UNITED STATES DISTRICT COURT
DISTRICT OF CONNECTICUT

CARL IGNACUINOS and PAMELA DAVIS, *on behalf of themselves and all others similarly situated*,
Plaintiffs,

v.

BOEHRINGER INGELHEIM PHARMACEUTICALS INC.,
Defendant.

No. 3:19-cv-672 (SRU)

RULING ON MOTION TO DISMISS

This purported class action seeks monetary and injunctive relief for injuries caused by the alleged deceptive design, manufacturing, and marketing of Boehringer Ingelheim Pharmaceuticals, Inc.'s ("Boehringer") pharmaceutical drug, Combivent Respimat ("Combivent"). Combivent is a metered dose inhaler that is prescribed to alleviate symptoms of chronic obstructive pulmonary disease ("COPD"). Carl Ignacuinos ("Ignacuinos") and Pamala Davis ("Davis") (collectively "the Plaintiffs") allege that Boehringer falsely represents that each Combivent inhaler ("the Product") contains 120 doses. The Plaintiffs bring a seventeen-count class action complaint seeking damages and an injunction prohibiting Boehringer from marketing and selling the Product with the alleged defects and misrepresentations. *See generally* Third Am. Compl. (Doc. No. 23). In addition, the Plaintiffs seek changes to the Product's design and labeling. *Id.*

Boehringer moves to dismiss the Third Amended Complaint in its entirety, primarily arguing that: (1) the Plaintiffs lack Article III standing; and (2) the Plaintiffs' state law claims are preempted by federal law. *See* Def's Mem. in Supp. Mot. to Dismiss ("Def's Mem.") (Doc. No.

24-1) at 1. On September 2, 2020, I held oral argument and took the motion under advisement. *See* Minute Entry, Doc. No. 39.

For the following reasons, Boehringer's motion to dismiss (doc. no. 24) is **granted**.

I. Standard of Review

A motion to dismiss for failure to state a claim pursuant to Rule 12(b)(6) is designed "merely to assess the legal feasibility of a complaint, not to assay the weight of evidence which might be offered in support thereof." *Ryder Energy Distrib. Corp. v. Merrill Lynch Commodities, Inc.*, 748 F.2d 774, 779 (2d Cir. 1984) (quoting *Geisler v. Petrocelli*, 616 F.2d 636, 639 (2d Cir. 1980)).

When deciding a motion to dismiss pursuant to Rule 12(b)(6), the court must accept the material facts alleged in the complaint as true, draw all reasonable inferences in favor of the plaintiff, and decide whether it is plausible that plaintiffs have a valid claim for relief. *Ashcroft v. Iqbal*, 556 U.S. 662, 678–79 (2009); *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555–56 (2007); *Leeds v. Meltz*, 85 F.3d 51, 53 (2d Cir. 1996).

Under *Twombly*, "[f]actual allegations must be enough to raise a right to relief above the speculative level," and assert a cause of action with enough heft to show entitlement to relief and "enough facts to state a claim to relief that is plausible on its face." 550 U.S. at 555, 570; *see also Iqbal*, 556 U.S. at 679 ("[w]hile legal conclusions can provide the framework of a complaint, they must be supported by factual allegations."). The plausibility standard set forth in *Twombly* and *Iqbal* obligates the plaintiff to "provide the grounds of his entitlement to relief" through more than "labels and conclusions, and a formulaic recitation of the elements of a cause of action." *Twombly*, 550 U.S. at 555 (quotation marks omitted). Plausibility at the pleading stage is nonetheless distinct from probability, and "a well-pleaded complaint may proceed even

if it strikes a savvy judge that actual proof of [the claims] is improbable, and . . . recovery is very remote and unlikely." *Id.* at 556 (quotation marks omitted).

II. Background

A. The Product

Combivent is a bronchodilator designed to provide relief to individuals suffering from COPD, a chronic inflammatory lung disease that constricts airflow to the lung's passageways. *See* Third Am. Compl. at ¶ 28. By delivering a combination of ipratropium bromide and albuterol through the Product, Combivent relaxes muscles in the lungs and expands air passageways so that it becomes easier to breathe. *Id.* at ¶ 29. The Product consists of the inhaler equipped with a mouthpiece and a cartridge that contains the medication itself. *See* Def's Mem. at 2. Boehringer represents that each use, or "actuation," of the Product will deliver a set, metered dose: "[e]ach actuation from the COMBIVENT RESPIMAT inhaler delivers 20 mcg ipratropium bromide (monohydrate) and 100 mcg albuterol (equivalent to 120 mcg albuterol sulfate) in 11.4 mcL of solution from the mouthpiece." Third Am. Compl. at ¶ 33. The recommended dose of the Product is "one inhalation four times a day, not to exceed six inhalations in 24 hours," and each Product is reported to contain 120 metered doses.[1] *Id*. at ¶¶ 35–36. In addition, Boehringer represents that the Product "will deliver 120 puffs and last 30 days if used 1 puff [actuation] four times daily." *Id*. at ¶ 37.

