UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

ADRIAN HOLLEY, et al.,

Plaintiffs,

v.

GILEAD SCIENCES, INC.,

Defendant.

Case No. 18-cv-06972-JST

ORDER GRANTING IN PART AND DENYING IN PART MOTION TO DISMISS

Re: ECF No. 45

Before the Court is Defendant Gilead Sciences, Inc.'s motion to dismiss. ECF No. 45. The Court will grant the motion in part and deny it in part.

I. BACKGROUND

This case alleges that individuals who have taken one or more of Gilead's drugs containing tenofovir disoproxil fumarate ("TDF") have suffered unnecessary kidney and bone damage resulting from Gilead's failure to provide adequate warnings and its decision to develop drugs containing TDF rather than the safer compound tenofovir alafenamide fumarate ("TAF"). The complaint alleges the following: Plaintiffs have taken one or more drugs manufactured by Gilead that contain TDF. ECF No. 1 ¶ 22. Since 2001, Gilead "has received FDA [Food and Drug Administration] approval for five TDF-based drugs for the treatment of HIV": Viread in 2001, Truvada in 2004, Atripla in 2006, Complera in 2011, and Stribild in 2012. *Id.* ¶¶ 188-93. Viread has also been approved to treat Hepatitis B, and Truvada has been approved for use "in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk." *Id.* ¶¶ 189, 190. Gilead has received FDA approval for three drugs containing TAF that are counterparts to its previously approved TDF drugs: Genvoya in 2015 and Odefsey and Descovy in 2016. *Id.* ¶¶ 196-98. Genvoya, Odefsey,

and Descovy are "identical to" to Stribild, Complera, and Truvada, respectively, "except for the substitution of TAF for TDF." *Id.*

Prior to the approval of Viread, Gilead had discovered TAF. *Id.* ¶ 194. "TDF and TAF are two prodrug versions of the same parent drug, tenofovir, though TAF requires a dose more than ten times smaller than TDF to obtain the same therapeutic effect." *Id.* "Because TAF can be administered at a much lower does than TDF, its use is associated with less toxicity and fewer side effects." *Id.* ¶ 7. Prior to selling its first TDF drug in 2001, "Gilead knew that TDF posed a safety risk to patients' kidneys and bones, . . . that the relatively high dose of TDF created a greater risk of toxic effects, and that bone and kidney toxicities were even more likely to be seen with long-term use of TDF for the treatment of a virus that, for the foreseeable future, has no cure." *Id.* ¶ 5. "Despite knowing that TAF could be given at a much lower, safer dose," "that TDF causes kidney and bone damage and that TAF is safer for patients' kidneys and bones, Gilead designed the TDF Drugs to contain TDF rather than safer TAF." *Id.* ¶¶ 7, 279. When Gilead began selling its TAF drugs, it "convinced doctors to switch their patients from TDF-based to TAF-based regimens by demonstrating TAF's superior safety profile over TDF with respect to kidney and bone toxicity – the very benefits that Gilead could have and should have incorporated into its prior product designs but withheld from doctors and patients for over a decade." *Id.* ¶ 11.

"Stribild is even more toxic to patients' kidneys and bones than Gilead's other TDF-based products" because it contains a higher dose of TDF than required. *Id.* ¶ 14. In addition to TDF, Stribild contains cobicistat, a "pharmacoenhancer or 'booster' that inhibits the breakdown of elvitegravir, another active ingredient in Stribild." *Id.* ¶ 12. Prior to submitting Stribild for FDA approval, Gilead knew that "TDF-associated renal toxicity occurs more frequently in patients taking TDF as part of a boosted regimen," and that the TAF dosage in Genvoya, the TAF-equivalent to Stribild, could be reduced "from 25 mg to 10 mg to account for the fact that cobicistat significantly increases tenofovir concentrations." *Id.* ¶¶ 13-14. Nonetheless, "Gilead did not reduce the dose of TDF when it designed Stribild." *Id.* ¶ 14.

Gilead also "failed to adequately warn physicians and patients about the risks and safe use of TDF. Gilead provided only the weakest, inadequate warnings to doctors and patients about the

need for frequent monitoring of all patients for TDF-associated kidney and bone damage – preventing doctors from detecting early signs of TDF toxicity." *Id.* ¶ 15. For example, "after May 21, 2007, the TDF labels do not disclose that adverse kidney and bone events occurred in patients without pre-existing risk factors – which, combined with the warning to only routinely monitor patients at risk – gives the false impression that TDF is only harmful to people otherwise at risk for kidney and bone injuries." *Id.* ¶ 346. "Gilead's monitoring instructions for at risk patients taking Viread, Truvada, Atripla, and Complera, and patients taking Stribild are also inadequate because they fail to recommend a specific, frequent monitoring schedule for doctors to assess patients' kidney function." *Id.* ¶ 347. "Regularly scheduled, frequent monitoring of kidney function is necessary to catch early signs of TDF-induced toxicity and prevent injury because patients are generally asymptomatic during the early stages." *Id.* ¶ 345. Early detection of toxicity "is key to preventing serious, potentially irreversible renal injury," and monitoring also "ensure[s] that patients' kidneys are healthy enough to continue treatment" or that patients receive necessary dosage adjustments. *Id.* ¶ 324, 338.

Plaintiffs allege a financial motive for Gilead's alleged conduct. They allege that Gilead stopped developing TAF in 2004, claiming that it was too similar to TDF to continue development, but in reality did so because "Gilead did not want to hurt TDF sales by admitting that its TDF-based products are unreasonably and unnecessarily unsafe." *Id.* ¶ 8. Gilead also stood to gain by having two different periods of drug exclusivity: first for TDF drugs and later for TAF drugs. "Only once Gilead realized billions in sales through most of the TDF patent life did it seek to market safer TAF-based versions of its HIV medications." *Id.* ¶ 10. Gilead "provides stronger monitoring warnings to physicians and patients in the European Union than it does in the United States for the exact same TDF products. . . . There is no scientific or medical rationale for these differences. Gilead was more concerned with increasing or maintaining crucial U.S. sales than it was in safeguarding patients from the known risks of TDF." *Id.* ¶ 16.

On the basis of these allegations, Plaintiffs assert design-defect and failure-to-warn claims under multiple states' product liability and negligence laws. Plaintiffs also assert state-law fraud and consumer protection claims, as well as claims for the breach of implied warranty and

merchantability.

The complaint names 140 plaintiffs from 31 states. ECF No. 1 ¶¶ 24-163. Plaintiffs' counsel filed a nearly identical case, *Dowdy v. Gilead Sciences, Inc.*, Case No. 3:19-cv-00481-JST, on behalf of 25 different plaintiffs from 10 of the 31 states involved in this case. Case No. 3:19-cv-00481-JST, ECF No. 1 ¶¶ 23-47. The parties filed consolidated briefing on Gilead's motion to dismiss in both cases. ECF Nos. 45, 54, 60; *Dowdy* ECF Nos. 30, 40, 45. The Court granted the parties' stipulation to consolidate these cases for pretrial purposes on April 29, 2019, and ordered that "[t]he master docket and master file for the consolidated actions shall be 3:18-cv-06972-JST and the consolidated action shall bear the caption *Holley, et al. v. Gilead Sciences Inc.*" ECF No. 67 at 6.

Gilead moves to dismiss all of Plaintiffs' claims as preempted under federal law. It also argues that Plaintiffs' failure-to-warn claims should be dismissed because they do not adequately allege causation, and that their claims under state fraud and consumer protection laws should be dismissed because they do not comply with the heightened pleading requirements of Federal Rule of Civil Procedure 9(b). Finally, Gilead argues that another court's decision, *AIDS Healthcare Foundation, Inc. v. Gilead Sciences, Inc.*, No. C 16-00443 WHA, 2016 WL 3648623, at *9 (N.D. Cal. July 6, 2016), *aff'd*, 890 F.3d 986 (Fed. Cir. 2018), establishes that it had no duty to introduce drugs containing TAF at an earlier date, and that Plaintiffs' claims based on that allegation should therefore be dismissed.

II. JURISDICTION

This case involves more than 100 plaintiffs, and Gilead does not contest that at least some of the plaintiffs are of diverse citizenship from Gilead, which Plaintiffs allege is a Delaware corporation with a principal place of business in California. ECF No. 1 ¶¶ 24-164. Gilead also does not contest that the total amount in controversy exceeds $5,000,000, exclusive of interest and costs, or that each Plaintiff's claims exceed $75,000. *Id.* ¶ 18. This case therefore meets the statutory requirements for a "mass action" under the Class Action Fairness Act of 2005 ("CAFA"), and the Court has subject matter jurisdiction under 28 U.S.C. § 1332(d). *Corber v. Xanodyne Pharm., Inc.*, 771 F.3d 1218, 1222 (9th Cir. 2014) (en banc) ("CAFA provides federal

district courts with original jurisdiction over 'mass actions' if the actions meet all of the statutory requirements. 28 U.S.C. § 1332(d).").

