regulation of Drug Labeling Generally**

3 The Federal Drug Administration ("FDA") is responsible for
4 enforcing the FDCA. In the FDCA, Congress broadly charged the
5 FDA with promoting "the public health by promptly and efficiently
6 reviewing clinical research and taking appropriate action on the
7 marketing of regulated products," 21 U.S.C. § 393(b)(1), and with
8 ensuring that "drugs are safe and effective," 21 U.S.C.
9 § 393(b)(2)(B). Congress also provided the FDA with exclusive
10 authority to enforce the FDCA, and litigants cannot enforce the
11 FDCA through private actions. 21 U.S.C. § 337(a); Buckman Co. v.
12 Plaintiffs' Legal Comm., 531 U.S. 341, 349 n.4 (2001).

13 As part of its regulatory mission, the FDA undertakes an
14 extensive review of new drugs before they are allowed on the
15 market. See 21 U.S.C. § 355 (outlining the New Drug Application
16 ["NDA"], which requires, among many other things, evidence
17 establishing whether the drug is safe and effective in its use
18 and proposed labeling). Most prescription drugs, including
19 Paxil, begin the regulatory approval process as a "new drug." 21
20 U.S.C. § 321(p). The FDA carefully reviews the NDA and
21 identifies the actual and potential safety risks the drug poses
22 and decides how these risks should be disclosed in the
23 prescribing information. The FDA approves the NDA only after it
24 concludes that a prescription drug is both "safe" and "effective"
25 under the conditions of use specified in the proposed prescribing
26 information. 21 C.F.R. §§ 201.56(d), 201.57 (FDA must be
27 satisfied that the drug's labeling accurately describes its
28 indications, dosages, administration, contraindications, warnings

1 and precautions, adverse reactions, interactions, and use in
2 specific populations). The FDA must disapprove a NDA if it finds
3 that: (1) investigations conducted to establish safety and
4 effectiveness were not adequate; (2) the prescription drug is not
5 safe for use under the conditions provided in the proposed
6 labeling; or (3) the proposed labeling is false and misleading.
7 21 U.S.C. § 355(d); 21 C.F.R. § 314.125(b)(2), (3), (6).

8 As part of the approval process, manufacturers of new drugs
9 submit to the FDA "specimens of the labeling proposed to be used
10 for such drug." 21 U.S.C. § 355(b)(1). While there are several
11 mandatory aspects of included drug information (see 21 C.F.R.
12 § 201.56-57), the aspect relevant to the present case involves
13 the "warnings" section. This section must describe "clinically
14 significant adverse reactions (including any that are potentially
15 fatal, are serious even if infrequent, or can be prevented or
16 mitigated through appropriate use of the drug)." 21 C.F.R.
17 § 201.57(c)(6)(I). Under the FDA's regulations, warnings must be
18 included on a label "as soon as there is reasonable evidence of a
19 casual association [of a serious hazard] with a drug." Id.²

20 The FDA communicates its decision to approve the NDA through
21 an approval letter that sets out FDA's terms for approving both
22 the drug and its labeling. FDA approval of a NDA is expressly
23 conditioned on the development and use of "final printed
24 labeling" (prescribing information) that is identical, in every

25
26 ² The FDA interprets the phrase "reasonable evidence of
27 an association" to mean that "evidence exists on the basis of
28 which experts qualified by scientific training and experience can
reasonably conclude that the hazard is associated with the drug."
44 Fed. Reg. 37434, 37447 (June 26, 1979).

1 material respect, to the labeling that accompanies the approval
2 letter. 21 C.F.R. § 314.105(b). Use of the FDA-approved
3 prescribing information is mandatory and failure to comply may
4 lead to civil and criminal enforcement. The FDCA envisions a
5 number of remedies against violators, including in rem
6 forfeiture, injunction, and/or criminal prosecution against the
7 manufacturer or responsible person if a "misbranded" drug is
8 distributed. 21 U.S.C. §§ 332(a), 333, 334(a), and 337(a). The
9 FDA may also seek to withdraw approval of a NDA. 21 C.F.R.
10 § 314.150(b).

11 A prescription drug is misbranded if its labeling is false
12 or misleading, lacks "adequate information for use," or omits
13 material facts. 21 U.S.C. §§ 352(a), (f)(1), 321(n); 21 C.F.R.
14 § 201.100(c)(1). Therefore, departing from the FDA-approved
15 prescribing information, failing to include a scientifically
16 valid warning FDA believes is necessary, or including warning
17 information not based on scientific evidence of known risks,
18 causes the drug labeling to be "false and misleading" and lacking
19 "adequate directions for use" and misbranded, in violation of the
20 FDCA. 21 U.S.C. § 352(a), (f)(1).

21 After approval of a NDA, the FDA continues to exercise
22 extensive control over the safety of prescription drugs and the
23 content of their labeling. The FDA can move to withdraw its
24 approval of a drug if it finds that scientific data shows that
25 the drug is unsafe for use under the conditions set forth when
26 the application was approved. 21 U.S.C. § 355(e). Additionally,
27 the FDA imposes comprehensive post-approval reporting
28 requirements on manufacturers, including reports of adverse

1 events and all published and unpublished clinical trials on the
2 drug. 21 C.F.R. § 314.80-81. If a manufacturer seeks NDA
3 approval for additional indications or dosage forms (as was done
4 for Paxil more than ten times between 1992 and 2004), then it
5 must provide new supporting data to the FDA, including updated
6 integrated summary of safety ("ISS") and effectiveness ("ISE").
7 21 C.F.R. § 314.50(d)(5)(vi)(a). If the FDA finds that any
8 information from a post-approval report or a new ISS report
9 merits a change in the drug's labeling, it will request that the
10 company make the change. If the company refuses to do so, the
11 FDA may pursue the administrative and enforcement actions
12 described above to secure the change.

13 FDA regulations also allow manufacturers to make certain
14 changes to their drug labels. With the exception of minor
15 editorial changes, a manufacturer must formally file a
16 "supplement" to the NDA to effect any change in a drug's
17 prescribing information. Two types of supplements are used for
18 labeling changes. The first, a "Prior Approval Supplement,"
19 requires FDA's prior approval before implementation. 21 C.F.R.
20 § 314.70(b)(2)(v). The second, a "Changes Being Effectuated"
21 supplement ("CBE"), does not require prior approval but must
22 nonetheless be submitted to the FDA for its review and final
23 approval.³ 21 C.F.R. § 314.70(c)(6)(iii). Among the changes
24

25 ³ If a company pursues the CBE route and immediately
26 implements a labeling change, FDA continues to retain the right
27 to disapprove or modify the change at any time. In the event FDA
28 disapproves a CBE change after it is in the marketplace, the
company must immediately comply with FDA's judgment and revise
the label accordingly. If the company refuses, its drug is

(continued...)

1 that can be unilaterally made by the manufacturer using a CBE
2 supplement are changes to "add or strengthen a contraindication,
3 warning, precaution or adverse reaction." 21 C.F.R.
4 § 314.70(c)(6)(iii)(A). These changes, like all warnings, remain
5 subject to Section 201.57(c)(6)(I) and may only be added when
6 there is reasonable evidence of an association of a serious
7 hazard with the drug.