In 2016, the FDA reviewed and approved an updated version of the labeling of the Product, including the package insert for physicians, patient information, and carton packaging, that remains in effect today. *See* Def's Mem. at 3. In a section of the labeling entitled "Answers

[1] The "Instructions for Use" provide that "[y]our inhaler contains 120 puffs (120 doses); or if you have a sample, your inhaler contains 60 puffs (60 doses) instead," and that Combivent "will deliver 120 puffs and last 30 days if used at 1 puff four times daily," Ex. 1 to Third Am. Compl. (Doc. No. 23-1) at 12, 13.

to Common Questions," the Instructions for Use note the possibility that "[t]he dose indicator on the COMBIVENT RESPIMAT reaches zero too soon" under certain circumstances involving user error. Ex. 1 to Third Am. Compl. at 14.

B. The Plaintiffs' Allegations

Ignacuinos, a Florida resident, is a long-time sufferer of COPD. *See* Third Am. Compl. at ¶ 22. Beginning in 2016, he was prescribed Combivent to alleviate his COPD symptoms. *Id*. Since he was first prescribed Combivent, Ignacuinos noticed that he was not receiving the full, or even close to, the 120 metered doses from the Product during each use. *Id*. at ¶ 24. Ignacuinos began logging the total number of doses he derived from each Combivent inhaler he was prescribed. *Id*. at ¶ 45. Over the course twenty-tour inhalers, Ignacuinos's inhalers delivered on average only 61 metered doses before each inhaler's dosage meter reached "0" and automatically locked, notwithstanding Boehringer's representations that each Product delivers 120 metered doses. *Id.* at ¶ 46.

Because the Product only delivers about half its advertised number of doses, Ignacuinos states that Combivent can only be used in accordance with Boehringer's one puff instruction, four times daily for approximately two weeks each month. *Id*. As a result, Ignacuinos uses less than four puffs daily so that he can preserve the lifespan of his Combivent inhaler for an entire month, until he is prescribed another inhaler by his health care provider after 30 days have lapsed. *Id.* Due to the Product's alleged defects, Ignacuinos routinely experiences bodily injury in the form of episodes with acute difficulty breathing because he does not have enough medication to alleviate his COPD symptoms. *Id*. at ¶ 48. In addition, Ignacuinos alleges that he is deprived of the benefit of the bargain each time he pays for the Product. *Id.* at ¶ 49.

Davis, an Indiana resident, is a COPD patient who was first prescribed and purchased Combivent in 2016 to treat her COPD symptoms. *Id*. at ¶ 23. After using approximately 30 Combivent inhalers since 2016, Davis reports that each Product delivers only about 70 doses. *Id*. at ¶ 52. Because her medication runs low well in advance of the date of her next available prescription, Davis takes less than the daily amount of puffs recommended by Boehringer to extend the lifespan of her inhaler. *Id*. at ¶ 53. Davis alleges that she has trouble breathing due to the Product's defects, which causes mental and emotional distress. *Id*. at ¶ 55.

The Plaintiffs note that other users of the Product have also complained about a shortfall in dosage. *See, e.g.*, *User Reviews & Ratings—Combivent Respimat inhalation*, WEBMD, https://www.webmd.com/drugs/drugreview-161259-Combivent+Respimat (last visited September 16, 2020)) ("I have had continuing problems with Combivent Respimat. It is supposed to have 120 doses for the month but has typically not lasted a full month. Last year 2017 it averaged less than 25 days. For May and June of 2018 it barely lasts two weeks and I am left without medication for the remainder of the month. Something is wrong with this product. I have talked to the company, sent them the defective inhalers but the problem persists."). The Plaintiffs further allege that "[t]he shortfall in dosage is not due to variance or any natural fluctuation in the manufacturing process. Instead, the consistent shortfall is based on the random sampling for each [Product he] receives, demonstrating a common scheme to defraud users." Third Am. Compl. at ¶ 50.