The statute excludes from the definition of "mass action" any civil action in which "the claims have been consolidated or coordinated solely for pretrial proceedings." 28 U.S.C. § 1332(d)(11)(B)(ii)(IV). Although the *Holley* and *Dowdy* actions have thus far been consolidated only for pretrial purposes, ECF No. 67 at 6, this does not prevent the Court from exercising jurisdiction because the *Holley* action alone satisfies the statutory requirements for a "mass action." In addition, all of the plaintiffs in the *Dowdy* action have diverse citizenship from Gilead, so the Court independently has jurisdiction over that action under 28 U.S.C. § 1332(a)(1).

III. LEGAL STANDARD

A complaint must contain "a short and plain statement of the claim showing that the pleader is entitled to relief." Fed. R. Civ. P. 8(a). Dismissal under Federal Rule of Civil Procedure 12(b)(6) "is appropriate only where the complaint lacks a cognizable legal theory or sufficient facts to support a cognizable legal theory." *Mendiondo v. Centinela Hosp. Med. Ctr.*, 521 F.3d 1097, 1104 (9th Cir. 2008). A complaint need not contain detailed factual allegations, but facts pleaded by a plaintiff must be "enough to raise a right to relief above the speculative level." *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555 (2007). "To survive a motion to dismiss, a complaint must contain sufficient factual matter, accepted as true, to 'state a claim to relief that is plausible on its face.'" *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009) (quoting *Twombly*, 550 U.S. at 570). "A claim has facial plausibility when the plaintiff pleads factual content that allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged." *Id.* While this standard is not a probability requirement, "[w]here a complaint pleads facts that are merely consistent with a defendant's liability, it stops short of the line between possibility and plausibility of entitlement to relief." *Id.* (internal quotation marks and citation omitted). In determining whether a plaintiff has met this plausibility standard, a court must "accept all factual allegations in the complaint as true and construe the pleadings in the light most favorable" to the plaintiff. *Knievel v. ESPN*, 393 F.3d 1068, 1072 (9th Cir. 2005).

Federal Rule of Civil Procedure 9(b) requires that "a party must state with particularity the

circumstances constituting fraud or mistake" but allows that "[m]alice, intent, knowledge, and other conditions of a person's mind may be alleged generally." Allegations of fraud must "be specific enough to give defendants notice of the particular misconduct so that they can defend against the charge and not just deny that they have done anything wrong. Averments of fraud must be accompanied by the who, what, when, where, and how of the misconduct charged." *Vess v. Ciba-Geigy Corp. USA*, 317 F.3d 1097, 1106 (9th Cir. 2003) (internal quotation marks, alteration, and citation omitted). However, "a plaintiff in a fraud by omission suit will not be able to specify the time, place, and specific content of an omission as precisely as would a plaintiff in a false representation claim," and such a claim "will not be dismissed purely for failure to precisely state the time and place of the fraudulent conduct." *Falk v. Gen. Motors Corp.*, 496 F. Supp. 2d 1088, 1098-99 (N.D. Cal. 2007); *Washington v. Baenziger*, 673 F. Supp. 1478, 1482 (N.D. Cal. 1987) ("[A] plaintiff cannot plead either the specific time of the omission or the place, as he is not alleging an act, but a failure to act.").

IV. DISCUSSION

A. *AIDS Healthcare Foundation v. Gilead*

AIDS Healthcare Foundation previously filed an antitrust action concerning Gilead's TDF- and TAF-based drugs that also sought a declaration of patent invalidity and relief under California and Nevada unfair competition laws. *AIDS Healthcare Found.*, 2016 WL 3648623, at *4. Among the plaintiff's theories was that:

> Gilead knew of the efficacy and safety benefits of TAF in 2004 but shelved its clinical trials until 2011, leading to FDA approval (and a grant of NCE exclusivity) in 2015, just before the patents on TDF were set to expire.
>
> This, AIDS Healthcare contends, delayed the expiration date of Gilead's NCE exclusivity and thus delayed the moment that competitors would seek to challenge Gilead's patents on TAF. Further, it left consumers to bear the higher bone and kidney toxicity of TDF longer than necessary.

Id. at *9.[1] The court dismissed the California unfair competition law ("UCL") claim, concluding

[1] New chemical entity ("NCE") exclusivity "bars the FDA from approving any application for a drug containing the covered new chemical entity for five years following approval of the first

that Gilead "had no obligation to introduce the improved product at an earlier date. Any competitor could have beaten Gilead to market (and thus NCE exclusivity)." *Id.* The court explained that delaying introduction of a new product did not violate antitrust law, and "AIDS Healthcare cannot recast its claim that Gilead unreasonably restrained competition by allegedly delaying the release of TAF as a claim under the unfair prong of the UCL." *Id.*

Gilead seeks to rely on this decision to bar Plaintiffs from asserting any claims based on the contention that Gilead had a duty to introduce TAF drugs earlier. However, the Court does not find *AIDS Healthcare Foundation* to be dispositive. First, the case was an antitrust action, which addressed the question of whether Gilead had engaged in anticompetitive conduct. Concluding that Gilead owed no duty to its competitors says nothing about any duties Gilead might owe to consumers under state tort law.[2] Moreover, the persuasive weight of the court's decision is

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NDA [new drug application] containing that ingredient. The FDA also cannot receive applications for drugs containing that ingredient until the fourth year following the approval of the first NDA." *AIDS Healthcare Found.*, 2016 WL 3648623, at *2.

[2] Even AIDS Healthcare Foundation's UCL claim was based on alleged anticompetitive conduct, rather than a violation of any duty to consumers under state-law theories of strict liability and negligence:

> AIDS Healthcare's second theory (which appears only in its brief, not in its complaint) fares no better. AIDS Healthcare contends that Gilead knew of the efficacy and safety benefits of TAF in 2004 but shelved its clinical trials until 2011, leading to FDA approval (and a grant of NCE exclusivity) in 2015, just before the patents on TDF were set to expire.
>
> This, AIDS Healthcare contends, delayed the expiration date of Gilead's NCE exclusivity and thus delayed the moment that competitors would seek to challenge Gilead's patents on TAF. Further, it left consumers to bear the higher bone and kidney toxicity of TDF longer than necessary.
>
> AIDS Healthcare fails to explain how this "delay" constituted *unfair competition.* Gilead's patents gave it a monopoly over both TDF and TAF. It had no obligation to introduce the improved product at an earlier date. Any competitor could have beaten Gilead to market (and thus NCE exclusivity). "Without more, it is not unlawful [under antitrust law] for any competitor in any market to delay the introduction of a new product or an entire line of new products until, as [the plaintiff] alleged in this case, the competition forces such introduction." *Foremost Pro Color, Inc. v. Eastman Kodak Co.*, 703 F.2d 534, 545 (9th Cir. 1983). Under *Chavez*, AIDS Healthcare

diminished by the facts that the plaintiff raised this theory only in its opposition brief and not in the complaint, and the court allowed the plaintiff to seek leave to amend. *Id.* at *9. Finally, Gilead does not even attempt to argue that the requirements for claim preclusion or issue preclusion are satisfied. *AIDS Healthcare Foundation* does not warrant dismissal of any of Plaintiffs' claims.

B. Preemption

Gilead argues that Plaintiffs' claims based on design defect and failure to warn are preempted by federal law because it is impossible to comply with both state and federal regulations.[3] Preemption analysis "must be guided by two cornerstones":

> First, "the purpose of Congress is the ultimate touchstone in every pre-emption case." Second, "[i]n all pre-emption cases, and particularly in those in which Congress has 'legislated . . . in a field which the States have traditionally occupied,' . . . we 'start with the assumption that the historic police powers of the States were not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress.'"

Wyeth v. Levine, 555 U.S. 555, 565 (2009) (citations omitted) (alterations in original) (quoting *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485 (1996)). "Impossibility pre-emption is a demanding defense," and the burden for demonstrating impossibility rests with the party asserting preemption. *Id.* at 573 (concluding that "Wyeth has failed to demonstrate that it was impossible for it to comply with both federal and state requirements").

In the past decade, the Supreme Court has considered three preemption cases concerning drug manufacturers. First, in *Wyeth v. Levine*, the Court considered "whether the FDA's drug labeling judgments 'preempt state law product liability claims premised on the theory that

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> cannot recast its claim that Gilead unreasonably restrained competition by allegedly delaying the release of TAF as a claim under the unfair prong of the UCL.

