NO. X03 HHD CV16-6065131S	:	STATE OF CONNECTICUT
CHARLES F. ADKINS	:	SUPERIOR COURT
v.	:	COMPLEX LITIGATION DOCKET
	:	JUDICIAL DISTRICT OF HARTFORD
BOEHRINGER INGELHEIM PHARMACEUTICALS, INC., ET AL.	:	MARCH 13, 2020

Ruling on Motion for Summary Judgment

Defendants Boehringer Ingelheim Pharmaceuticals, Inc., and Boehringer Ingelheim International GMBH (defendant or BI) move for summary judgment in this Pradaxa product liability case brought by the plaintiff, Charles F. Adkins. The issue is whether federal law preempts the plaintiff's state law failure to warn claims. The court will address the effect of its prior ruling in *Roberto v. Boehringer Ingelheim Pharmaceuticals, Inc.* No. CPLHHDCV166068484S, 2019 WL 5068452, *9-*21 (Conn. Super. Ct. Sept. 11, 2019) (*Roberto),* in favor of federal preemption. The court heard oral argument on February 13, 2020.

I

For purposes of summary judgment, the historical facts are undisputed. The plaintiff is a resident of Yawkey, West Virginia. The defendant is a German pharmaceutical company with U.S. headquarters in Ridgefield, Connecticut that manufactures an anticoagulant medication called Pradaxa.

On or about November 22, 2010, the plaintiff was prescribed Pradaxa for the treatment of atrial fibrillation, which is an irregular heart rhythm. On or about May 3, 2014, the plaintiff suffered an internal bleeding event for which he was hospitalized at Thomas Memorial Hospital in

FILED

MAR 13 2020

HARTFORD J.D.

133.00

South Charleston, West Virginia for a period of approximately fourteen days. At the time of his injury, the plaintiff suffered from renal impairment and was taking Amiodarone, which is a P-gp inhibitor designed to improve the delivery of therapeutic agents.

The plaintiff alleges that the use of Pradaxa was a substantial contributing factor in causing or exacerbating the bleeding event. The plaintiff also claims that the defendant did not provide warnings on the label[1] that adequately warned doctors prescribing Pradaxa about the risks of bleeding, particularly when concentrations of Pradaxa in the blood plasma are already high.[2] More specifically, the plaintiff asserts that the defendant's labeling neither adequately warns physicians of the impact of plasma concentrations on bleeding risks nor instructs physicians about the need to monitor plasma concentrations to confirm that those concentrations are not above the "upper limit for Pradaxa levels to avoid unnecessary risk of bleeding." In other words, according to the plaintiff, the Pradaxa label fails to warn adequately about patients who are "overexposed to Pradaxa" or "over-anticoagulated." (Entry #106.00 (Plaintiff's Expert Disclosure), pp. 2-3.)

---

[1]The United States Supreme Court has stated: "Although we commonly understand a drug's 'label' to refer to the sticker affixed to a prescription bottle, in this context the term refers more broadly to the written material that is sent to the physician who prescribes the drug and the written material that comes with the prescription bottle when the drug is handed to the patient at the pharmacy.... These (often lengthy) package inserts contain detailed information about the drug's medical uses and health risks." *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1672-73 (2019).

[2]Connecticut law, which applies in this case, employs the "learned intermediary" doctrine, in which "adequate warnings to prescribing physicians obviate the need for manufacturers of prescription products to warn ultimate consumers directly. The doctrine is based on the principle that prescribing physicians act as learned intermediaries between a manufacturer and consumer and, therefore, stand in the best position to evaluate a patient's needs and assess [the] risks and benefits of a particular course of treatment." (Internal quotation marks omitted.) *Vitanza v. Upjohn Co.*, 257 Conn. 365, 376, 778 A.2d 829, 836–37 (2001)

II

The court applies the accepted standards governing summary judgment motions. "Practice Book § [17–49] requires that judgment shall be rendered forthwith if the pleadings, affidavits and any other proof submitted show that there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law. A material fact is a fact that will make a difference in the result of the case.... The facts at issue are those alleged in the pleadings....

"In seeking summary judgment, it is the movant who has the burden of showing the nonexistence of any issue of fact. The courts are in entire agreement that the moving party for summary judgment has the burden of showing the absence of any genuine issue as to all the material facts, which, under applicable principles of substantive law, entitle him to a judgment as a matter of law. The courts hold the movant to a strict standard. To satisfy his burden the movant must make a showing that it is quite clear what the truth is, and that excludes any real doubt as to the existence of any genuine issue of material fact.... As the burden of proof is on the movant, the evidence must be viewed in the light most favorable to the opponent....