8 **B. Pertinent Aspects⁴ of Paxil's Regulatory History**

9 **1. FDA Review & Approval of Original Paxil NDA (1989-1992)**

10 On November 20, 1989, SmithKline Beecham Pharmaceuticals
11 ("SB")⁵ filed a NDA for paroxetine (Paxil) seeking FDA approval
12 for the treatment of depression in adults.⁶ (Pls.' Opp'n to
13 GSK's Stmt. of Undisputed Facts [Docket # 142-2], filed Nov. 14,
14 2007 ["UF"], ¶ 7.)⁷ SB submitted extensive data and information
15

16 ³(...continued)
17 misbranded and distribution is prohibited under the FDCA. (See
18 Arning Decl., filed Oct. 6, 2007, ¶s 16-17.)

18 ⁴ An exhaustive description of Paxil's regulatory history
19 is provided by GSK in its moving points and authorities (see
20 Docket #98 at 10-21). In many respects, plaintiffs object to
21 GSK's description. The entirety of Paxil's regulatory history,
22 however, is not pertinent to the court's resolution of the
23 motion, and as such, it recounts herein only that portion of the
24 history which it finds relevant to determination of the motion.
25 To the extent the history is repeated here, and as more fully
26 explained below, the court overrules any evidentiary objections
27 posed by plaintiffs.

28 ⁵ SB and GlaxoWellcome entities merged in or about
December 2000 to form GSK PLC. (UF ¶ 8.) This orders refers to
SB and GSK interchangeably at times.

⁶ Prescription Paxil is one of a class of drugs known as
selective serotonin reuptake inhibitors ("SSRIs"). (UF ¶ 6.)

⁷ Plaintiffs object to the vast majority of GSK's
proffered undisputed facts, primarily on the basis of irrelevancy
(continued...)

1 in this initial submission and in numerous amendments to the NDA
2 throughout the following three year period. These submissions to
3 the Paxil NDA included information describing any incidents of
4 suicidality in patients given placebo, Paxil or active control
5 drugs during clinical studies. (UF ¶ 9.)⁸

6 _____
7 ⁷(...continued)
8 (Fed. Rs. Evid. 402, 403) or improper authentication (Fed. R.
9 Evid. 602). More specifically, plaintiffs assert their
10 irrelevancy objections largely at GSK's proffered evidence
11 concerning a similar SSRI, Prozac. (See Pls.' Objs. and Mtn. to
12 Strike Evid. [Docket #151], filed Nov. 14, 2007.) Plaintiffs'
13 objections are unavailing; GSK has amply demonstrated the
14 multiple ways in which said evidence is relevant to this motion
15 (see Opp'n to Mtn. to Strike [Docket #160], at 9-11), and courts
16 considering similar motions and objections have rejected the
17 plaintiffs' similar irrelevancy claims (see Dusek v. Pfizer, 2004
18 WL 2191804, at *7 (S.D. Tex. Feb. 20, 2004) (rejecting argument
19 in Zolof case that the court should not consider FDA's
20 evaluation of Prozac's labeling when deciding a similar
21 preemption motion). As to plaintiffs' authentication objections,
22 they object to the authenticity and foundation of GSK's own
23 documents and publicly available FDA documents. Again,
24 plaintiffs' objections are unavailing. GSK's documents have been
25 authenticated by Dr. Arning and a proper foundation has been laid
26 to satisfy the business records exception to the hearsay rule.
27 (See GSK's Opp'n to Pls.' Add'l Disputed Facts [Docket #161],
28 filed Nov. 21, 2007, at 2-3.) As to the variety of FDA documents
submitted by GSK, these documents have likewise been properly
authenticated by GSK and clearly satisfy the business records
exception to the hearsay rule. (Id. at 3.) Indeed, despite
asserting these objections to the FDA related documents,
plaintiffs themselves cite and rely upon these documents in their
statement of additional disputed facts. Plaintiffs obviously
cannot have it both ways.

Ultimately, where the court describes herein any fact
objected to by plaintiffs on these grounds, plaintiffs'
objections are overruled, and the court finds the fact
undisputed. To the extent these issues are raised in plaintiffs'
motion to strike evidence (Docket #151), plaintiffs' motion is
denied.

⁸ Despite FDA's ultimate findings to the contrary,
plaintiffs contend that these initial submissions by SB, in 1989,
showed a statistically significant, greater than eight fold
increased risk of suicidal behavior--suicide and suicide
attempts--for adult patients put on Paxil when compared to
patients put on placebo (dummy) pills. Plaintiffs contend this
(continued...)

1 In late 1990 and early 1991, two groups filed "Citizen
2 Petitions" pursuant to 21 C.F.R. § 10.30, asking the FDA to
3 withdraw approval of the NDA for Prozac, the only approved SSRI
4 at the time. These petitions alternatively sought warning
5 statements in SSRI labeling regarding an increased risk of
6 suicide. (UF ¶s 12, 14.)

7 On October 3, 1990, because of the questions raised about an
8 increased risk of suicidality in Prozac, the FDA requested data
9 on suicidality from SB while the NDA for Paxil was under review.
10 (UF ¶ 11 [Specifically, FDA requested SB prepare a report
11 discussing the relationship between Paxil and "violence-ideation
12 and suicide ideation."].) On May 10, 1991, SB submitted an
13 analysis based on its worldwide clinical database that showed
14 that patients randomized to Paxil therapy were at no greater risk

15
16 ⁸(...continued)
17 information was not acted upon by the FDA because SB submitted
18 reports that included events or conclusory statements that
19 obscured or falsely stated the true reports. (See GSK's Resp. to
20 Pls.' Stmt. of Add'l Disputed Facts ["ADF"], filed Nov. 21, 2007,
21 ¶ 1-10.) More specifically, plaintiffs contend SB improperly
22 included pre-baseline events (run-ins) as post-baseline placebo
23 events. Pre-baseline means before a study actually begins, while
24 potential participants are being evaluated to determine if they
25 meet inclusion criteria as dictated by the clinical trial's
26 protocol. Plaintiffs maintain that it was improper to have
27 included run-in events in tabulations of post-baseline suicidal
28 behavior events and risk rates.

23 This dispute between the parties does not preclude entry of
24 summary judgment in favor of GSK on this motion for the reasons
25 set forth more fully below. In short, to the extent plaintiffs'
26 argument sounds in a claim of fraud, *i.e.*, that GSK defrauded the
27 FDA in obtaining approval of Paxil, such a claim is not
28 cognizable under Buckman v. Plaintiffs' Legal Comm., 531 U.S.
341, 348 (2001) (holding that the plaintiffs' state-law
fraud-on-the-FDA claims conflict with, and are therefore
impliedly pre-empted by federal law). Additionally, plaintiffs'
proffered evidence does not raise a triable issue of fact that
GSK was aware, at the time, of reasonable evidence of an
association between Paxil and suicidality in *pediatric* patients.