Based on those allegations, the Plaintiffs filed the Third Amended Complaint on behalf of themselves and all others similarly situated. The Plaintiffs seek to represent "[a]ll persons who purchased Combivent Respimat in the United States within the applicable limitations period, and/or such subclasses as the Court may deem appropriate." *Id*. at ¶ 74. In the alternative,

Ignacuinos seeks to represent a Florida class of Combivent purchasers and Davis seeks to represent an Indiana class of purchasers. *See id*.

The Plaintiffs asserts the following claims against Boehringer:

> A product liability claim under the Connecticut Product Liability Act ("CPLA"), Conn. Gen. Stat. §§ 52-572m, *et seq*., based on (a) manufacturing defect, (b) failure to warn, (c) design defect, (d) negligence, (e) negligent design, (f) fraud, misrepresentation, and concealment, (g) negligent misrepresentation, (h) breach of express warranties, and (i) breach of implied warranties (Count I);
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> A statutory consumer protection claim under the Connecticut Unfair Practices Act ("CUTPA"), Conn. Gen. Stat. §§ 42-110g, *et seq*. (Count II);
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> Florida common law claims for Strict Liability—Manufacturing Defect (Count III) Strict Liability—Failure to Warn (Count IV); Strict Liability—Design Defect (Count V); Strict Liability—Fraudulent Misrepresentation (Count VI); Negligent Design Defect (Count VII); Negligent Misrepresentation (Count VIII); Breach of Express Warranties (Count IX); and Breach of Implied Warranties (Count X);
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> Violations of the Florida Deceptive and Unfair Trade Practices Act ("FDUTPA"), Fla. Stat. § 501.201, *et seq*. (Count XI);
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> Violations of the Indiana Product Liability Act ("IPLA"), Ind. Code §§ 34-20-1-1, *et seq*., based on (a) manufacturing defect, (b) failure to warn, and (c) design defect, (Count XII);
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> A breach of express warranties claim under Indiana law (Count XIII);
>
> A breach of implied warranties claim under Indiana law (Count XIV);
>
> Violations of the Indiana Deceptive Consumer Sales Act Ind. Code §§ 24-5-0.5-1, *et seq.* (Count XV);
>
> A constructive fraud claim under Indiana law (Count XVI);
>
> A common Law Fraud claim under either Connecticut, Florida, or Indiana law (Count XVII).

Id. at ¶¶ 83–327.

The Plaintiffs also seek injunctive relief in the form of: "(1) changes to the Product's labeling and 'Instructions for Use' to reflect the fact that it does not live up to its unequivocal promise that the Combivent Respimat inhaler will deliver 120 metered doses; (2) a change in the

design of the Product so that it actually delivers 120 metered doses; or (3) to the extent that the Product's design is sound, but the manufacturing process is compromised, improvements in the manufacturing process." *Id*. at ¶ 62.

III. Discussion

A. Standing

As a threshold matter, Boehringer argues that the Plaintiffs lack Article III standing. To establish Article III standing the Plaintiffs must allege: "(1) [an] injury-in-fact, which is a 'concrete and particularized' harm to a 'legally protected interest'; (2) causation in the form of a 'fairly traceable' connection between the asserted injury-in-fact and the alleged actions of the defendant; and (3) redressability, or a non-speculative likelihood that the injury can be remedied by the requested relief." *Tweed-New Haven Airport Auth. v. Tong*, 930 F.3d 65, 70 (2d Cir. 2019), *cert. denied*, 140 S. Ct. 2508, 206 L. Ed. 2d 463 (2020) (quoting *W.R. Huff Asset Mgmt. Co. v. Deloitte & Touche LLP*, 549 F.3d 100, 106–07 (2d Cir. 2008)).

First, Boehringer argues that the Plaintiffs have not alleged sufficient facts to establish that their "bodily injur[ies]—primarily in the form of episodes where they experience acute difficulty breathing," are fairly traceable to its conduct. Def's Mem. at 24 (quoting Third Am. Compl. at ¶ 13). Although the Plaintiffs allege that the Product does not contain 120 doses, Boehringer asserts that there is nothing on the label that precludes the Plaintiffs from either obtaining additional medicine when they run out or procuring a different medication to treat their COPD. *See id*. at 25. "If [the] Plaintiffs are unable to procure more than one [Product] or COPD medication within 30 days, this must be attributable to some independent restriction imposed by another entity, perhaps a physician, pharmacy, or insurer . . . . [T]he complaint, [however], does

not identify what that independent restriction is, much less allege that it is traceable to Boehringer." *Id.*