Id. at *9 (emphasis and alterations in original). Gilead's attempt to recast *AIDS Healthcare Foundation* as a "consumer protection" case by quoting selectively from this passage, ECF No. 60 at 16-17, falls flat when the language is read in its entirety.

[3] Gilead argues that "Plaintiffs' remaining causes of action are based on the same flawed theories as their design defect and failure to warn claims" and are therefore preempted for the same reasons. ECF No. 45 at 22.

different labeling judgments were necessary to make drugs reasonably safe for use.'" 555 U.S. at 563 (quoting petition for certiorari). Like Gilead, Wyeth manufactured a brand-name drug, Phenergan, and contended that it "would have been impossible for it to comply with the state-law duty to modify Phenergan's labeling without violating federal law." *Id.* The Court explained the relevant provisions of the Federal Food, Drug, and Cosmetic Act ("FDCA"):

> The FDA's premarket approval of a new drug application includes the approval of the exact text in the proposed label. *See* 21 U.S.C. § 355; 21 CFR § 314.105(b) (2008). Generally speaking, a manufacturer may only change a drug label after the FDA approves a supplemental application. There is, however, an FDA regulation that permits a manufacturer to make certain changes to its label before receiving the agency's approval. Among other things, this "changes being effected" (CBE) regulation provides that if a manufacturer is changing a label to "add or strengthen a contraindication, warning, precaution, or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product," it may make the labeling change upon filing its supplemental application with the FDA; it need not wait for FDA approval. §§ 314.70(c)(6)(iii)(A), (C).

Id. at 568. The Court also explained that the CBE regulation was amended in 2008 to provide "that a manufacturer may only change its label 'to reflect newly acquired information.'" *Id.* (quoting 73 Fed. Reg. 49603, 49609). "Newly acquired information . . . may include (but is not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events, or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA." 21 C.F.R. § 314.3(b). "The rule accounts for the fact that risk information accumulates over time and that the same data may take on a different meaning in light of subsequent developments." *Levine*, 555 U.S. at 569. Although Wyeth had previously worked with the FDA to change Phenergan's labeling after the first incident of gangrene and amputation resulted from a Phenergan injection in 1967, the Court found persuasive that, "[i]n later years, as amputations continued to occur, Wyeth could have analyzed the accumulating data and added a stronger warning about IV-push administration of the drug." *Id.* at 569-70. The FDA "retains authority to reject labeling changes made pursuant to the CBE regulation in its review of the manufacturer's supplemental application," but this fact was not dispositive: "[A]bsent clear evidence that the FDA would not

have approved a change to Phenergan's label, we will not conclude that it was impossible for Wyeth to comply with both federal and state requirements."[4] *Id.* at 571.

In *PLIVA, Inc. v. Mensing*, 564 U.S. 604 (2011), the Supreme Court reached a different result when considering failure-to-warn claims against generic, rather than brand-name, drug manufacturers. The Court explained that "brand-name and generic drug manufacturers have different federal drug labeling duties." *Id.* at 613. "A brand-name manufacturer seeking new drug approval is responsible for the accuracy and adequacy of its label," but "[a] manufacturer seeking generic drug approval, on the other hand, is responsible for ensuring that its warning label is the same as the brand name's." *Id.* The Court concluded that generic manufacturers cannot use "the CBE process to unilaterally strengthen their warning labels" and assumed without deciding that FDA regulations require that "[g]eneric drug manufacturers that become aware of safety problems must ask the agency to work toward strengthening the label that applies to both the generic and brand-name equivalent drug." *Id.* at 614, 616-17. The Court found it would be impossible for generic manufacturers to comply with both state and federal duties: "Although requesting FDA assistance would have satisfied the Manufacturers' federal duty, it would not have satisfied their state tort-law duty to provide adequate labeling. State law demanded a safer label; it did not instruct the Manufacturers to communicate with the FDA about the possibility of a safer label." *Id.* at 619. "[F]ederal law would permit the Manufacturers to comply with the state labeling requirements if, and only if, the FDA and the brand-name manufacturer changed the brand-name label to do so." *Id.* at 620. This was sufficient to establish impossibility preemption because the manufacturers could not "independently do under federal law what state law requires of it," *id.* – that is, "federal law directly conflicts with state law," *id.* at 624 n.8. "[W]hen a party cannot satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for pre-emption purposes." *Id.* at 623-24. The Court explained that

[4] On January 7, 2019, the Supreme Court heard oral argument in *Merck Sharp & Dohme Corp. v. Albrecht* (No. 17-290), an appeal from *In re Fosamax (Alendronate Sodium) Products Liability Litigation*, 852 F.3d 268 (3d Cir. 2017), *cert. granted sub nom.*, 138 S. Ct. 2705 (June 28, 2018), in which the Third Circuit opined on the "clear evidence" standard.

Levine "is not to the contrary." *Id.* at 624. "The Court in [*Levine*] asked what the drug manufacturer could independently do under federal law, and in the absence of clear evidence that Wyeth could not have accomplished what state law required of it, found no pre-emption." *Id.* at 624 n.8.

In the third case to consider preemption in this context, the Supreme Court held that "state-law design-defect claims that turn on the adequacy of a drug's warnings are pre-empted by federal law" as to generic manufacturers. *Mut. Pharm. Co. v. Bartlett*, 570 U.S. 472, 476 (2013). The Court "[began] by identifying [a drug manufacturer's] duties under state law" and determined that New Hampshire law "requires manufacturers to ensure that the products they design, manufacture, and sell are not 'unreasonably dangerous.' The New Hampshire Supreme Court has recognized that this duty can be satisfied either by changing a drug's design or by changing its labeling." *Id.* at 480, 482. A generic manufacturer could not change the drug's design, both because federal law "requires a generic drug to have the same active ingredients, route of administration, dosage form, strength, and labeling as the brand-name drug on which it is based," and because, in this case, the drug had a "simple composition" that "is chemically incapable of being redesigned." *Id.* at 483-84. As a result, the only way for Mutual to comply with New Hampshire law would be for it to strengthen the drug's warning label. *Id.* at 484. But, "[a]s [*Mensing*] made clear, federal law prevents generic drug manufacturers from changing their labels. Thus, federal law prohibited Mutual from taking the remedial action required to avoid liability under New Hampshire law." *Id.* at 486 (citations omitted). The Court rejected the "'stop selling' rationale," adopted by the Court of Appeals, that compliance with both laws was not impossible because Mutual could have chosen not to manufacture the drug at all. *Id.* at 488. The Court explained that its "pre-emption cases presume that an actor seeking to satisfy both his federal- and state-law obligations is not required to cease acting altogether in order to avoid liability." *Id.*

Reading these cases together, this Court discerns the following two-step analysis for impossibility preemption in the drug-manufacturing context: First, courts must determine whether a drug manufacturer may independently take action that complies with both state and federal law. An action is independent under this analysis if the manufacturer can take such action without prior

FDA approval, even if the FDA may subsequently reject approval of the action post hoc. If independent action is not possible, then the state-law claims are preempted. If independent action is possible, then the claims are preempted only if there is clear evidence that the FDA would not grant approval. *Levine*, 555 U.S. at 571 ("[A]bsent clear evidence that the FDA would not have approved a change to Phenergan's label, we will not conclude that it was impossible for Wyeth to comply with both federal and state requirements").

1. Design-Defect Claims Based on Drug Composition

Plaintiffs allege that Gilead violated various state laws by designing and submitting for FDA approval drugs that contained TDF rather than TAF, which they allege was a safer alternative available at the time. Plaintiffs also allege that Gilead should have designed Stribild with a lower dose of TDF. Gilead argues that these design-defect claims based on drug composition are preempted.