1 for suicidal ideation or behavior than patients who were
2 randomized to placebo or other active medication. (UF ¶ 13.)⁹
3 On June 19, 1991, Dr. Martin Brecher, the lead FDA safety
4 reviewer for the Paxil NDA issued his report, finding: "there is
5 no signal in this large data base that paroxetine exposes a
6 subset of depressed patients to additional risk for suicide,
7 suicide attempts or suicidal ideation." (UF ¶ 15.)

8 In September 1991, FDA convened a Psychopharmacological
9 Drugs Advisory Committee ("PDAC") meeting to consider further
10 whether there was an association between SSRIs and suicide. (UF
11 ¶ 16.) The PDAC concluded, in agreement with prior findings of
12 the FDA itself (UF ¶s 18, 19), that no credible evidence existed
13 to conclude that antidepressants cause the "emergence and/or
14 intensification of suicidality and/or other violent behavior."
15 (UF ¶ 20.)

16 Ultimately, the FDA denied the citizen petitions regarding
17 Prozac, finding that there was no "reasonable evidence of an
18 association between the use of Prozac and suicidality." (UF ¶s
19 21, 22.)

20 Similarly, on October 5, 1992, during the PDAC panel meeting
21 on Paxil, FDA officials presented their analyses of the Paxil
22 NDA, including clinical trial data on safety and efficacy. (UF ¶
23 24.) Dr. Thomas Laughren reported that "there was no suggestion

24
25 ⁹ Plaintiffs dispute this fact, arguing that when GSK
26 responded to the FDA's request it again, as in 1989,
27 intentionally obscured the risks by improper inclusion of the
28 run-in events in the post-baseline tabulations (ADF ¶s 16-20);
according to plaintiffs' experts, when analyzed correctly, the
net result is that the adult patients on Paxil had a
statistically significant greater than eight-fold increase in
suicidal behavior. (UF ¶ 13.)

1 here of emergence of suicidality with paroxetine." (UF ¶ 26.)

2 The PDAC found Paxil safe and effective for use in the treatment
3 of adult depression and voted unanimously in favor of approval.

4 (UF ¶ 27.)

5 On December 29, 1992, the FDA issued an approval letter for
6 Paxil which made clear that the approval was conditioned on the
7 use of the FDA-approved prescribing information. (UF ¶ 29.) The
8 original FDA-approved labeling did not include any warning or
9 other statement indicating there was an increased risk of suicide
10 or suicidality from Paxil. The only references to "suicide" or
11 "suicide attempt" in the labeling appeared in the description of
12 "a major depressive episode" and a precaution that suicide is an
13 inherent risk in depressed patients. (UF ¶ 30.)¹⁰

14 During the period from Paxil's original approval in 1992
15 through January 2004, the FDA reviewed and approved at least 12
16 supplemental NDAs for new therapeutic indications for Paxil, and
17 two additional NDAs for new formulations of Paxil, an oral
18 suspension and a controlled release version of the drug. (UF ¶

19
20 ¹⁰ Following the 1992 approval of Paxil for the treatment
21 of adult depression, SB approved in August 1993 a clinical trial,
22 "Study 329," involving a multi-center, double blind, placebo
23 controlled study of paroxetine and imipramine in adolescents
24 (ages 12 to 18 years, 11 months old) with unipolar major
25 depression. (ADF ¶ 32.) Plaintiffs contend that beginning in
26 1994 through 1996, SB received reports from clinical
27 investigators of adolescents experiencing suicidality on Paxil.
28 (ADF ¶s 34-37.) GSK disputes these facts, arguing plaintiffs
misreport the investigators' true findings (*id.*), and regardless,
SB did not break the blind on the acute phase of the trial until
October 1997, after Benjamin's death (UF ¶ 43). The results of
this study were not submitted to the FDA until May 2003,
following GSK's April 2002 application for approval of Paxil for
children. For the reasons set forth below, the court finds that
evidence pertaining to Study 329 does not raise a triable issue
as to whether SB/GSK was aware of an association of suicidality
and pediatric patients prior to February 1997.

1 31.) Each approval was conditioned on the verbatim use of the
2 FDA-approved prescribing information and warnings. (UF ¶ 33.)
3 Where required, SB and GSK submitted to the FDA ISSs, which
4 included all available information about the safety of the drug
5 product, including adverse events. (UF ¶ 35.) The FDA used
6 these opportunities to review updated safety information and
7 require certain changes to Paxil's labeling. (UF ¶ 34.) None of
8 these reviews, however, required labeling relating to an
9 association between Paxil and suicide or suicidality in adult or
10 pediatric patients. (UF ¶ 39.)

11 **2. FDA's Continued Monitoring of Paxil's Safety (1995-**
12 **2003)**

13 On June 9, 1995, in response to the FDA's request, SB
14 submitted data and reported that studies indicated no increased
15 suicidality associated with paroxetine or clomipramine when
16 compared with placebo. (UF ¶ 40.)

17 In 1997, another citizen petition was filed with the FDA
18 which sought to require a warning in the prescribing information
19 for Prozac that "people who are considered at risk for suicide
20 and who begin to take [Prozac] should be carefully observed and
21 should consider taking a sedative as well." On June 25, 1997,
22 the FDA rejected the petition, explaining that it "carefully
23 considered the issue of whether Prozac was associated with
24 suicidal ideation and suicidality and concluded that no labeling
25 revisions were warranted." (UF ¶s 41, 42.)

26 At various times between July 1999 and February 2003, in
27 response to FDA requests or on its own, SB and/or GSK submitted
28

1 data to the FDA regarding the incidence of suicide in randomized
2 controlled trials for Paxil. (UF ¶s 45-48.)

3 **3. FDA Public Health Advisories, Advisory Committee**
4 **Meetings and Labeling Changes for SSRIs regarding**
5 **Pediatric Suicidality (2003-2004)**

6 On May 23, 2003, GSK submitted to the FDA analyses of the
7 reports of possible "suicide attempts" and "possibly suicide-
8 related" events from the pediatric-only clinical trials. During
9 the "on-therapy plus 30 days post-therapy period," there was a
10 statistically significant difference between paroxetine and
11 placebo when the data from all pediatric studies included in the
12 analyses were pooled together. (UF ¶ 49.) On June 19, 2003, the
13 FDA issued a Talk Paper, reporting that it was "reviewing reports
14 of a possible increased risk of suicidal thinking and suicide
15 attempts in children and adolescents under the age of 18 treated
16 with the drug Paxil for major depressive disorder (MDD)." The
17 advisory stated: "Although the FDA had not completed its
18 evaluation of the new safety data, FDA is recommending that Paxil
19 not be used in children and adolescents for the treatment of
20 MDD." (UF ¶ 50.) The FDA did not take any action with respect
21 to Paxil's labeling and warnings at that time. (UF ¶ 51.)

22 On October 27, 2003, the FDA issued a Public Health Advisory
23 and corresponding Talk Paper, stating that the "data do not
24 clearly establish an association between the use of these drugs
25 and increased suicidal thoughts or actions by pediatric
26 patients." The Paper also provided, however, that it was "not
27 possible at this point to rule out an increased risk of these
28 adverse events [suicidality] for any of these drugs, including
Paxil" (UF ¶ 52.) The FDA scheduled an advisory

1 committee meeting for February 2, 2004 to discuss the available
2 data and pertinent regulatory actions. (UF ¶ 54.)