Second, Boehringer contends that the Plaintiffs fail to allege economic injuries that are traceable to its conduct. Although the Plaintiffs "assert that they 'experience financial injury each time the Product fails to deliver on its 120 metered doses representation,' Boehringer highlights that the "Plaintiffs continued to pay [the same] amounts for several years after allegedly discovering that [the Product] delivers fewer than 120 metered doses." Def's Mem. at 26 (citing Third. Am. Compl. at ¶ 26). As a result, Boehringer argues that the Plaintiffs do not have any "benefit of the bargain" losses, which are defined under Connecticut law as the "difference in value between the property actually conveyed and the value of the property as it would have been if there had been no false representation." *Leisure Resort Tech., Inc. v. Trading Cove Assocs*., 277 Conn. 21, 33 (2006)).[2]

Drawing all reasonable inferences in the Plaintiffs' favor, I conclude that they plausibly alleged a causal connection between their physical and economic injuries and Boehringer's conduct. There is a reasonable inference that the alleged misrepresentations on the Product's label, which advise both patients and prescribers of the Product's recommend dosage, caused the Plaintiffs' injuries. Accepting those allegations as true, Boehringer's conduct exacerbated the Plaintiffs' COPD symptoms and caused them to pay more for their prescribed medication.

[2] The definition is similar under both Florida and Indiana law. *See Soltero v. Swire Dev. Sales, Inc.*, 485 F. App'x 377, 379 (11th Cir. 2012) ("[The] benefit-of-the-bargain method requires proof of the difference between the actual value of the property and its value had the alleged facts regarding it been true.") (internal quotations omitted); *Sanchez v. Benkie*, 799 N.E.2d 1099, 1102 (Ind. Ct. App. 2003) ("[T]he applicable measure of damages is the 'benefit of the bargain' or difference between the value of the property conveyed and the value of the property as it was warranted to be.").

Under Boehringer's view, the Plaintiffs standing is destroyed through their continued use of the Product because they could either ask their health care provider for a refill or use another medication. The Third Amended Complaint, however, clearly alleges that "[the] Plaintiffs experience bodily injury each time the Product fails to deliver on [Boehringer's] representations that it will deliver 120 metered doses." Third Am. Compl. at ¶ 25. The continued use of the Product may reduce a claim for damages but does not destroy standing. *See Gustavsen v. Alcon Labs., Inc*., 903 F.3d 1, 9 (1st Cir. 2018) ("There can be no real dispute that plaintiffs' claim of injury traces itself directly to the challenged conduct. Nor can there be any doubt that plaintiffs' financial injury can be redressed by damages. Plaintiffs, therefore, have standing to assert their cause of action.").

Accordingly, I **deny** Boehringer's motion to dismiss on standing grounds.

B. Preemption

Boehringer's also argues that the Plaintiffs' state law claims based on manufacturing and design defects are preempted by federal law. "Plaintiffs misrepresentation claims are preempted because federal law prohibits [Boehringer] from modifying the language in the label without prior FDA approval. Federal law likewise preempts Plaintiffs' product defect claims because it prohibits [Boehringer] from physically altering Combivent without prior FDA approval. Plaintiffs' claims must therefore be dismissed in their entirety." Def's Mem. at 10. I agree.

The Supremacy Clause of the U.S. Constitution establishes that federal law "shall be the supreme Law of the Land . . . any Thing in the Constitution or Laws of any State to the Contrary notwithstanding." U.S. Const., Art. VI, cl. 2. Therefore, "[w]here state and federal law directly conflict, state law must give way." *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 617 (2011) (internal quotations omitted). "State and federal law conflict where it is 'impossible for a private party to

comply with both state and federal requirements.'" *Id*. at 618 (quoting *Freightliner Corp. v. Myrick*, 514 U.S. 280, 287 (1995)) (footnote omitted).

In *PLIVA*, the Supreme Court held the doctrine of "impossibility" preemption applies to state law claims that impose additional duties on drug manufacturers after a drug has been approved by the FDA. *Id.* at 620. In that case, the Plaintiffs asserted numerous state-law claims alleging that drug manufactures failed to provide adequate warning labels for generic metoclopramide, in violation of Minnesota and Louisiana law. *Id*. at 611. The labeling requirements under state law were arguably more demanding than the FDA's requirements. *Id*. at 617. The generic drug manufacturers argued that the Plaintiffs state law claims were preempted because federal law required "that generic drug labels be the same at all times as the corresponding brand-name drug labels." *Id*. at 618 (citing 21 C.F.R. § 314.150(b)(10)). The Court agreed, holding that it was "impossible for the Manufacturers to comply with both their state-law duty to change the label and their federal-law duty to keep the label the same." *Id*.