Before considering whether a manufacturer can comply with both state and federal law, courts must determine a manufacturer's duties under each law. *E.g.*, *Bartlett*, 570 U.S. at 480 ("We begin by identifying petitioner's duties under state law."); *Mensing*, 564 U.S. at 611 ("Pre-emption analysis requires us to compare federal and state law. We therefore begin by identifying the state tort duties and federal labeling requirements applicable to the Manufacturers."). The parties here have not attempted to describe Gilead's duties under any particular state law.[5] The question presented by Gilead's motion is therefore not whether any particular state law is preempted but, rather, whether *all* state-law claims based on pre-approval drug composition are preempted. For purposes of this analysis, the Court assumes without deciding that the state laws

[5] On reply, Gilead makes a cursory argument that one of the cases relied on by Plaintiffs "ultimately *dismissed* plaintiff's pre-approval design defect claim as a matter of state law, because 'courts throughout the country have held that a party may not show a reasonable alternative design *by pointing to the availability of a different drug available for the same purpose*.'" ECF No. 60 at 10-11 (emphasis in original) (quoting *Young v. Bristol-Myers Squibb Co.*, No. 4:16-CV-00108-DMB-JMV, 2017 WL 706320, at *10 (N.D. Miss. Feb. 22, 2017)). But "[i]t is inappropriate to consider arguments raised for the first time in a reply brief." *Ass'n of Irritated Residents v. C & R Vanderham Dairy*, 435 F. Supp. 2d 1078, 1089 (E.D. Cal. 2006). Moreover, the *Young* court noted that whether an alleged alternative design is instead a different product is generally a question of fact. *Young*, 2017 WL 706320, at *11. It nonetheless concluded that the plaintiff's allegations failed as a matter of law because they "point[ed] to drugs which by their very nature perform a different function." *Id.* The allegations in this case are distinguishable.

invoked by Plaintiffs required Gilead to use TAF rather than TDF, and to use a lower dose of TDF before submitting Stribild to the FDA for approval.

The Supreme Court has not addressed whether federal law preempts design-defect claims against a brand-name manufacturer on grounds that, prior to initial FDA approval, the drug should have had a different composition.[6] Some language from *Bartlett* could arguably be read broadly to cover all design-defect claims, including those brought against brand-name manufacturers. *E.g.*, 570 U.S. at 477 ("Once a drug – whether generic or brand-name – is approved, the manufacturer is prohibited from any major changes to the 'qualitative or quantitative formulation of the drug product, including active ingredients, or in the specifications provided in the approved application.'" (quoting 21 C.F.R. § 314.70(b)(2)(i))); *id.* at 490 ("[A]s discussed at length above, we hold that state-law design-defect claims like New Hampshire's that place a duty on manufacturers to render a drug safer by either altering its composition or altering its labeling are in conflict with federal laws that prohibit manufacturers from unilaterally altering drug composition or labeling." (citation omitted)). However, *Bartlett* involved only a generic manufacturer, and the Supreme Court has recognized that brand-name and generic manufacturers are subject to different federal requirements. *E.g.*, *Mensing*, 564 U.S. at 613. As the Sixth Circuit case relied on heavily by Gilead, and which the Court discusses below, explained, "the *Bartlett* Court did not reach the sweeping conclusion that all design defect claims are preempted by federal law, but rather applied the impossibility preemption analysis to the plaintiff's design defect claim regarding a generic drug, and clarified that preemption cannot be avoided if the only way a manufacturer can comply with both federal and state law is to exit the market." *Yates v. Ortho-McNeil-Janssen Pharm., Inc.*, 808 F.3d 281, 296 (6th Cir. 2015).

The Sixth Circuit is the only Court of Appeals to have ruled on whether pre-approval design-defect claims against a brand-name manufacturer are preempted. In *Yates*, the court noted

[6] Plaintiffs' opposition makes clear that they are not pursuing claims that Gilead should have pursued a different drug composition after approval. ECF No. 54 at 9 (arguing that "no federal law prevented Gilead from designing its TDF drugs to be safer before U.S. Food and Drug Administration ('FDA') approval"); *id.* at 21 ("Gilead's remaining cases are inapposite because they did not address allegations that the manufacturer should have changed the drug design before approval."). The Court therefore does not consider whether post-approval claims are pre-empted.

that "counsel for defendants has cited no federal law that restricts a brand-name drug manufacturer from designing a reasonably safe product prior to FDA approval"; that the plaintiff argued that the existence of a different contraceptive that was chemically distinct and marketed in other countries "shows that redesign of ORTHO EVRA® [the contraceptive at issue] was possible prior to submitting for FDA approval"; and that the defendants "have offered no evidence that the FDA would have exercised its authority to prohibit defendants from creating and submitting such a design for approval." 808 F.3d at 299. Relying on *Mensing*, the court found that these facts were insufficient to escape preemption:

> But Yates's argument regarding defendants' pre-approval duty is too attenuated. To imagine such a pre-approval duty exists, we would have to speculate that had defendants designed ORTHO EVRA® differently, the FDA would have approved the alternate design. Next, we would have to assume that Yates would have selected this method of birth control. Further yet, we would have to suppose that this alternate design would not have caused Yates to suffer a stroke. This is several steps too far. Even if New York law requires defendants to produce and market a different design, the ultimate availability to Yates is contingent upon whether the FDA would approve the alternate design in the first place. . . . Defendants could not have complied with whatever pre-approval duty might exist without ultimately seeking the FDA's approval prior to marketing ORTHO EVRA®, and certainly prior to Yates's use of the drug.

Id. at 299-300. The court also concluded that allowing a pre-approval claim to proceed would run afoul of *Bartlett*'s admonition that an actor seeking to comply with both state and federal law need not "cease acting altogether in order to avoid liability." *Id.* at 300 (quoting *Bartlett*, 570 U.S. at 488). "In contending that defendants' pre-approval duty would have resulted in a birth control patch with a different formulation," the court reasoned, "Yates essentially argues that defendants should never have sold the FDA-approved formulation of ORTHO EVRA® in the first place. We reject this never-start selling rationale for the same reasons the Supreme Court in *Bartlett* rejected the stop-selling rationale of the First Circuit." *Id.*

District courts that have considered the question have ruled both ways. Of those courts that are not bound by the Sixth Circuit's ruling in *Yates*, a majority has found no preemption under these circumstances. *In re Xarelto (Rivaroxaban) Prods. Liab. Litig.*, No. MDL 2592, 2017 WL 3188456, at *6 (E.D. La. July 21, 2017); *Young v. Bristol-Myers Squibb Co.*, No. 4:16-CV-00108-

DMB-JMV, 2017 WL 706320, at *7-8 (N.D. Miss. Feb. 22, 2017); *Guidry v. Janssen Pharm., Inc.*, 206 F. Supp. 3d 1187, 1206-09 (E.D. La. 2016); *Sullivan v. Aventis, Inc.*, No. 14-CV-2939-NSR, 2015 WL 4879112, at *6 (S.D.N.Y. Aug. 13, 2015); *Estate of Cassel v. Alza Corp.*, No. 12-CV-771-WMC, 2014 WL 856023, at *2-6 (W.D. Wis. Mar. 5, 2014). Gilead cites only two district court cases outside the Sixth Circuit that have addressed pre-approval claims. In the first, the court did not rely on *Yates* but reached the same conclusion: "The complaint's allegations of harm due to the design defect go to the nature of the composition of the drug. The defendants had no ability to alter that composition without prior approval of the FDA." *Utts v. Bristol-Myers Squibb Co.*, 226 F. Supp. 3d 166, 186 (S.D.N.Y. 2016). The court therefore dismissed the design-defect claims with prejudice. *Id.* In addition to being against the weight of authority, the *Utts* decision is unpersuasive because it relied on portions of the lead opinion in *Mensing* that did not constitute the opinion of the Court. *Id.* (quoting *Mensing*, 564 U.S. at 622-23); *see Mensing*, 564 U.S. at 607 (syllabus noting that Part III-B-2 of Justice Thomas's opinion was joined by only three other Justices). In the second case, the court cited *Yates* for the proposition that "it is likely, even if Enbrel [the drug in question] is capable of redesign, that any claim that Defendants should have changed Enbrel's design before seeking FDA approval would likewise be preempted." *Small v. Amgen, Inc.*, No. CV 2:12-476-FTM29-CM, 2016 WL 4942078, at *2 (M.D. Fla. Jan. 25, 2016). But the court went on to determine that the questions "are matters for post-discovery dispositive-motion practice, not a motion for judgment on the pleadings." *Id.* It therefore does not support dismissal on preemption grounds.

Additionally, a case raising similar allegations against Gilead regarding its TDF and TAF drugs is currently pending in California state court. The judge in that case recently distinguished *Yates* and overruled Gilead's demurrer as to the plaintiffs' pre-approval design-defect claims. *Lujano v. Gilead Scis., Inc.*, No. BC702302, at 2-4 (Cal. Sup. Ct. Feb. 13, 2019) (ECF No. 55-1 at 3-5).