3 On February 2, 2004, an FDA advisory committee convened to
4 discuss the possible relationship between antidepressants and
5 suicidal thinking in pediatric patients, specifically patients 18
6 years of age and younger. (UF ¶ 61.) The committee ultimately
7 recommended that the FDA reanalyze the data on pediatric use,
8 warn the public and physicians of the possibility of suicidality
9 in the pediatric population and change the labeling for
10 antidepressants. (UF ¶ 64.) The committee met again in
11 September 2004, and concluded that in the aggregate, the data
12 reflected an increased risk of suicidality in pediatric patients
13 and recommended that the FDA consider new class labeling changes.
14 (UF ¶s 66, 67.)

15 On October 15, 2004, FDA issued a Public Health Advisory and
16 a letter directing all manufacturers to add a "black box" warning
17 and expanded warning statements to the labeling of all
18 antidepressant medications describing the increased risk of
19 suicidality in children and adolescents. (UF ¶ 68.)

20 On November 12, 2004, GSK submitted labeling supplements
21 seeking to add FDA's October 15, 2004 warnings to Paxil's
22 labeling. (Arning Decl., ¶ 56.) On January 12, 2005, FDA
23 approved GSK's application. (Id. at ¶ 58.) On January 26, 2005,
24 FDA notified GSK that it decided to "modify the new PI [package
25 insert] slightly so that the language in the 'Warnings Section'
26 of the PI more precisely mirrors the language set forth in the
27 black box warning." (UF ¶ 70.) Specifically, the FDA stated:
28

1 The sentence in the current "Warnings Section" of the
2 PI that reads, "A causal role of antidepressants in inducing
3 suicidality has been established in pediatric patients"
4 should be excised and replaced with the following:
5 "Antidepressants increased the risk of suicidal thinking
6 and behavior (suicidality) in short term studies in children
7 and adolescents with Major Depressive Disorder (MDD) and
8 other psychiatric disorders."

9 (Id.) On January 26, 2005, FDA approved the labeling supplements
10 for Paxil submitted by the company on November 12, 2004. (UF ¶
11 71.)¹¹

12 **C. Undisputed Facts Regarding Benjamin Bratt's Death**

13 Benjamin had a history of depression that predated both his
14 suicide and his ingestion of Paxil. (UF ¶ 1.) On February 6,
15 1997, Paxil was prescribed for Benjamin by his nurse
16 practitioner. (UF ¶s 2, 3.) On February 14, 1997, Benjamin
17 attempted to commit suicide by hanging himself. (UF ¶ 4.) On
18 February 15, 1997, Benjamin died from injuries sustained from his
19 suicide attempt. (UF ¶ 5.)

20 Plaintiffs, Benjamin's parents, filed this action on April
21 14, 2006 in El Dorado County Superior Court. Former co-defendant
22 McKesson Corporation (now dismissed) removed the action on the
23 basis of diversity jurisdiction to this court on May 15, 2006.
24 Plaintiffs' complaint asserts the following claims against GSK:
25 (1) negligence; (2) strict products liability; (3) breach of
26 express warranty; (4) fraud; and (5) negligent infliction of
27 emotional distress.

28 ¹¹ Certain other changes to Paxil's labeling were
conducted during 2005-2007 regarding adult suicidality. (See UF
¶s 70-91.) These facts are not pertinent to the instant motion,
and thus the court does not recount that portion of Paxil's
regulatory history.

1 STANDARD

2 A. Summary Judgment

3 The Federal Rules of Civil Procedure provide for summary
4 judgment where "the pleadings, depositions, answers to
5 interrogatories, and admissions on file, together with the
6 affidavits, if any, show that there is no genuine issue as to any
7 material fact." Fed. R. Civ. P. 56(c); see California v.
8 Campbell, 138 F.3d 772, 780 (9th Cir. 1998). The evidence must
9 be viewed in the light most favorable to the nonmoving party.
10 See Lopez v. Smith, 203 F.3d 1122, 1131 (9th Cir. 2000) (en
11 banc).

12 The moving party bears the initial burden of demonstrating
13 the absence of a genuine issue of fact. See Celotex Corp. v.
14 Catrett, 477 U.S. 317, 325 (1986). If the moving party fails to
15 meet this burden, "the nonmoving party has no obligation to
16 produce anything, even if the nonmoving party would have the
17 ultimate burden of persuasion at trial." Nissan Fire & Marine
18 Ins. Co. v. Fritz Cos., 210 F.3d 1099, 1102-03 (9th Cir. 2000).
19 However, if the nonmoving party has the burden of proof at trial,
20 the moving party only needs to show "that there is an absence of
21 evidence to support the nonmoving party's case." Celotex Corp.,
22 477 U.S. at 325.

23 Once the moving party has met its burden of proof, the
24 nonmoving party must produce evidence on which a reasonable trier
25 of fact could find in its favor viewing the record as a whole in
26 light of the evidentiary burden the law places on that party.
27 See Triton Energy Corp. v. Square D Co., 68 F.3d 1216, 1221 (9th
28 Cir. 1995). The nonmoving party cannot simply rest on its

1 allegations without any significant probative evidence tending to
2 support the complaint. See Nissan Fire & Marine, 210 F.3d at
3 1107. Instead, through admissible evidence the nonmoving party
4 "must set forth specific facts showing that there is a genuine
5 issue for trial." Fed. R. Civ. P. 56(e).

6 **B. Conflict Preemption**

7 The United States Constitution and federal laws and treaties
8 "shall be the supreme Law of the Land; and the Judges in every
9 State shall be bound thereby, any Thing in the Constitution or
10 Laws of any State to the Contrary notwithstanding." U.S. Const.
11 Art. VI, Cl. 2. In applying this standard, the United States
12 Supreme Court has recognized three types of federal preemption of
13 state law. First is express preemption, where Congress states
14 explicitly the preemptive effect of its legislation on state law.
15 English v. General Electric Co., 496 U.S. 72, 78-79 (1990).
16 Second is field preemption, where Congress intends for federal
17 law to occupy exclusively an entire field of regulation. Id. at
18 79. Third is conflict preemption, the type of preemption
19 advocated by GSK in this case. Conflict preemption can be either
20 direct or indirect. Direct conflict, or "impossibility
21 preemption," occurs where it is "impossible for a private party
22 to comply with both state and federal requirements;" indirect
23 conflict, or "obstacle preemption," exists "where state law
24 stands as an obstacle to the accomplishment and execution of the
25 full purposes and objectives of Congress." Sprietsma v. Mercury
26 Marine, 537 U.S. 51, 64 (2002) (internal quotations and citations
27 omitted); see also Witczak v. Pfizer, Inc., 377 F. Supp. 2d 726,
28 728 (D. Minn. 2005) (discussing the two forms of conflict

1 because it finds a direct conflict of law and thus bases its
2 decision on a finding of "impossibility preemption."