The Second Circuit in *Gibbons v. Bristol-Myers Squibb Co.*, 919 F.3d 699, 707 (2d Cir. 2019), ruled that the Food, Drug, and Cosmetics Act ("FDCA") limits a drug manufacturer's "ability to unilaterally change the labels on their products." *Id*. A manufacturer, however, may change a drug label on its own if the change complies with the "changes being effected" ("CBE") regulation, set forth in 21 C.F.R. § 314.70(c)(6)(iii). *Id*. That regulation allows drug manufacturers to change a label without the FDA's preapproval if the changes "add or strengthen a contraindication, warning, precaution, or adverse reaction," or "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product," in order to "reflect newly acquired information."[3] 21 C.F.R. § 314.70(c)(6)(iii). "Because

[3] Newly Acquired Information is defined as "data, analyses, or other information not previously submitted to the Agency, which may include (but is not limited to) data derived from new clinical studies, reports of adverse events,

manufacturers may unilaterally update a drug's label if the change complies with the CBE regulation, a state law failure-to-warn claim that depends on newly acquired information – information that Defendants could have added to their label without FDA approval – is not preempted." *Gibbons*, 919 F.3d at 708. Therefore, "to state a claim for failure-to-warn that is not preempted by the FDCA, a plaintiff must plead a labeling deficiency that [Defendants] could have corrected using the CBE regulation." *Id.* (internal citation omitted). A change under the CBE regulation must be for the purpose of accomplishing at least one of the five following objectives:

> (A) To add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling . . . ;
>
> (B) To add or strengthen a statement about drug abuse, dependence, psychological effect, or overdosage;
>
> (C) To add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product;
>
> (D) To delete false, misleading, or unsupported indications for use or claims for effectiveness; or
>
> (E) Any labeling change normally requiring a supplement submission and approval prior to distribution of the drug product that FDA specifically requests be submitted under this provision.

In re Celexa & Lexapro Mktg. & Sales Practices Litig., 779 F.3d 34, 37 (1st Cir. 2015) (quoting 21 C.F.R. § 314.70(c)(6)(iii)) (internal citations and quotations omitted).

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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).

"If the Plaintiffs meet that standard, the burden shifts to the party asserting a preemption defense to demonstrate that there is clear evidence that the FDA would not have approved a change to the [prescription drug's] label." *Gibbons*, 919 F.3d at 708 (internal quotations omitted).

Here, Boehringer contends that the Plaintiffs' manufacturing defect claims, which allege that it violated state law by misrepresenting on the Combivent label the true number of doses available in each Product, are preempted because federal law prohibits it from changing the label without FDA approval. *See* Def's Mem. at 11. There is no dispute that Combivent and its labeling was FDA-approved before the Product was brought to market. The parties disagree about whether the Plaintiffs' proposed changes invoke the CBE regulation, allowing Boehringer to implement a label change without FDA preapproval based on "newly acquired information." 21 C.F.R. § 314.3(b).

Boehringer argues that the Plaintiffs have failed to plausibly allege the existence of "newly acquired information" because their anecdotal allegations are not equivalent to "new clinical studies, reports of adverse events, or new analyses of previously submitted data" that may constitute "newly acquired information." Def's Mem. at 14 (quoting 21 C.F.R. § 314.3(b)). An "adverse event" is defined as "any untoward medical occurrence associated with the use of a drug in humans whether or not considered drug related." 21 C.F.R. § 312.32(a).

Boehringer also contends that the Plaintiffs' state law claims asserting a design defect are also preempted by federal law. Under federal regulations, modifications to the "fill volume" of a specific drug are considered "major changes" under 21 C.F.R. § 314.70(b)(2)(i) and "must be submitted [to the FDA] in a prior approval supplement." Ex. F to Def's Mot., FDA Guidance for Industry (Doc. No. 24-7) at 9. In addition, Boehringer contends that redesigning the Product to

adjust the amount dispensed by each actuation would constitute a "major change" requiring prior approval from the FDA because it would require a "[c]hange[] in a drug product container closure system that controls the drug product delivered to a patient." Def's Mem. at 31 (quoting 21 C.F.R. § 314.70(b)(2)(vi)).