The Court finds persuasive the weight of authority against a finding of preemption. As noted above, the Court must first consider whether Gilead could take independent action in compliance with both state and federal law. The question is not whether a drug manufacturer can

"independently sell pharmaceutical drugs without FDA approval"; it is whether "a drug manufacturer [can] independently design a reasonably safe drug in compliance with its state-law duties before seeking FDA approval." *Guidry*, 206 F. Supp. 3d at 1208. That a brand-name manufacturer cannot market a redesigned version of an approved drug without first seeking additional FDA approval does not address whether the "manufacturer was required to use the allegedly defective design in the first place." *Trahan v. Sandoz, Inc.*, No. 3:13-cv-350-J-34MCR, 2015 WL 2365502, at *6 n.5 (M.D. Fla. Mar. 26, 2015). Gilead "has cited no federal law that restricts a brand-name drug manufacturer from designing a reasonably safe product *prior* to FDA approval" and, in particular, has identified no federal law that would have prevented it from developing and submitting for approval drugs that contained TAF rather than TDF, or from presenting for approval a version of Stribild with a lower dose of TDF. *Sullivan*, 2015 WL 4879112, at *6 (emphasis in original). At this stage of the proceedings, the Court therefore concludes that Gilead could have independently complied with both state and federal law prior to submitting the TDF drugs for FDA approval. Because Gilead has not presented "clear evidence" that the FDA would not have approved the allegedly safer versions of the drugs that Plaintiffs contend would have complied with state law, Plaintiffs' pre-approval design-defect claims are not preempted. *Levine*, 555 U.S. at 571.

The Court rejects the *Yates* court's "too attenuated" theory because, as the *Guidry* court reasoned:

> [T]he Sixth Circuit merely outlines the requisite assumptions for *all* defective design claims. . . . Indeed, every defective design claim requires consideration of hypothetical scenarios – what different steps *could have* been taken that *may have* prevented the plaintiff's injury. The only added assumption in the pharmaceutical context is that the FDA would have approved the safer, hypothetical drug. It is not too attenuated to assume that the FDA would approve a safer, alternative design of a drug that it has already approved.

206 F. Supp. 3d at 1208 (emphasis in original). This is especially true where, as here, Plaintiffs allege that three of the allegedly safer drugs were actually approved by the FDA years later. *Lujano* at 3-4 (ECF No. 55-1 at 4-5).

Similarly, the Court agrees that "*Yates* misstates the 'stop selling' rationale explained in

Bartlett." *Young*, 2017 WL 706320, at *8. Under *Bartlett*, "an actor seeking to satisfy both his federal- and state-law obligations is not required to cease acting altogether in order to avoid liability." 570 U.S. at 488. But "[t]he preapproval theory does not argue that a manufacturer should have stopped acting, just that it should have acted *differently*." *Young*, 2017 WL 706310, at *8 (emphasis in original). A pre-approval theory of liability in this case "does not run afoul of the admonition in *Bartlett*" because "Plaintiffs' argument would not require [Gilead] to stop selling in order to comply with both state and federal law." *Lujano* at 4 (ECF No. 55-1 at 5). Plaintiffs do not argue that Gilead "should have complied with both federal and state law by not selling a drug. Rather Plaintiffs contend that, under state law, [Gilead] should have offered for FDA approval a drug formulation with fewer side effects, and that [Gilead] could have complied with both state and federal law by formulating a drug with TAF, a formulation that eventually was approved by the FDA." *Id.* Thus, *Bartlett*'s rejection of the "stop-selling" rationale does not mandate preemption of Plaintiffs' state-law design-defect claims.

At this stage of the proceedings, Gilead has not satisfied the "demanding" defense of impossibility preemption as to those claims. *Levine*, 555 U.S. at 573.

2. Failure-to-Warn Claims

Gilead argues that Plaintiffs' failure-to-warn claims are preempted under *Buckman Company v. Plaintiffs' Legal Committee*, in which the Supreme Court held that "[s]tate-law fraud-on-the-FDA claims" – i.e., claims that a defendant caused injuries based on its fraudulent representations to the FDA – are preempted. 531 U.S. 341, 348 (2001). The Court disagrees. Claims are preempted under *Buckman* where they are based on a "fraud-on-the agency theory" or "exist solely by virtue of the FDCA disclosure requirements" and not "traditional state tort law principles." *Id.* at 352-53. By contrast, where "failure-to-warn claims . . . [do] not arise solely by virtue" of federal law, there is no preemption under *Buckman* because "there is no suggestion that Congress intended to displace traditional tort law by making all policing of medical labels and warnings the exclusive province of the FDA." *McClellan v. I-Flow Corp.*, 776 F.3d 1035, 1040-41 (9th Cir. 2015). Plaintiffs' claims here are similar to the claim at issue in *McClellan*, where the plaintiff alleged that defendant "negligently failed to warn that its pain pump should not

be used in intra-articular spaces such as the glenohumeral joint." *Id.* at 1037. Gilead argues that *McClellan* is distinguishable based on the following excerpt:

> The allegations at issue occur outside the context of the regulatory process, unlike in *Buckman*. Where the plaintiff in *Buckman* alleged that the defendant made fraudulent representations *during* the market approval process, *to the FDA*, McClellan's requested instructions here have little to do with direct regulatory interaction with the FDA.

Id. at 1041 (emphasis in original) (citation omitted). But the allegations at issue here *did* occur outside the regulatory process in the same way that McClellan's did: They are based on an alleged failure to warn consumers, and not on any contention that Gilead made misrepresentations to the FDA. Plaintiffs' claims are not preempted under *Buckman*.

a. Pre-Approval

Nor are Plaintiffs' claims preempted to the extent that Plaintiffs contend that Gilead should have submitted different warnings as part of their initial submissions for FDA approval. Just as Gilead has pointed to no federal law that would have prevented it from submitting TAF drugs rather than TDF drugs for approval in the first instance, it has also cited no federal law that would prevent a drug manufacturer from submitting a different warning label to the FDA prior to initial approval of a drug.[7] As one district court has explained, "[a]lthough defendants are correct in stating the labeling language must not deviate from that which was approved by the FDA, defendants still possessed the ability to implement stronger warning language into labeling, by submitting stronger warning language for FDA approval." *In re Actos (Pioglitazone) Prods. Liab. Litig.*, No. 12-CV-00064, 2014 WL 60298, at *7 (W.D. La. Jan. 7, 2014) (also noting that a manufacturer may seek FDA approval "by way of a CBE or prior approval submissions," a post-approval option that the Court discusses below).

The Court does not find the cases relied on by Gilead to be persuasive. The First Circuit interpreted *Levine* as barring claims "based on information available at the commencement of marketing, while allowing the states to reach contrary conclusions when new information not

[7] As with claims regarding drug composition, the parties do not discuss Gilead's duties under particular state laws regarding drug labeling. For purposes of this motion, the Court assumes without deciding that the state laws invoked by Plaintiffs require Gilead to use different labeling.

considered by the FDA develops." *In re Celexa & Lexapro Mktg. & Sales Practices Litig.*, 779 F.3d 34, 41 (1st Cir. 2015). Similarly, a district court has interpreted *Levine* as "plainly preempt[ing]" any claim "based on information known to the FDA . . . when the label at issue here was approved." *Maze v. Bayer Healthcare Pharm. Inc.*, No. 4:18-CV-21-TAV-CHS, 2019 WL 1062387, at *3 (E.D. Tenn. Mar. 6, 2019). But *Levine* rejected Wyeth's contention that, "[o]nce the FDA has approved a drug's label, a state-law verdict may not deem the label inadequate, regardless of whether there is any evidence that the FDA has considered the stronger warning at issue." 555 U.S. at 573-74. And the Supreme Court considered only a manufacturer's duties once a drug, including its labeling, had already been approved. Although, as discussed below, the question of what information was presented to the FDA is relevant in the post-approval context, the Court does not read *Levine* as requiring preemption of all failure-to-warn claims, including pre-approval claims, based on material that has been presented to the FDA. Gilead also relies on the *Utts* court's conclusion that, "[t]o the extent that the failure to warn claims are premised on the adequacy of the label as approved by the FDA when the drug was first marketed in the United States, they are preempted." 226 F. Supp. 3d at 184 (citing regulations setting forth FDA labeling requirements). But the cited labeling requirements provide only that a new drug application must contain certain proposed information. *See* 21 U.S.C. § 355(b)(1)(F); 21 C.F.R. § 314.50(c)(2)(i). They do not conflict with any state-law duties regarding adequacy of warnings, and it is therefore not impossible for a manufacturer to comply with both state and federal law prior to submitting a new drug application to the FDA for approval. Plaintiffs' pre-approval failure-to-warn claims are not preempted.

b. Post-Approval

Levine, 555 U.S. 555, presents the relevant analytical framework for Plaintiffs' post-approval failure-to-warn claims. As discussed above, the Supreme Court held in *Levine* that such claims against brand-name manufacturers are not preempted if the manufacturer could independently alter the drug label under the CBE regulation and there is not "clear evidence that

the FDA would not have approved a change to [the drug's] label."[8] *Id.* at 568-72. "[T]o properly plead and then prove a state law failure-to-warn claim based on post-drug-release information . . . that is not preempted by the FDCA, a plaintiff must plead 'a labeling deficiency that [Defendants] could have corrected using the CBE regulation.'" *Gibbons v. Bristol-Myers Squibb Co.* 919 F.3d 699, 708 (2d Cir. 2019) (alteration in original) (quoting *In re Celexa*, 779 F.3d at 41).