3 A direct conflict of law exists in this case because GSK
4 could not have been in compliance with federal law in February
5 1997 and have included the suicidality warning plaintiffs urge.
6 In other words, had GSK included the warning that plaintiffs
7 insist upon, GSK would have risked misbranding Paxil in violation
8 of the FDCA. Therein lies the actual and direct conflict
9 presented in this case--comply with federal law and be held
10 liable under state law tort claims, or, to avoid state tort
11 liability, add a warning without reasonable evidence and violate
12 federal law.

13 As the court will explain below, GSK and plaintiffs agree on
14 one critical point: GSK could not have changed the Paxil labeling
15 to include a warning of a potential association of suicidality in
16 pediatrics taking Paxil absent "reasonable evidence" of an
17 association. 21 C.F.R. § 201.57(c)(6)(I). The court cannot
18 find, however, on the evidence proffered by plaintiffs, that such
19 evidence existed *prior to* Benjamin's death in February 1997. In
20 fact, the evidence submitted by GSK suggests the contrary.
21 Clearly, plaintiffs' state law claims conflict directly with the
22 FDA-mandated labeling and warning for Paxil, at the relevant
23 time. Had GSK included the warning plaintiffs urge, contrary to
24 the FDA's approvals and absent reasonable evidence available at
25 the time, it would have misbranded the drug in violation of the
26 FDCA. Thus, plaintiffs' claims are preempted.

27 Before addressing these findings, the court notes
28 preliminarily that in reaching its decision it does not rely on

1 the preemption opinions of the FDA, as either expressed in the
2 various amicus briefs submitted by GSK in support of its motion¹²
3 or as stated in the 2006, so-called "Preemption Preamble."¹³
4 Since this is a case of conflict preemption, no formal statement
5

6 ¹² In their motion to strike evidence (Docket #151),
7 plaintiffs also seek to exclude all amicus briefs filed by GSK in
8 support of its motion. The submitted amicus briefs were filed by
9 the FDA in other failure to warn litigation relating to SSRIs.
10 While the court does not rely on these briefs in reaching its
11 decision herein, it does not strike the evidence as requested by
12 plaintiffs. Plaintiffs' primary objection on hearsay grounds is
13 unpersuasive. Courts routinely consider amicus briefs filed in
14 other litigation. See e.g. In re Bextra and Celebrex Mktg. Sales
15 Practices & Prod. Liab. Litig., 2006 WL 2374742, at *5 (N.D. Cal.
16 Aug. 16, 2006); Witczak v. Pfizer, Inc., 377 F. Supp. 2d 726, 730
17 n. 6 (D. Minn. 2005). Moreover, even if the amicus briefs were
18 considered hearsay evidence, the briefs fall under the public
19 records exception to the hearsay rule. Fed. R. Evid. 803(8).
20 The briefs also do not need to be purely factual to be
21 admissible. See e.g. Breech Aircraft Corp. v. Rainey, 488 U.S.
22 153, 170 (1988); Gilbrook v. City of Westminster, 177 F.3d 839,
23 858-59 (9th Cir. 1999). Finally, plaintiffs assert a number of
24 other bases for exclusion of these briefs, none of which the
25 court finds persuasive. (See Opp'n to Mtn. to Strike at 6-9.) As
26 a result of these findings, the court denies plaintiffs' motion
27 to strike evidence (Docket #151) in its entirety.
28

18 ¹³ In 2006, the FDA issued its most recent labeling rule;
19 in the preamble to the rule, it explained the implications of its
20 labeling regulations on products liability claims, expressly
21 finding that: "under existing preemption principles, FDA approval
22 of labeling under the act, whether it be in the old or new
23 format, preempts conflicting or contrary State law." 71 Fed.
24 Reg. 3922, 3934 (Jan. 24, 2006). In making this finding, the FDA
25 provided certain examples of when it believes state laws are
26 preempted, with one situation specifically pertinent to this
27 case: "FDA believes that State laws conflict with and stand as an
28 obstacle to achievement of the full objectives and purposes of
Federal law when they purport to compel a firm to include in
labeling or advertising a statement that FDA has considered and
found scientifically unsubstantiated. In such cases, including
the statement in the labeling or advertising would render the
drug misbranded under the act (21 U.S.C. § 352(a) and (f))." 71
Fed. Reg. 3922, 3935. More specifically, the FDA found that
claims that a drug sponsor breached an obligation to warn by
failing to include contraindications or warnings that are not
supported by evidence that meets the standards set forth in this
rule are preempted. Id. at 3936.

1 of Congressional intent to preempt is necessary, nor is a
2 statement of agency intent required. Geier, 529 U.S. at 884; see
3 also Pennsylvania Employees Benefit Trust Fund v. Zeneca, Inc.,
4 2007 WL 2376312, at *6 (3rd Cir. Aug. 17, 2007) (recognizing that
5 conflict preemption arises absent an "express congressional
6 command"). Thus, consideration of the preemption views of the
7 FDA is not necessary to resolution of the motion. As such, the
8 court does not discuss herein the parties' various and lengthy
9 arguments in favor and against paying deference to the FDA's
10 views on whether cases such as this one are preempted by federal
11 law. Instead, this court's decision is driven by the facts of
12 this case, which point to only one conclusion--that at the
13 relevant time, GSK could not have complied with both federal and
14 state law requirements for the warning at issue. See accord
15 Dobbs v. Wyeth Pharma., 2008 WL 169021, at *13 (W.D. Okla. Jan.
16 17, 2008) (declining to pay deference to the "relatively broad
17 scope of preemption set forth in the Preamble and *amicus* briefs
18 filed [by the FDA] since 2000" since the particular facts of that
19 case "present[ed] a narrower issue").

20 **A. FDA-Mandated Labeling and Warnings for Paxil Pre-February**
21 **1997**

22 **Federal law requires GSK to follow FDA's labeling and to use**
23 the FDA-approved labeling verbatim. 21 U.S.C. § 314.105(b). If
24 GSK departs from these federal requirements and inserts
25 unsubstantiated warnings, the drug labeling will be false and/or
26 misleading, and the company could be subjected to enforcement
27 actions. See 21 U.S.C. § 352(a), (f).
28

1 Here, plaintiffs do not dispute that prior to February 1997,
2 the FDA did not require that SB/GSK warn of an increased risk of
3 suicidality in patients taking Paxil, adult or adolescent. While
4 Paxil's NDA was under review during 1989 through 1992, the FDA
5 considered whether any credible evidence existed to find that
6 antidepressants cause the emergence and/or intensification of
7 suicidality and/or violent behavior, and concluded that no such
8 evidence existed. (UF ¶ 20.) Ultimately, the FDA denied two
9 citizen petitions directed at Prozac, a similar SSRI to Paxil, on
10 the basis of this conclusion. (UF ¶s 21, 22.) Similarly, the
11 PDAC panel on Paxil specifically concluded that "there is no
12 suggestion here of emergence of suicidality with paroxetine."
13 (UF ¶ 26.) The panel found Paxil safe and effective for use in
14 the treatment of adult depression and voted unanimously in favor
15 of approval. (UF ¶ 27.) The original FDA-approved labeling,
16 which SB/GSK was mandated to use (UF ¶ 29), did not include any
17 warning or other statement indicating there was an increased risk
18 of suicide or suicidality from Paxil. The only references to
19 "suicide" or "suicide attempt" in the labeling appeared in the
20 description of "major depressive episode" and a precaution that
21 suicide is an inherent risk in depressed patients. (UF ¶ 30.)