In response, the Plaintiffs contend that their manufacturing and design defect claims are not preempted because: (1) the proposed changes to the product invoke the CBE regulation because their allegations are reports of adverse events; and (2) the proposed changes constitute "minor" or "moderate" changes under 21 C.F.R. § 314.70(c) and (d). Pls' Opp. (Doc. No. 27) at 3.

First, the Plaintiffs argue that the labeling changes they propose are consistent with the plain language of subsections (C) ("To add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product") and (D) ("To delete false, misleading, or unsupported indications for use or claims for effectiveness") of the CBE regulation at 21 C.F.R. § 314.70(c)(6)(iii)(C) & (D). *Id.* at 4.

Second, they argue that directing Boehringer to manufacture a Product that actually conforms to its 120-metered-dose representations constitutes only a "minor" change within the meaning of 21 C.F.R. § 314.70(d) or "moderate" changes under 21 C.F.R. § 314.70(c). *Id.* at 4–5. Under 21 C.F.R. § 314.70(c)(2)(i), "[a] change in the container closure system that does not affect the quality of the drug product" is considered moderate. *Id*. Similarly, "[a]n addition to a specification or changes in the methods or controls to provide increased assurance that the drug substance or drug product will have the characteristics of identity, strength, quality, purity, or potency that it purports or is represented to possess" is considered a "moderate" change. 21 C.F.R. § 314.70(c)(6)(i).

The Plaintiffs primarily rely on the Supreme Court's decision in *Wyeth v. Levine*, 555 U.S. 555, 559 (2009), where the Court held that state-law failure to warn claims were not preempted by federal law when the drug manufacturer could have amended its labeling under the CBE regulation. In *Wyeth*, the plaintiff filed suit after her arm was amputated as a result of taking an injunction of Phenergan. *Id*. at 558. The drug manufacturer argued that her state law claims were preempted by the FDCA. *Id*. at 558–60. The Court disagreed, commenting that the drug manufacturer, and not the FDA, was ultimately responsible for the warning label because the manufacturer retains the ability to update a warning label under the CBE regulation.

> [T]hrough many amendments to the FDCA and to FDA regulations, it has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times. It is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market. *See, e.g.*, 21 C.F.R. § 201.80(e) (requiring a manufacturer to revise its label "to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug").

Id. at 570–71.

Plaintiffs also cite the Tenth Circuit's decision in *In re MDL 2700 Genentech Herceptin (Trastuzumab) Mktg. & Sales Practice Litig.*, 960 F.3d 1210, 1238 (10th Cir. 2020), where the court, citing *Wyeth*, rejected a drug manufacturer's preemption argument, concluding that the evidence:

> suggests that Genentech, as it continued to manufacture Herceptin, obtained and exercised a high degree of control over its manufacturing process, and, in turn, may have knowingly targeted an amount of trastuzumab per vial lower than the 440 mg target stated in the BLA. In other words, the evidence suggests that the downward trend of the average quantity of trastuzumab per vial was not the result of "unavoidable deviations in good manufacturing practice," but instead may have been the result of intentional acts on the part of Genentech.

Id. (quoting 21 C.F.R. § 201.51(g)).

1. *The Plaintiffs' Allegations do not Constitute "Newly Acquired Information"*

I conclude that the Plaintiffs' state law claims are preempted by federal law. To avoid preemption, the Plaintiffs must show that Boehringer could have corrected the alleged labeling discrepancy through the CBE regulation. *See Gibbons*, 919 F.3d at 708. To invoke the CBE regulation, the Plaintiffs must provide "newly acquired information" with the meaning of 21 C.F.R. § 314.3(b). In this case, the Plaintiffs rely on their own self-reporting and other negative online reviews to show that the Product discharges less than 120 doses. Those self-reports and online reviews are, at best, "reports of adverse events" under 21 C.F.R. § 314.3(b). Case law defining what types of "reports of adverse events" constitute "newly acquired information," provides that "new information must have some degree of scientific validity and conclusiveness to constitute 'newly acquired information' under the CBE regulation." *Roberto v. Boehringer Ingelheim Pharm., Inc*., 2019 WL 5068452, at *14 (Conn. Super. Ct. Sept. 11, 2019).