The parties dispute whether Plaintiffs' allegations satisfy this test. Specifically, Gilead argues that Plaintiffs do not allege any "newly acquired information," as required by the 2008 amendments to the CBE regulation. Federal regulations define "newly acquired information" as "data, analyses, or other information not previously submitted to the Agency." 21 C.F.R. § 314.3(b). It "may include (but is not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events, or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA." *Id.* The Supreme Court explained that:

> The rule accounts for the fact that risk information accumulates over time and that the same data may take on a different meaning in light of subsequent developments: "[I]f the sponsor submits adverse event information to FDA, and then later conducts a new analysis of data showing risks of a different type or of greater severity or frequency than did reports previously submitted to FDA, the sponsor meets the requirement for 'newly acquired information.'"

Levine, 555 U.S. at 569 (quoting 73 Fed. Reg. at 49607). *Levine* arose after trial, and the Supreme Court noted that "[t]he record is limited concerning what newly acquired information Wyeth had or should have had about the risks of IV-push administration of Phenergan because Wyeth did not argue before the trial court that such information was required for a CBE labeling change." *Id.* The label "warned of the danger of gangrene and amputation following inadvertent intra-arterial injection," but "Levine alleged that the labeling was defective because it failed to instruct clinicians to use the IV-drip method of intravenous administration instead of the higher risk IV-push method." *Id.* at 560. The Court found it sufficient that Levine "present[ed] evidence of at

[8] Gilead does not argue that there exists "clear evidence" that the FDA would not have approved the labeling changes that Plaintiffs contend were necessary. The Court therefore does not address that component of the preemption analysis.

least 20 incidents prior to her injury in which a Phenergan injection resulted in gangrene and an amputation" and that, "[i]n later years, as amputations continued to occur, Wyeth could have analyzed the accumulating data and added a stronger warning about IV-push administration of the drug." *Id.* at 569-70. Although it is not clear from the opinion, it appears that the Supreme Court found these later incidents qualified as "newly acquired information" in part because Wyeth only notified the FDA "[a]fter the first such incident came to Wyeth's attention in 1967," and not after subsequent incidents occurred. *Id.* at 569.

The Ninth Circuit has not considered sufficiency of claims in this context, but two other circuits have affirmed dismissal of failure-to-warn claims that, in their views, failed to adequately allege "newly acquired information," and another circuit has found claims to be preempted based on the plaintiff's failure to present such information at trial. The First Circuit found claims to be preempted where the labeling change sought by the plaintiffs "was plainly known to the FDA prior to approving the label," and the CBE procedure therefore could not have been used to implement that change. *In re Celexa*, 779 F.3d at 43. Similarly, the Second Circuit found preempted claims based on allegations that "[b]efore and after marketing Eliquis, [D]efendants became aware of many reports of serious hemorrhaging in users of [their] drugs" and that "[n]umerous . . . studies published after Eliquis' approval in 2012 confirm the problematic bleeding events associated with Eliquis." *Gibbons*, 919 F.3d at 708 (alterations in original). The court explained that the complaint "provides no basis upon which the court could conclude that the bleeding events covered by the alleged 'reports' and 'studies' presented a different type of risk than those the company had discussed with the FDA, or were more severe or more frequent than bleeding events that the government already knew about." *Id.* Finally, the Seventh Circuit found claims to be preempted when the plaintiff failed to present at trial any information that was either a new analysis or data that had not been previously submitted to the FDA. *Dolin v. GlaxoSmithKline LLC*, 901 F.3d 803, 816 (7th Cir. 2018), *petition for cert. filed*, 87 U.S.L.W. 3280 (Dec. 19, 2018) (No. 18-803).

i. Pre-2008

The CBE regulation was not amended to include the requirement that the labeling change

be based on "newly acquired information" until 2008. *Levine*, 555 U.S. at 568. Thus, as to the three drugs approved prior to 2008 – Viread, Truvada, and Atripla – Gilead could have made a labeling change via the CBE regulation regardless of whether the change presented "newly acquired information." Gilead does not dispute this and, on reply, argues only that the 2008 amendment requires "newly acquired information" as to post-approval failure-to-warn claims regarding Stribild and Complera, which were approved after 2008. ECF No. 60 at 13 & n.7. Plaintiffs' pre-2008 claims as to Viread, Truvada, and Atripla are not preempted.

ii. Post-2008

Regarding post-2008 claims, Gilead correctly notes that Plaintiffs allege that the company knew that TDF posed risks to patients' kidneys and bones before the first TDF drug was approved by the FDA. For example, the complaint alleges that:

> *Before Gilead began selling its first TDF Drug, Viread, in 2001*, Gilead knew that TDF posed a safety risk to patients' kidneys and bones. Gilead knew that two of its other antiviral drugs with structures similar to tenofovir, cidofovir and adefovir dipivoxil, had been highly nephrotoxic (i.e., toxic to kidneys) and that preclinical data for TDF showed that it could cause significant kidney and bone damage. Gilead also knew that the relatively high dose of TDF created a greater risk of toxic effects, and that bone and kidney toxicities were even more likely to be seen with long-term use of TDF for the treatment of a virus that, for the foreseeable future, has no cure.

ECF No. 1 ¶ 5 (emphasis added); *see also id.* ¶ 210 ("Since scientists first synthesized TDF, studies [including one published in 1999] have consistently shown that it could cause significant kidney and bone damage."). Similarly, Plaintiffs allege that:

> Gilead knew years before it developed Stribild that: (a) higher tenofovir concentrations in patients' blood, as opposed to the target cells, endangers the kidneys; (b) tenofovir concentrations in patients' blood increase significantly when patients take tenofovir with a booster; and (c) TDF-associated renal toxicity occurs more frequently in patients taking TDF as part of a boosted regimen.

Id. ¶ 13.

However, the complaint also alleges that Gilead acquired additional information after FDA approval. For example, Plaintiffs allege that Gilead became aware of "increasing post-approval marketing evidence that patients with and without prior risk factors were experiencing kidney and

bone adverse effects, and expanding support within the scientific community to frequently monitor multiple indicators of renal function in all patients." *Id.* ¶ 363. Plaintiffs also allege that "Gilead's knowledge of the toxic effects of TDF only grew as patients began treatment with and were injured by each successive TDF product. By the time Gilead designed Stribild, it had ten years' worth of cumulative evidence that TDF injured patients' kidneys and bones." *Id.* ¶ 6. Plaintiffs further allege that, "less than one month after Viread entered the market, the first published case of TDF-associated acute renal failure occurred. Thereafter, additional reports of TDF-associated kidney damage, including but not limited to Fanconi syndrome, renal failure, renal tubular dysfunction, and nephrogenic diabetes insipidus began to appear in the medical literature. Many of those adverse events occurred in patients without preexisting kidney dysfunction." *Id.* ¶ 214. Additionally, Plaintiffs make the following allegations: "Gilead was also seeing renal adverse events in its postmarketing safety data. In fact, the most common serious adverse events reported to Gilead were renal events, including renal failure, Fanconi syndrome, and serum creatinine increase," *id.* ¶ 215 (footnotes omitted); "Gilead's long-term clinical data also demonstrated that TDF was damaging patients' bones," *id.* ¶ 218; and "[a]fter Gilead brought Truvada to market, the medical literature continued to identify cases of TDF-associated kidney damage, including in patients without pre-existing renal dysfunction or co-administration with another nephrotoxic drug," *id.* ¶ 219. Finally, Plaintiffs allege that various studies from 2006 to 2012 reported adverse renal events in TDF patients and "continued to show that TDF caused a significant loss of renal function in HIV-infected patients." *Id.* ¶¶ 220-21, 226-28.