22 Prior to February 1997, the FDA considered two supplemental
23 NDAs for new therapeutic indications for Paxil (for obsessive
24 compulsive disorder and panic disorder), ultimately approving
25 these NDAs. Again, the FDA's approval was conditioned on the
26 verbatim use of the FDA-approved prescribing information and
27 warnings; like the initial approval, the required labeling did
28 not require any warning relating to an association between Paxil

1 and suicide or suicidality in adult or pediatric patients. (See
2 UF ¶s 31, 33-34, 39.)

3 It was not until June 2003, *six years* after Benjamin's
4 death, that the FDA first recognized "a possible increased risk
5 of suicidal thinking and suicide attempts in children and
6 adolescents under the age of 18 treated with the drug Paxil for
7 major depressive disorder (MDD)." (UF ¶ 50.) In an advisory
8 issued June 19, 2003, the FDA recommended that Paxil not be used
9 in children and adolescents for the treatment of MDD. (Id.)
10 The FDA did not take any action with respect to Paxil's labeling
11 and warnings at that time. (UF ¶ 51.)

12 The FDA continued to study the issue (UF ¶ 52),
13 commissioning an advisory committee to meet in February 2004 to
14 discuss the possible relationship between antidepressants and
15 suicidal thinking in pediatric patients. (UF ¶ 61.) Following
16 that meeting and in conformance with the committee's final
17 recommendations of September 2004 for class-wide labeling
18 changes, on October 15, 2004, the FDA issued a Public Health
19 Advisory and letter directing all manufacturers to add a "black
20 box" warning and expanded warning statements to the labeling of
21 all antidepressant medications describing the increased risk of
22 suicidality in children and adolescents. (UF ¶ 68.) Thus, it
23 was not until over *seven years* after Benjamin's death that the
24 FDA required labeling changes to warn of the risk plaintiffs
25 assert SB/GSK should have implemented prior to February 1997.

26 Thus, the record indicates that the type of warning which
27 plaintiffs claim SB/GSK should have included in its Paxil label
28 had been considered and rejected by the FDA because such a

1 warning was not supported by reasonable evidence at the time of
2 Benjamin's death. A state law determination, to the contrary,
3 that such a warning was required creates a conflict between
4 federal and state law and imposes inconsistent federal and state
5 obligations, thus warranting a finding of preemption.

6 A number of other courts have found similarly. For example,
7 in Tucker v. SmithKline Beecham Corp., 2007 WL 2726259, at *10
8 (S.D. Ind. Sept. 19, 2007) , the court held that "[b]ecause
9 [plaintiff's] state law [failure-to-warn] claims seeking to
10 impose liability on GSK represent an obstacle to the FDA's
11 efforts to ensure the proper use of Paxil, [the] claims are
12 preempted;" see also Sykes v. Glaxo-SmithKline, 484 F. Supp. 2d
13 289, 318 (E.D. Pa. 2007) (holding the plaintiffs' failure-to-warn
14 claims, regarding certain pediatric vaccines, conflict with the
15 FDCA, because the warnings "[were] not scientifically supported
16 and would have been false and misleading under federal law");
17 accord Dobbs v. Wyeth Pharmaceuticals, 2008 WL 169021, at *13
18 (Jan. 17, 2008) (same Effexor); Colacicco v. Apotex, Inc., 432 F.
19 Supp. 2d 514 (E.D. Pa. 2006) (same Paxil); Dusek v. Pfizer, Inc.,
20 2004 WL 3191804, at *8-10 (S.D. Tex. Feb. 20, 2004) (same
21 Zoloft); Needleman v. Pfizer, Inc., 2004 WL 1773697, at *5 (N.D.
22 Tex. Aug. 6, 2004) (same Zoloft); Ehlis v. Shire Richwood, Inc.,
23 233 F. Supp. 2d 1189, 1197 (D.N.D. 2002) (same Adderall); In re
24 Bextra and Celebrex Mktg. Sales Pracs. & Prods. Liab. Litig.,
25 2006 WL 2374742, at *9 (N.D. Cal. Aug. 16, 2006) (same Celebrex);

1 Conte v. Wyeth, Inc., 2006 WL 2692469, at *6 (Cal. Sup. Ct. Sept.
2 14, 2006) (same metroclopramide).¹⁴

3 Here, plaintiffs assert claims based on the failure to
4 include a warning unsubstantiated by reasonable evidence, and
5 thus, create a direct conflict with federal law. Because
6 plaintiffs assert claims based on a type of warning which the FDA
7 considered and rejected due to lack of reasonable evidence during
8 the relevant time period, this case presents the precise conflict
9 that courts have previously identified.

10 Nevertheless, plaintiffs maintain that the FDA did not
11 appreciate the necessity for a suicidality warning earlier
12 because SB obscured or falsely stated its data submitted to the
13

14 ¹⁴ The court acknowledges that there are other lower
15 courts (although none of these cases involved Paxil specifically)
16 which have declined to find preemption in prescription drug
17 cases. (See GSK's Mem. of P. & A. at 26 n. 14 [citing cases].)
18 Primarily, these courts reason that FDA drug labeling
19 requirements impose only "minimum standards" that may be
20 supplemented by state law, and therefore the state laws do not
21 conflict with federal law. The conclusion that FDA labeling
22 requirements are merely minimum standards emphasizes the FDA
23 regulations permitting a drug manufacturer to add warnings to its
24 label without prior FDA approval. However, for the reasons set
25 forth below, this court does not find that argument persuasive
26 because these courts (like plaintiffs here) fail to acknowledge
27 the significance of the other regulations which only require such
28 additions to a warning if "reasonable evidence" of an association
of a hazard with the drug exists. See Cartwright v. Pfizer, Inc.
369 F. Supp. 2d 876 (E.D. Tex. 2005). Where such evidence is not
present, as is the case here, there can be a finding of
impossibility preemption because state law may require precisely
what federal law does not. Moreover, even some of the courts
that have found no preemption on a theoretical level have
acknowledged that where the facts demonstrate that the FDA
actually considered and rejected a similar warning, conflict
preemption, via "impossibility preemption," may be found. See
e.g. Kelly v. Wyeth, 2007 WL 1302589 (Mass. Sup. 2007); Perry v.
Novartis Pharma. Corp., 456 F. Supp. 2d 678 (E.D. Pa. 2006).
Such are the facts in this case, which warrant a preemption
holding.

1 FDA in 1989 and 1991. According to plaintiffs, when analyzed
2 correctly, without including pre-baseline run-in events as if
3 they were post-baseline events, the net result is that patients
4 on Paxil have a statistically significant greater than eight-fold
5 increase in suicidal behavior. (ADF ¶s 1-11, 16-20.) According
6 to plaintiffs' experts, Drs. Glenmullen and Grimson, when
7 properly viewed, there are two overall conclusions that can be
8 drawn from the Paxil data regarding suicidality submitted in 1989
9 and 1991: (1) a patient treated with Paxil is at between three to
10 nine times greater risk of suicidality than if treated with a
11 placebo and this is a statistically (beyond chance) association;
12 and (2) if a Paxil treated patient experiences suicidality, then
13 more likely than not (68% to 89%) the suicidality is attributable
14 to Paxil. (Id.) Thus, plaintiffs contend that a warning
15 regarding suicidality should have been included in the Paxil
16 label from the outset.