Under federal regulations, newly acquired information "'must provide *reasonable evidence* of a causal association of a clinically significant adverse reaction linked to a drug.' A clinically significant adverse reaction 'ha[s] a significant impact on therapeutic decision-making, such as a risk that is *potentially fatal or otherwise serious.*'" *McGrath v. Bayer HealthCare Pharm. Inc.*, 393 F. Supp. 3d 161, 167 (E.D.N.Y. 2019) (quoting 21 C.F.R. § 201.57(c)(6)(i)) (emphasis in original). The FDA imposes that high standard because it "recognize[s] that exaggeration of risk, or *inclusion of speculative or hypothetical risks*, could discourage appropriate use of a beneficial drug . . . or decrease the usefulness and accessibility of important information by diluting or obscuring it. Indeed, labeling that includes theoretical hazards not well-grounded in scientific evidence can cause meaningful risk information to lose its significance." *Id.* (quoting *Utts v. Bristol-Myers Squibb Co*., 251 F. Supp. 3d 644, 659

(S.D.N.Y. 2017), *aff'd sub nom. Gibbons v. Bristol-Myers Squibb Co.*, 919 F.3d 699 (2d Cir. 2019)).

Accordingly, "reports of adverse events" must be scientific in nature and provide sufficient evidence that links the alleged defect to the information reported on the drug label. *See Utts*, 251 F. Supp. 3d at 659–60. ("By expressly requiring that a CBE supplement only reflect newly acquired information and 'be based on sufficient evidence of a causal association,' the FDA ensures 'that scientifically accurate information appears in the approved labeling.'") (quoting Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices,73 Fed. Reg. 49603, 49604 (Aug. 22, 2008)). For instance, newly acquired information "could be an increasing body of data [detailing] an inherent risk with [a certain] drug." *In re Celexa*, 779 F.3d at 42 (citing *Wyeth*, 555 U.S. at 571).

Multiple courts within the Second Circuit have held that newly acquired information must be scientific in nature. For example, in *McGrath*, the court considered whether a new study that linked a drug to significant metabolic disorders and kidney injury in mice constituted "newly acquired information" under the CBE regulation. 393 F. Supp. 3d at 169. The court ruled that it did not, observing that "the study has yet to be replicated, and only demonstrates an adverse reaction in mice" and therefore did not satisfy the FDA's standard. *Id*. at 170. In *Utts*, the court analyzed nine different reports, studies, and articles supporting the assertion that the defendant's drug labeling was inadequate and held that each one failed to constitute "newly acquired information." *See* 251 F. Supp. 3d at 670 ("The article does not purport to offer new analyses of previously submitted data. Rather, it explores the limitations of the clinical data and offers guidance to prescribing physicians in light of these limitations. Accordingly, it does not constitute newly acquired information.") (internal citations and quotations omitted). In *Gayle v.*

Pfizer Inc., 2020 WL 1685313, at *5 (S.D.N.Y. Apr. 7, 2020), the court held that 6,000 adverse reports sent to Pfizer alleging that its drug Lipitor caused type 2 diabetes did not constitute newly acquired information because the Plaintiffs offered no analysis to accompany the reports.

> Courts have also rejected the notion that analyses based on adverse event reports—much less the reports standing alone—can constitute newly acquired information . . . . Here, Plaintiffs offer no analysis on the adverse event reports. Instead, they merely proffer the adverse event reports by themselves to conclude that Pfizer could have updated the Lipitor label. Under the applicable regulations and case law, Plaintiffs' argument misses the mark.

Id. (citing *Utts*, 251 F. Supp. 3d at 663–64) (internal citations and quotations omitted) (emphasis in original).

Applying those principles here, I conclude that the Plaintiffs' self-reporting and collection of online reviews are not "reports of adverse events" within the meaning of "newly acquired information" because they are not grounded in scientific research. Although Ignacuinos and Davis diligently recorded their daily doses of the Product for an extended period, there is no suggestion that their own research was subjected to peer-review or "well-grounded in scientific evidence" as required by the FDA to alter a preapproved label. The same is true for the Plaintiffs' reliance on online consumer reviews from website such as *WebMD* and *Drugs.com*. *See* Third Am. Compl. at *Id.* at ¶¶ 57–60. Even if the Plaintiffs' reporting and the cited online reviews did constitute "reports of adverse events," the Plaintiffs do not provide any additional scientific analysis to accompany those reports or reviews. *See Gayle*, 2020 WL 1685313, at *5.

Therefore, I **grant** Boehringer's motion to dismiss the Plaintiffs' manufacturing defect claims on preemption grounds.[4]

[4] Accordingly, the Plaintiffs' manufacturing defect claims (Counts I and XII in part and Count III) are dismissed.