The problem with Plaintiffs' allegations is that it is not possible to discern from the complaint whether – and, if so, when – any such information was provided to the FDA. Plaintiffs allege that the risks of TDF drugs were known before Gilead submitted its first TDF drug for approval. It would be an unreasonable inference to conclude that Gilead did not present any information concerning the risks of TDF drugs to the FDA, especially when Plaintiffs allege that Gilead submitted multiple applications for different TDF drugs and that it also "update[d] its Viread labeling at least four times [between 2002 and 2006] to describe the kidney damage patients experienced when taking TDF," *id.* ¶ 217, and again modified its labeling (as to

unspecified drugs) in 2007 and twice in 2008, *id.* ¶¶ 224-25. Such changes could not have been made without application to the FDA for approval. *See Levine*, 555 U.S. at 568 (noting the general rule that "a manufacturer may only change a drug label after the FDA approves a supplemental application" before explaining that the CBE regulation provides that a manufacturer may make certain changes "upon filing its supplemental application with the FDA"). Without more, the Court cannot conclude that Plaintiffs have plausibly alleged the existence of "newly acquired information" – i.e., "data, analyses, or other information *not previously submitted to the [FDA]*" – such that it could have made post-2008 labeling changes under the CBE regulation. 21 C.F.R. § 341.3(b) (emphasis added). Consequently, Plaintiffs have not plausibly alleged that Gilead could have made, under the CBE regulation or any other federal law allowing changes without prior FDA approval, the post-2008 labeling changes Plaintiffs contend were required to comply with state law.[9] As pleaded, those claims are therefore preempted. The Court will grant leave to amend because it is not clear that amendment could not cure the deficiencies identified in this order.

In short, as currently pleaded, Plaintiffs' failure-to-warn claims are preempted as to post-approval, post-2008 labeling changes. They are not preempted as to pre-approval labeling changes or pre-2008 labeling changes to Viread, Truvada, or Atripla, the three TDF drugs that were approved prior to 2008.

C. Adequacy of Causation Allegations in Failure-to-Warn Claims

Gilead argues that Plaintiffs have not adequately alleged causation on their failure-to-warn claims. Plaintiffs do not dispute that they must allege that the allegedly inadequate warnings caused them injury, or that the state laws they invoke require warnings to Plaintiffs' physicians and not to Plaintiffs directly. Instead, Plaintiffs argue that they "have alleged what Gilead says is required – i.e., that but for Gilead's warning failures, Plaintiffs' physicians 'would have acted

[9] The *Lujano* court found sufficient the plaintiffs' allegations that Gilead "should have viewed the accumulating evidence of the risks associated with Viread, Truvada and Atripla with respect to potential kidney damage, including Fanconi syndrome, and with respect to bone loss as requiring strengthened warning labels." *Lujano*, at 5 (ECF No. 55-1 at 6). However, it did not discuss whether the "accumulating evidence" satisfied the definition of "newly acquired evidence," including that it not have been previously submitted to the FDA.

differently.'" ECF No. 54 at 27 (quoting ECF No. 45 at 25).

Gilead asserts that Plaintiffs must allege that their physicians would not have prescribed the TDF drugs had Gilead given different warnings, but that position is not supported by the case law. Although choosing not to prescribe a particular medication or device is one way that a physician might have acted differently, it is not the only adequate means of demonstrating causation on a failure-to-warn claim. To the contrary, as the first case cited by Gilead demonstrates, the relevant question is whether the plaintiff's physician would have "prescribed the drug *in the same manner*." *Byrd v. Janssen Pharm., Inc.*, 333 F. Supp. 3d 111, 127 (N.D.N.Y. 2018) (emphasis added) (quoting *Alston v. Caraco Pharm., Inc.*, 670 F. Supp. 2d 279, 285 (S.D.N.Y. 2009)). Thus, for example, courts have found triable issues of causation where plaintiffs have presented evidence that their physicians would have used monitoring tests if adequately warned to do so, or that they would have altered their prescription practices in a way that may have prevented injury. *In re Xarelto (Rivaroxaban) Prods. Liab. Litig.*, No. 2592, 2017 WL 1393480, at *2-3 (E.D. La. Apr. 17, 2017) (denying summary judgment where the plaintiff presented evidence that her doctor "would have used [monitoring tests] had they been adequately instructed to do so, and therefore . . . would have known [the plaintiff] was not anticoagulated and would have proceeded with her surgery much sooner," thus avoiding "significant medical issues"); *Georges v. Novartis Pharm. Corp.*, No. CV 06-5207 SJO (VBKx), 2012 WL 9083365, at *6 (C.D. Cal. Nov. 2, 2012) (noting multiple courts have "held that even where physicians admitted that they still recommended the Treatment Drugs knowing of their . . . risks [of causing deterioration of bones in the jaw], the changes to their prescription and treatment procedure nonetheless created triable questions of fact on specific causation"). Changed prescription practices might include cautioning the patient about risk factors or reducing the prescribed dosage. *Georges*, 2012 WL 9083365, at *6. In addition, at least in some jurisdictions, causation can be demonstrated by evidence that any of the plaintiff's treating physicians would have acted differently with additional knowledge, even if the prescribing physician would still have prescribed the drug with adequate warnings. *In re Aredia & Zometa Prods. Liab. Litig.*, No. 3:06-MD-1760, 2009 WL 2497692, at *2 (M.D. Tenn. Aug. 13, 2009).

Plaintiffs' causation allegations here are sufficient. First, Plaintiffs allege that their physicians would have acted differently if Gilead's warning labels had contained different monitoring instructions: "Had Gilead adequately warned and instructed Plaintiffs' doctors, Plaintiffs' doctors would have read and heeded such adequate warnings and instructions" and "would have monitored Plaintiffs differently."[10] ECF No. 1 ¶¶ 421-22, 493. Plaintiffs further allege that increased monitoring "would have detected TDF toxicity earlier, thus preventing or lessening Plaintiffs' injuries." *Id.* ¶ 422, 493; *see also id.* ¶¶ 339, 344 (Gilead's "fail[ure] to warn doctors to monitor all patients for TDF-associated toxicity" and "to monitor additional markers of all patients' kidney function . . . delayed the diagnosis of TDF-associated harm, causing or enhancing injuries that would have been prevented or lessened through early detection."). Plaintiffs plausibly allege why "early detection is key to preventing serious, potentially irreversible renal injury": because "a patient experiences even greater exposure to tenofovir as the kidneys become impaired – causing even greater harm. Frequent monitoring for TDF-induced toxicity is also critical because patients are typically asymptomatic in the early stages." *Id.* ¶ 324. "Without using sufficiently sensitive markers of kidney function, substantial kidney injury can occur before it is measurable. As a result, the detection of TDF-induced nephrotoxicity often comes too late, resulting in kidney injury that may be irreversible." *Id.* ¶ 341; *see also id.* ¶ 345 ("By the time a doctor assesses a patient's kidney function when 'clinically appropriate,' the patient is likely to have already experienced adverse toxic effects, some of which might be irreversible. Regularly scheduled, frequent monitoring of kidney function is necessary to catch early signs of TDF-induced toxicity and prevent injury because patients are generally asymptomatic during the early stages."). Plaintiffs further allege that "[f]requent monitoring of all patients' kidney function is necessary to ensure that patients' kidneys are healthy enough to continue treatment or patients receive a needed dose interval adjustment." *Id.* ¶ 338. These

[10] The Court recognizes a difference of opinion as to whether such allegations are sufficient to state a claim. For example, one court dismissed as "merely conclusory" an allegation that "had [the plaintiff's] physician been adequately informed about the extensive dangers associated with the use of the Ventralex patch, his physician would not have implanted the device in Plaintiff." *Hammarlund v. C.R. Bard, Inc.*, No. 2:15-cv-05506-SVW-JEM, 2015 WL 5826780, at *5 (C.D. Cal. Oct. 2, 2015). The Court disagrees.

allegations are sufficient to allege a plausible causal link between Gilead's alleged failure to warn and Plaintiffs' alleged injuries. To the extent Gilead argues the complaint is deficient because it does not allege specific treatment that would have lessened Plaintiffs' kidney and bone damage, the Court disagrees; the contours of what Plaintiffs' physicians might have done differently if Gilead had provided different warnings can be explored during discovery.