17 Plaintiffs acknowledge that this early data pertained to
18 adults only. However, they contend that even with respect to the
19 pediatric population specifically, SB/GSK was aware of the need
20 for a suicidality warning prior to Benjamin's death in February
21 1997. Plaintiffs maintain that shortly after Paxil's 1992
22 approval for use in the treatment of adult depression, SB/GSK
23 became aware, via Study 329, that pediatric patients taking Paxil
24 were at an increased risk of suicide. According to plaintiffs,
25 SB/GSK began receiving reports from clinical investigators of
26 adolescents experiencing suicidality on Paxil as early as late
27 1994 and that by the Fall of 1996, a "substantial number of the
28 adolescents taking Paxil had experienced an adverse event

1 involving suicidality and/or hostility." (Opp'n at 9:8-9; ADF ¶s
2 34-37.)

3 Plaintiffs' counsel conceded at oral argument that to the
4 extent these arguments sound in a claim of fraud allegedly
5 perpetrated on the FDA by SB/GSK, such claim would be preempted
6 by the Supreme Court's decision in Buckman. In Buckman, the
7 Court held that patients' "state-law-fraud-on-the-agency" claims
8 against a manufacturer's representative were impliedly preempted
9 because the state claim of fraud would "inevitably conflict with
10 the FDA's responsibility to police fraud consistently with the
11 Administration's judgment and objectives." Buckman Co. v.
12 Plaintiffs' Legal Comm., 531 U.S. 341, 350 (2001). The court
13 found that as a practical matter, complying with the FDA's
14 detailed regulatory regime in the shadow of 50 States' tort
15 regimes would dramatically increase the burdens facing potential
16 applicants--burdens that were not contemplated by Congress in
17 enacting the FDCA. Id.¹⁵ Recognizing Buckman's parameters,
18 plaintiffs' counsel clarified plaintiffs' position at oral
19 argument.¹⁶ Significantly, counsel stated clearly that
20 plaintiffs are not pressing a Buckman-theory. He conceded that
21 there may well be a direct conflict of law in this case between

22
23 ¹⁵ The Court explained further that fraud-on-the-FDA
24 claims would also cause applicants to fear that their disclosures
25 to the FDA, although deemed appropriate by the Administration,
26 will later be judged insufficient in state court. Applicants
would then have an incentive to submit a deluge of information
that the Administration neither wants nor needs, resulting in
additional burdens on the FDA's evaluation of the application.
Id. at 351.

27 ¹⁶ Plaintiffs did not clearly make this concession in
28 their briefs; nor did they clearly articulate their theory for
why a direct conflict of law is not present in this case.

1 what the FDA required, at the time, and what plaintiffs' state
2 tort claims seek to impose. However, plaintiffs contend
3 nonetheless that there is no "impossibility preemption" in this
4 case because their theory rests not on what *the FDA* required of
5 SB/GSK with respect to the labeling and warnings for Paxil but
6 what *SB/GSK* was obligated to do by virtue of the federal statutes
7 and regulations at issue. In particular, the CBE regulation, 21
8 C.F.R. § 314.70(c)(6)(iii)(A), permitting a manufacturer to
9 unilaterally make changes, without prior FDA approval, to "add or
10 strengthen a contraindication, warning, precaution or adverse
11 reaction." Under this and the corollary laws, plaintiffs contend
12 SB/GSK was obligated to include the very warning plaintiffs seek
13 based on the evidence it had in its possession as early as 1989.
14 According to plaintiffs, federal and state law consistently
15 required the warning plaintiffs urge, and thus, there is no
16 conflict of law warranting a finding of preemption.

17 Therefore, the critical inquiry is whether reasonable
18 evidence existed to support the warning plaintiffs urge under the
19 federal standards. Both parties agree that SB/GSK was only
20 obligated to warn of the claimed risk if there was reasonable
21 evidence of an association of a serious hazard with the drug. 21
22 C.F.R. § 201.57(c)(6)(I). The parties, however, dispute whether
23 such evidence existed at the relevant time.

24 **B. No Reasonable Evidence Supported Contrary Label or Warning**
25 **Pre-February 1997**

26 Plaintiffs' proffered evidence is not sufficient to
27 demonstrate that prior to February 1997 there was reasonable
28 evidence of an association between Paxil and an increased risk of

1 suicidality in pediatric patients. With respect to the 1989 and
2 1991 data submitted by SB to the FDA, said data related to adults
3 only. Plaintiffs have not shown through their experts' testimony
4 or otherwise, that this data, even assuming plaintiffs' analysis
5 is correct, demonstrates that SB was aware or should have been
6 aware of an increased risk of suicidality in *pediatric* patients.
7 At best, this initial data represents an increased risk in adult
8 patients;¹⁷ however, plaintiffs proffer no evidence that this
9 data is translatable to the pediatric population. (See generally
10 Decls. of Drs. Grimson and Glenmullen, filed Nov. 14, 2007
11 [Docket #s 149 and 150], attaching expert reports, filed under
12 seal.) Indeed, plaintiffs' expert, Dr. Joseph Glenmullen,
13 testified at deposition that: "I can't represent to you what
14 they [SB/GSK] did and did not know as of February, '97 from the
15 pediatric data." (Glenmullen Dep., filed Oct. 10, 2007, at
16 174:2-174:4 [Docket #122].)

17 As to plaintiffs' reliance on Study 329, which did involve
18 clinical trials of adolescents taking Paxil, GSK could not have
19 known whether the study revealed a reasonable association of any
20 risk for pediatric patients until after Benjamin's death in
21 February 1997. It is undisputed that the results of Study 329
22 were not available for evaluation until after *October* 1997 when
23 GSK broke the blind on the acute phase of the study. (UF ¶

24
25
26 ¹⁷ However, the court notes that the FDA's current
27 position with respect to an increased risk of suicidality in
28 adults, over the age of 24, is to the contrary. While presently
a warning regarding an increased risk of suicidality is required
by the FDA with respect to pediatric patients, no such warning is
similarly required regarding some adults. (See UF ¶s 70-91.)

1 43.)¹⁸ Any clinical investigator reports that GSK may have
2 received prior to this time were not actionable as they did not
3 represent the final results of the study, and as explained by
4 GSK's counsel at oral argument, GSK would have been penalized for
5 breaking the blind on the study early. Thus, Study 329 is not
6 evidence which raises a triable issue of fact that GSK was aware
7 or should have been aware of an increased risk of suicidality in
8 pediatric patients *prior* to Benjamin's death in February 1997.¹⁹

9 In sum, plaintiffs' contention that because a statutory
10 procedure existed to petition the FDA for a label change, GSK
11 could have included a suicide warning regarding pediatric
12 patients in Paxil's labeling in February 1997 is unavailing.