"The party opposing a motion for summary judgment must present evidence that demonstrates the existence of some disputed factual issue.... The movant has the burden of showing the nonexistence of such issues but the evidence thus presented, if otherwise sufficient, is not rebutted by the bald statement that an issue of fact does exist.... To oppose a motion for summary judgment successfully, the nonmovant must recite specific facts ... which contradict those stated in the movant's affidavits and documents.... The opposing party to a motion for summary judgment must substantiate its adverse claim by showing that there is a genuine issue of material fact together with the evidence disclosing the existence of such an issue.... The existence

of the genuine issue of material fact must be demonstrated by counteraffidavits and concrete evidence...." (Citations omitted; internal quotation marks omitted.) *Morrissey-Manter v. Saint Francis Hospital & Medical Center*, 166 Conn. App. 510, 517, 142 A.3d 363, cert. denied, 323 Conn. 924, 149 A.3d 962 (2016).

III

At the outset, the court must address several procedural issues raised by the plaintiff's brief. In *Roberto,* the court addressed a claim of impossibility preemption – that prevailing federal law made it impossible for the defendant to conform to the plaintiff's state law claims. See generally *Gibbons v. Bristol-Myers Squibb Co.,* 919 F.3d 699, 707-08 (2d Cir. 2019). Specifically, the defendant posited that regulations promulgated under the federal Food, Drug and Cosmetic Act (FDCA); 21 U.S.C. §301 et seq; made it impossible to change the Pradaxa label to meet the plaintiff's state law claims of failure to warn.

The plaintiff claims that in this context a "state law claim is preempted **only** when there is 'clear evidence' that the FDA would not have approved a change to the drug's label." (Emphasis in original) (Pl. Br., p. 2.) This statement, which the plaintiff and his lawyers have made repeatedly, is not correct.[3] There are actually two theories of preemption in this context and the "clear evidence" theory is the second to consider chronologically. The first, or threshold, theory addresses whether the pharmaceutical company had authority under federal law to change the label on its own to conform to the plaintiff's state law demands. If it did not, then it would also be impossible for the company to comply with state law.

---

[3]The plaintiff's lawyers are the lead counsel in the Consolidated Pradaxa Docket, CPL HHD-CV135036974S, which involves approximately 2800 similar cases, and were the plaintiff's lawyers in *Roberto.*

The first theory involves the concepts of the "changes being effected" or CBE regulation and "newly acquired information." "The FDA can direct a pharmaceutical manufacturer to change a drug's label after it has entered the market, see 21 U.S.C. § 355(o)(4), but manufacturers, not the FDA, bear primary responsibility for their drug labeling at all time .... Nevertheless, drug manufacturers are limited in their ability to unilaterally change the labels on their products. Specifically, to make a change on their own, a manufacturer must comply with the 'changes being effected' or 'CBE' regulation set forth at 21 C.F.R. §314.70(c)(6)(iii). 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 dosing and administration that is intended to increase the safe usage of the drug product," in order to "reflect *newly acquired information.*"'" (Emphasis added.) *Gibbons v. Bristol-Myers Squibb Co.*, supra, 919 F.3d 707.[4]

The phrase "newly acquired information" is the key component of the CBE regulation. "Because manufacturers may unilaterally update a drug's label if the change complies with the

---

[4]The actual CBE regulation is lengthy and complex. 21 C.F.R. § 314.70 is entitled: "Supplements and other changes to an approved NDA." Subsection (c) is entitled: "Changes requiring supplement submission at least 30 days prior to distribution of the drug product made using the change (moderate changes)." Paragraph 6 provides: "The agency may designate a category of changes for the purpose of providing that, in the case of a change in such category, the holder of an approved NDA may commence distribution of the drug product involved upon receipt by the agency of a supplement for the change. These changes include, but are not limited to:" Subparagraph (iii) (A) through (C) then provides as follows: "Changes in the labeling to reflect newly acquired information, except for changes to the information required in § 201.57(a) of this chapter (which must be made under paragraph (b)(2)(v)(C) of this section), to accomplish any of the following: (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 under § 201.57(c) of this chapter; (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 ...."