D. Fraud and Consumer Protection Law Claims

Gilead moves to dismiss Plaintiffs' fraud and consumer protection claims for failure to comply with Rule 9(b)'s heightened pleading requirements. The rule applies to state-law fraud claims, as well as to consumer protection claims that "sound in fraud" – i.e., that allege "a unified course of fraudulent conduct and rely entirely on that course of conduct as the basis of that claim." *Kearns v. Ford Motor Co.*, 567 F.3d 1120, 1125 (9th Cir. 2009). But where a plaintiff "choose[s] not to allege a unified course of fraudulent conduct in support of a claim" and instead "allege[s] some fraudulent and some non-fraudulent conduct . . . , only the allegations of fraud are subject to Rule 9(b)'s heightened pleading requirements." *Vess*, 317 F.3d at 1104. "The rule does not require that allegations supporting a claim be stated with particularity when those allegations describe non-fraudulent conduct." *Id.*

The Court agrees with Plaintiffs that not all of their claims sound in fraud. For example, Plaintiffs allege that "Gilead knowingly designed unreasonably dangerous TDF Drugs that injured Plaintiffs to make more money – conduct which is 'unfair' under the laws of numerous states." ECF No. 54 at 29 (citations omitted). Gilead does not argue that such conduct would not be "unfair," but it argues that Rule 9(b) nonetheless applies because the alleged conduct is part of a unified course of fraudulent conduct.[11] However, whether Gilead acted unfairly by designing unreasonably dangerous drugs for financial gain does not require that Gilead also acted fraudulently. *Cf. Haskins v. Symantec Corp.*, No. 13-cv-01834-JST, 2013 WL 6234610, at *8 (N.D. Cal. Dec. 2, 2013) ("The Court does not agree that Plaintiff's claims under the ['unfair

[11] As with the design-defect and failure-to-warn claims, the parties do not present argument on the specific requirements under state law. For purposes of this motion, the Court assumes without deciding that Plaintiffs are correct that the alleged conduct would be considered "unfair" under various state laws.

practices' and 'fraudulent practices'] prongs are coterminous; she also appears to argue that it was unfair practice for Defendant to sell a product it knew to be compromised, regardless of the content of its advertisements."). Rule 9(b) therefore does not apply to these claims.

Rule 9(b) does, however, govern Plaintiffs' fraud claims and their consumer protection claims to the extent that the latter allege a course of fraudulent conduct. Plaintiffs contend that their claims are based only on omissions and not affirmative misrepresentations, but Gilead correctly observes that the complaint also alleges misrepresentations. For example, in the count alleging violation of consumer protection laws, Plaintiffs allege that:

> Gilead *intentionally misrepresented material facts in its promotional, marketing, and labeling communications* about the risks and benefits of the TDF Drugs to Plaintiffs and Plaintiffs' doctors, including but not limited to, that the TDF Drugs: 1) presented limited risk of kidney and bone toxicity resulting from purportedly unavoidable side effects of tenofovir; and 2) did not require careful, frequent monitoring of all TDF Drug patients for TDF-associated kidney and bone toxicity.

ECF No. 1 ¶ 536 (emphasis added); *see also id.* ¶¶ 539-43 (referring to "misrepresentations" as well as "omissions"). Plaintiffs elsewhere allege that Gilead "misrepresent[ed] the safety profile of TDF when promoting TDF to doctors" and gave "misleading marketing messages" to doctors, including "that Viread was a 'miracle drug,' 'extremely safe,' and 'extremely well-tolerated' with 'no toxicities.'" *Id.* ¶¶ 327, 333. Similarly, Plaintiffs allege that Gilead "misrepresent[ed]: (a) that any tenofovir-induced toxicity was rare and unavoidable; (b) why Gilead had purportedly abandoned development of TAF in 2004; and (c) that TAF was 'new' once Gilead finally introduced the safer TAF design over a decade later." *Id.* ¶ 511; *see also id.* ¶ 332 (alleging that "Gilead continued to downplay the risks of TDF-induced toxicity when promoting its TDF Drugs to doctors by misrepresenting the drug as safe, dismissing case reports of acute renal failure and other TDF-associated adverse events as purportedly unavoidable side effects of tenofovir in an otherwise 'safe' drug, and discouraging doctors from monitoring patients for drug-induced toxicity using more sensitive markers of kidney function"). Even Plaintiffs' opposition brief argues that "Plaintiffs' fraud by omission and consumer protection claims . . . are based, in part, on Gilead's omissions *and misrepresentations* with respect to TDF and TAF." ECF No. 54 at 26-

27 (emphasis added). Thus, at least as currently pleaded, Plaintiffs' claims are not only about omissions, and Plaintiffs may not rely on the lower level of specificity allowed for claims based on alleged omissions to avoid dismissal of their misrepresentation claims. Plaintiffs do not argue that they have satisfied Rule 9(b) as to those claims, and the Court will therefore dismiss those claims with leave to amend.

However, Plaintiffs' omissions-based claims are sufficiently pleaded. In *MacDonald v. Ford Motor Co.*, 37 F. Supp. 3d 1087 (N.D. Cal. 2014), this Court considered allegations that Ford failed to disclose a coolant pump defect to consumers. Ford argued in its motion to dismiss that the plaintiffs failed to plead omission with particularity. The Court disagreed and concluded that:

> Plaintiffs adequately allege the "who what when and how," given the inherent limitations of an omission claim. In short, the "who" is Ford, the "what" is its knowledge of a defect, the "when" is prior to the sale of Class Vehicles, and the "where" is the various channels of information through which Ford sold Class Vehicles.

Id. at 1096. Likewise, here, as Plaintiffs observe in their opposition: "The 'who' is Gilead, the 'what' is an adequate warning about the risks and safe use of TDF and the fact that Gilead was withholding safer designs of the TDF Drugs, the 'when' is prior to Plaintiffs' doctors' prescribing and monitoring decisions, and the 'where' is in Gilead's drug labeling, marketing, and promotional materials." ECF No. 54 at 31. For example, the complaint alleges:

> Gilead intentionally suppressed, concealed, and omitted material facts in its promotional, marketing, and labeling communications about the risks and benefits of the TDF Drugs to Plaintiffs and Plaintiffs' doctors, including but not limited to, that: 1) all TDF patients should be carefully and frequently monitored for adverse kidney and bone effects on a frequent schedule; 2) Gilead had already developed the safer TAF design for delivering tenofovir into the body but nevertheless designed the TDF Drugs to contain TDF, and withheld the safer [TAF] design, in order to maximize profits on its TDF-based products and extend its ability to profit on its HIV franchise for years to come; and 3) Gilead knew that the tenofovir prodrug dose should be reduced when combined in a fixed dose combination pill with cobicistat, but did not reduce the TDF dose in Stribild.

ECF No. 1 ¶ 535; *see also id.* ¶ 507 ("Gilead intentionally omitted from its prescriber and patient labeling an adequate warning regarding the need for doctors to monitor all TDF patients, on a frequent, specific schedule, for the adverse effects of TDF-associated bone and kidney toxicity.").

The complaint is "specific enough" as to omissions "to give defendants notice of the particular misconduct so that they can defend against the charge and not just deny that they have done anything wrong." *Vess*, 317 F.3d at 1106 (internal quotation marks and alteration omitted). Plaintiffs' claims based on omissions are therefore not subject to dismissal under Rule 9(b).

The Court denies Gilead's alternate request to require Plaintiffs to submit a more definite statement under Federal Rule of Civil Procedure 12(e). First, Gilead's moving papers made this argument only in a footnote. ECF No. 45 at 30 n.15. "Arguments raised only in footnotes, or only on reply, are generally deemed waived" and need not be considered. *Estate of Saunders v. Comm'r*, 745 F.3d 953, 962 n.8 (9th Cir. 2014); *see Sanders v. Sodexo, Inc.*, No. 2:15-cv-00371-JAD-GWF, 2015 WL 4477697, at *5 (D. Nev. July 20, 2015) ("Many courts will disregard arguments raised exclusively in footnotes." (quoting Bryan Garner, *The Redbook: A Manual on Legal Style* 168 (3d ed.2013))). Moreover, on the merits, the Court does not find the complaint to be "so vague or ambiguous that [Gilead] cannot reasonably prepare a response." Fed. R. Civ. P. 12(e).

CONCLUSION

Gilead's motion to dismiss is granted in part and denied in part. The motion is granted as to Plaintiffs' failure-to-warn claims based on post-approval, post-2008 labeling changes, and as to Plaintiffs' fraud and consumer protection claims to the extent those claims are based on misrepresentations and not omissions. Plaintiffs are granted leave to amend the dismissed claims. The motion is denied in all other respects.

As confirmed at the April 23, 2019 case management conference, the parties have agreed that Plaintiffs can amend the complaint "to allege consumer protection claims for damages under the state consumer protection laws of Alabama, California, Indiana, and Texas." ECF No. 59 at 5; ECF No. 62. Plaintiffs should also consider whether to incorporate the *Dowdy* plaintiffs' claims into the amended complaint, such that there is a single consolidated complaint for these cases.

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Any amended complaint must be filed on or before May 31, 2019. Failure to file a timely amended complaint will result in dismissal with prejudice of the claims dismissed by this order.

IT IS SO ORDERED.

Dated: May 10, 2019

JON S. TIGAR
United States District Judge