13
14 ¹⁸ Indeed, plaintiffs' expert, Dr. Glenmullen, analyzed
15 the data from Study 329, as reflected in GSK's "Final Clinical
16 Report on Study 329," which was completed on November 24, 1998,
17 over a year after Benjamin's death. Thus, Dr. Glenmullen's
18 ultimate finding that GSK obscured, like with the 1989 and 1991
19 data on adults, a "statistically significant risk of Paxil-
20 induced suicidality in children" by inappropriately coding
21 treatment-emergent suicidality as emotional lability, hostility,
22 worsening depression, and euphoria, is not relevant to the
instant motion. (Ex. 2 to Glenmullen Decl. at 73.) Plaintiffs
correctly chose not to rely expressly on this opinion in their
briefing. Instead, plaintiffs only point to certain investigator
reports made during the study (which occurred from April 24, 1994
to May 7, 1997) and which pre-dated Benjamin's death. (See ADF
¶s 34-37.) However, these reports, even assuming the truth
thereof, cannot raise a triable issue of fact since Study 329 was
not finalized until 1998.

23 ¹⁹ In fact, by early 2004, the FDA had reviewed three
24 Paxil studies regarding suicidality and children and adolescents
25 and concluded that the studies were inconsistent with one another
26 because "a signal emerges from 1 study (329), but without even a
27 weak signal from the other 2 studies in the program." (Arning
28 Decl. at Ex. 25 at 16.) Not until October 2004, after the FDA
completed its review of the *aggregate* data from antidepressants
generally did the agency conclude that there may be an increased
risk of suicidality in pediatric patients. At this point, the
FDA directed all manufacturers of antidepressants to add a "black
box" warning of an association between pediatric patients and
suicidality.

1 Plaintiffs' argument fails to acknowledge the significance of the
2 fact that GSK was under this obligation by statute *only if* there
3 was reasonable evidence to support such a warning. 21 C.F.R.
4 § 201.57(c)(6)(I). As set forth above, plaintiffs have failed to
5 raise a triable issue of fact that such evidence existed. As
6 Tucker and Bextra make clear, to prevail on this argument,
7 plaintiffs must overcome the fact that "reasonable evidence" of
8 an association between Paxil and an increased risk of suicide in
9 pediatric patients was lacking prior to February 1997 to support
10 such a warning. That later clinical studies ultimately led to a
11 clear signal of pediatric suicidality, and that these studies
12 arguably reflected the initial data in 1989 and 1991 of similar
13 associations among adults, simply does not provide "reasonable
14 evidence" of the association of pediatric suicidality in February
15 1997.

16 Absent reasonable evidence of a risk, GSK had no basis to
17 petition FDA and simply did not have the option under federal law
18 to include or secure a lawful warning for that risk in the drug's
19 labeling. Had it done so, GSK would have misbranded the drug in
20 violation of the FDCA and subjected itself to a possible federal
21 enforcement action against it or the withdrawal of its NDA by the
22 FDA. Stated otherwise, the obligation under state law on GSK
23 that plaintiffs advance is flatly contrary to GSK's obligations
24 under federal law. As such, plaintiffs' claims must be found
25 preempted.

26 A final, alternative argument, plaintiffs contend that, at
27 least in part, there is no conflict in this case, because their
28 claims are not limited to Paxil's warning labeling, but extend to

1 "promotion, advertising and 'Dear Doctor' letters." (Pls.' Opp'n
2 at 23.) This argument is illogical. All promotional material
3 must be consistent with a drug's labeling. See 21 C.F.R. §
4 202.1. If the warning is prohibited in the labeling (the
5 prescribing information), the warning is not permitted in
6 promotional material. The FDA has comprehensive statutory
7 authority over all aspects of safety, efficacy, labeling,
8 marketing, advertising, and promotion of prescription drugs. The
9 FDCA and the FDA's regulations define "labeling" to include all
10 hard-copy promotional material "upon" or "accompanying" the drug,
11 which includes the package insert for the drug, and everything
12 from booklets to calendars, if the material is textually related
13 to the drug. 21 U.S.C. § 321(m); 21 C.F.R. § 202.1(1)(2). FDA's
14 regulation of prescription drug labeling would be meaningless if
15 GSK were free to undermine and contradict FDA-mandated warnings
16 through other publication means.²⁰ See Dowhal v. SmithKline
17 Beecham Cons. Healthcare, 32 Cal. 4th 910, 929 (2004) ("Warnings
18 through point-of-sale posters or public advertising could have
19 the same effect of frustrating the purpose of federal policy.")

20
21 ²⁰ The court finds that Perry v. Novartis Pharma. Corp.,
22 456 F. Supp. 2d 678 (E.D. Pa. 2006), the sole case relied upon by
23 plaintiffs in support of this argument, is wrongly decided as
24 contrary to the FDA statutes and regulations described above. In
25 Perry, the court denied the defendant's motion to dismiss,
26 finding that even if it were inclined to find that the defendant
27 could not have modified the FDA-approved labeling for Elidel to
28 include a warning about pediatric cancers, the court would still
deny the motion to dismiss because the plaintiffs were not
specific about the types of warnings they asserted defendant
should have provided; the court found that regardless of the
label warning, a plaintiff may have a viable, non-preempted claim
relating to another type of warning; for example, if the
plaintiff claimed that a manufacturer was negligent in not
sending an appropriate letter to prescribing physicians. Id. at
686.

1 **CONCLUSION**

2 The court's preemption holding herein is a narrow one. The
3 court does not hold that FDA drug approvals in general preempt
4 state law failure-to-warn claims. Rather, it finds on the
5 specific facts of this case, the precise state law failure-to-
6 warn claims plaintiffs assert are preempted because they are in
7 direct, actual conflict with federal law. Prior to February
8 1997, it is undisputed that the FDA had considered the issue of
9 an increased risk of suicidality and SSRIs, including Paxil, and
10 found that no casual relationship existed to merit a specific
11 suicidality warning for adults or pediatric patients. It was not
12 until 2004, seven years after Benjamin's death that the FDA
13 required such a warning for pediatric patients; to date, no such
14 warning is required for adults over the age of 24. Importantly,
15 GSK had no obligation to include a warning for pediatric patients
16 prior to February 1997 because there was no reasonable evidence
17 of an association between the drug and suicidality in children
18 and adolescents.

19 The court acknowledges that there is an understandable sense
20 of frustration when clinical studies reveal critical conclusions
21 after the fact as in this case, after the tragic suicide of
22 Benjamin Bratt. However, the failure of those studies to timely
23 signal adverse effects on pediatric patients does not overcome
24 conflict preemption here.

25 Thus, for the foregoing reasons, GSK's motion for summary
26 judgment on preemption grounds is GRANTED. Plaintiffs' complaint
27 against GSK is dismissed in its entirety. The Clerk of the Court
28

1 is directed to close this file.²¹

2 IT IS SO ORDERED.

3 DATED: January 30, 2008

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5 
6 FRANK C. DAMRELL, JR.
UNITED STATES DISTRICT JUDGE

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27 ²¹ The April 25, 2008 hearing on GSK's other pending
28 motions (Docket #s 91, 111, 116) is hereby VACATED and the
motions are DENIED as moot.