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." (Internal citations omitted; internal quotation marks omitted.) Id., 708. That is, "[a]s a general rule ... state law can hold a brand-name manufacturer liable for failing to use its powers under the CBE regulation to add a new warning to a drug label." *Dolin v. GlaxoSmithKline LLC*, 901 F.3d 803, 811 (7th Cir. 2018), cert. denied, 139 S. Ct. 2636 (2019). Conversely, if there is no newly acquired information, then the manufacturer is under no duty to change its label and related state failure to warn claims are preempted. See *Utts v. Bristol-Myers Squib Co.*, 251 F. Supp.3d 644, 673 (S.D.N.Y. 2017) ("the plaintiffs' failure to warn claims are preempted because the information upon which the [plaintiff] relies to plausibly plead these claims does not, upon examination, demonstrate that any newly acquired information exists to support a label change pursuant to CBE regulations.")[5]

Contrary to the plaintiff's suggestion, the May, 2019 decision of the United States Supreme Court in *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668 (2019) (*Albrecht*), did not eliminate the first, CBE prong of the preemption test. It is true that, in *Albrecht,* the Court focused on the second prong of preemption which, as noted, involves the issue of whether there is "clear evidence" that the FDA would not have approved a change to the drug label. The Court

---

[5]The court refers to the *Roberto* decision for an extensive discussion of the meaning of "newly acquired information." *Roberto,* *13-*14. For the present purposes, the court will reiterate that federal regulations define "newly acquired information" as "[D]ata, analyses, or other information not previously submitted to the [FDA], which 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).

defined "clear evidence" to mean evidence showing that the drug manufacturer "fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the drug manufacturer that the FDA would not approve a change to the drug's label to include that warning." Id., 1678.

Although the *Albrecht* Court did not specifically identify the test as being two-pronged, it nonetheless acknowledged the concept of "newly acquired information"; id., 1673, 1679; and noted that Merck, the manufacturer of Fosamax, the drug in question, "conceded that the FDA's CBE regulation would have permitted Merck to try to change the label to add a warning before 2010, but Merck asserted that the FDA would have rejected that attempt." Id., 1675. It also "[assumed] ... that ... there is sufficient evidence to find that [the manufacturer] violated state law by failing to add a warning about atypical femoral fractures to the Fosamax label." Id., 1678. Thus, there was no need to address the newly acquired information prong any further in that case.

A post-*Merck* decision of the Third Circuit cited by the plaintiff, while primarily relying on the "clear evidence" prong of preemption, also recognized the argument that the absence of newly acquired information would make it impossible to change the label. See *In re Avandia Marketing, Sales & Product Liability Litigation*, No. 18-1010, 2019 WL 6873681, at *7 (3d Cir. Dec. 17, 2019) ("Finally, we are not persuaded by any of *GSK's arguments that the Plans' claims are preempted because GSK allegedly was unable to avail itself of the CBE process* for various reasons. GSK primarily argues that it could not use the CBE process to introduce a warning on ischemic risks prior to mid-2006, when it submitted its Prior Approval Supplement. GSK reasons that ICT-42 served as the basis for its belief that an ischemic-risk warning should be included on the label, and because that study was completed in mid-2006, *it did not have the 'newly acquired*

information' necessary to make a labeling change prior to that time. This argument, however, is undermined by GSK's own admissions." [Emphasis added.]) Other post-*Albrecht* decisions from outside the Second Circuit have continued to acknowledge that the absence of newly acquired information is a basis for preemption. See *In re Testosterone Replacement Therapy Product Liability Litigation Coordinated Pretrial Proceedings*, No. 14 C 1748, 2019 WL 7290560, at *7-*8 (N.D. Ill. Dec. 30, 2019) (Court examined, although ultimately rejected on the merits, manufacturer's argument "that [plaintiff's] claims are preempted because he has not identified 'newly acquired information ....'"); *Klein v. Bayer Healthcare Pharmaceuticals, Inc.*, No. 218CV01424APGEJY, 2019 WL 3945652, at *5 (D. Nev. Aug. 21, 2019) ("Ingeborg does not plead facts showing that Bayer had or should have had newly acquired information permitting it to unilaterally add her desired warning under the CBE regulation.")

Although the federal Circuit and District courts have differed in their phrasing of the first prong, the court is ultimately guided by the decision of the Second Circuit, to which Connecticut state courts afford "particularly persuasive weight" in the interpretation of federal statutes. *Webster Bank v. Oakley*, 265 Conn. 539, 555 n.16, 830 A.2d 139 (2003), cert. denied, 541 U.S. 903 (2004). In *Gibbons v. Bristol-Myers Squibb Co.*, supra, 919 F.3d 708, the Second Circuit stated: "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 ....If the plaintiff meets 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." [Citations omitted; internal quotation marks omitted.]) While the present case does not involve a challenge to the complaint or to the plaintiff's pleading, *Gibbons*