2. *The Plaintiffs' Proposed Changes are "Major" Changes*

The Plaintiffs' design defect claims are also preempted by federal law because their proposed changes would constitute "major changes," requiring FDA approval. The Plaintiffs request that Boehringer manufacture or design a Product that "actually conforms to its 120-metered-dose representations." Pls' Opp. at 4. Although the Plaintiffs contend that any proposed labeling, design, or manufacturing change are "at most, 'moderate' in nature under 21 C.F.R. § 314.70(c)," *id*. at 4–5, federal regulations define a "moderate" change concerning a drug dosage as "[a] change in the size and/or shape of a container for a nonsterile drug product, except for solid dosage forms, *without a change in the labeled amount of drug product* or from one container closure system to another." 21 C.F.R. § 314.70(c)(6)(ii) (emphasis added). Similarly, a "minor" change is defined as "a change in the labeling concerning the description of the drug product or in the information about how the drug product is supplied, *that does not involve a change in the dosage strength or dosage form*." 21 C.F.R. § 314.70(d)(2)(ix). (emphasis added).

Based on the proposed changes in the Third Amended Complaint,[5] the Plaintiffs requests would *require* "a change in the labeled amount of" Combivent available in each Product or include "a change in the dosage strength." 21 C.F.R. § 314.70(c)(6)(ii), (d)(2)(ix). Such changes are considered "major" and would require a supplemental submission and additional approval by the FDA. 21 C.F.R. § 314.70(b). Plaintiffs are correct that an "addition to a specification or changes in the methods or controls to provide increased assurance that the drug substance or

[5] As discussed above, the Plaintiffs seek "(1) *changes to the Product's labeling* and 'Instructions for Use' to reflect the fact that it does not live up to its unequivocal promise that the Combivent Respimat inhaler will deliver 120 metered doses; (2) a *change in the design of the Product* so that it actually delivers 120 metered doses; or (3) to the extent that the Product's design is sound, but the manufacturing process is compromised, improvements in the manufacturing process." Third Am. Compl. at ¶ 62 (emphasis added).

drug product will have the characteristics of identity, strength, quality, purity, or potency that it purports or is represented to possess" are "moderate" changes. 21 C.F.R. § 314.70(c)(6)(i). Their requests, however, involve changes to the labeling on the Product (proposed change no. 1), changes to the dosage amount (proposed change no. 2), or changes to the design or manufacturing processes (proposed changes nos. 2–3), which all require prior FDA approval.[6] *See* Third Am. Compl. at ¶ 62.

Therefore, I **grant** Boehringer's motion to dismiss the Plaintiffs' design defect claims as well[7] as claims alleging that the FDA approved label is inadequate, negligent, or fraudulent [8]

IV. Conclusion

For the reasons stated above, I **grant** Boehringer's motion to dismiss the Third Amended Complaint (doc. no. 24). The Clerk shall enter judgment in favor of the Defendant and close the case.

So ordered.

Dated at Bridgeport, Connecticut, this 23rd day of September 2020.

/s/ STEFAN R. UNDERHILL
Stefan R. Underhill
United States District Judge

[6] Indeed, the FDA Guidance for Industry expressly states that any change to "the valve or actuator of a metered-dose inhaler" constitutes a "[m]ajor [c]hange" that requires prior FDA approval. Ex. E to Def's Mem., FDA Guidance for Industry, April 2004 (Doc. No. 24-6) at 20. Likewise, a change to the "fill volume of a drug product involves a change to the specification and must be submitted in a prior approval supplement." Ex. F to Def's Mem., FDA Guidance for Industry, January 2001 (Doc. No. 24-7) at 9.

[7] Counts I and XII in part and Counts V and VII.

[8] Those counts include each statutory consumer protection claim (Counts II, XI, and XV) as well as all product liability and common law claims to the extent they are based on a theory of misrepresentation, fraud, or false statement regarding the Product's labeling (Counts I and XII in part and Count IV, Failure to Warn under Florida law; Count VI, Fraudulent Misrepresentation under Florida law; Count VIII, Negligent Misrepresentation under Florida law; Count IX, Breach of Express Warranties under Florida law; Count X, Breach of Implied Warranties under Florida law; Count XIII, Breach of Express Warranties under Indiana law; Count XIV, Breach of Implied Warranties under Indiana law; Count XVI, Constructive Fraud under Indiana law, and Count XVII, Common Law Fraud under Connecticut law, or alternatively under Florida and Indiana law).