makes clear that the threshold issue is whether there is a "labeling deficiency that [Defendants] could have corrected using the CBE regulation ...." As discussed, that labeling correction can only take place if there is newly acquired information. At least two other courts within the Second Circuit have continued, after *Albrecht,* to apply a two-pronged preemption test in which the first prong requires a showing that the manufacturer "was prohibited by federal law from [unilaterally] modifying the FDA-approved labeling ...." (Internal quotation marks omitted.) *McGrath v. Bayer HealthCare Pharmaceuticals, Inc.*, 393 F. Supp. 3d 161, 167 (E.D.N.Y. 2019). Accord *Saboi v. Bayer Healthcare Pharmaceuticals, Inc.,* No. 18 CIV. 11169 (VM), 2020 WL 705170, at *11 (S.D.N.Y. Feb. 12, 2020) ("Bayer must (1) demonstrate that Sabol fails to allege facts showing that it could have unilaterally changed Magnevist's label under CBE, or (2) present clear evidence that the FDA would not have approved a change to the drug's label," citing *Wyeth v. Levine*, 555 U.S. 555, 568-73 (2009)). Thus, the absence of newly acquired information is still a basis for preemption in these cases.[6]

III

The plaintiff admits that "[a] judge, not a jury, must decide the pre-emption question." (Pl. Br., p. 3.) Yet the plaintiff's brief repeatedly asserts that the court should deny the summary judgment motion because there are factual disputes, implicitly suggesting that these factual disputes should be resolved at trials which, in these cases, have been to a jury. These positions

---

[6]The plaintiff's suggestion at oral argument that the plaintiff merely has to come forward with what he alleges to be newly acquired information and that the defendant does not have a right to be heard on that issue is simply contrary to the basic adversary nature of our judicial system. (2/13/20 Tr., p. 94.) Even if the plaintiff agrees that the court could review the plaintiff's submission to ensure that it meets the definition of newly acquired information, the court cannot do so effectively and reliably unless it hears from both sides on the issue.

are obviously contradictory.[7]

The *Albrecht* Court held with respect to the second, "clear evidence" prong of the analysis that the "question is a legal one for the judge, not a jury." *Albrecht*, supra, 139 S. Ct. 1679. See also id., 1672 ("We here determine that this question of pre-emption is one for a judge to decide, not a jury.") The Court reasoned that "judges are better suited than are juries to understand and to interpret agency decisions in light of the governing statutory and regulatory context." Id., 1680. The Court added that "sometimes contested brute facts will prove relevant to a court's legal determination about the meaning and effect of an agency decision." Id. The Court observed: "[W]e consider these factual questions to be subsumed within an already tightly circumscribed legal analysis. And we do not believe that they warrant submission alone or together with the larger pre-emption question to a jury. Rather, in those contexts where we have determined that the question is 'for the judge and not the jury,' we have also held that courts may have to resolve subsidiary factual disputes that are part and parcel of the broader legal question." (Internal quotation marks omitted.) Id.

Although the issues and analysis on the first prong of the preemption test, involving newly acquired information, are not identical to those involved in the second, clear evidence prong, it seems unlikely that the Supreme Court would hold that the first prong is triable to the jury while the second prong is not. Both prongs involve complicated legal analysis. The question of whether there is newly acquired information seems ill-suited for a jury. Accordingly, the court concludes that both the legal issues and any "subsidiary factual questions" in deciding whether

---

[7]To compound matters, the plaintiff's brief does not specifically identify the alleged factual disputes.

there is newly acquired information are matters for a court, not a jury, to decide. (Internal quotation marks omitted.) Id. See also *Ridings v. Maurice,* No. 4:15-cv-00020-JYM (W. D. Mo. Oct. 20, 2019) ("Consistent with *Albrecht*, the Court will be the factfinder on the question of whether Boehringer's affirmative defense of preemption can be established so as to bar Ridings' state law failure-to-warn claims." [footnote deleted]).

Related to the characterization of the preemption issue is the question of the burden of proof. The plaintiff maintains that the defendants have the burden of proof on preemption because preemption is a special defense. This statement is only partly correct. As the court ruled in *Roberto*, the burden of going forward and identifying the purported newly acquired information must fall on the plaintiff because "it would be virtually impossible for the defendants to prove a negative and negate the existence of newly acquired information without knowing exactly what newly acquired information the plaintiff relies upon." *Roberto*, *11 n.19. Although this point could become important in future cases, it is essentially academic in this case because the plaintiff has cited numerous purported examples of newly acquired information.

For a case, such as the present one, arising on summary judgment, our courts have traditionally applied a burden-shifting approach in which the defendant must initially make a showing of entitlement to judgment as a matter of law and the plaintiff must then show a genuine issue of material fact. See *Morrissey-Manter v. Saint Francis Hospital & Medical Center*, supra, 166 Conn. App. 516–18. That approach applies even when the defendant seeks summary judgment on an affirmative defense. See *Riley v. Pierson*, 126 Conn. App. 486, 490–92, 12 A.3d 581 (2011); *Petro, Inc. v. U.S. Coffee, Inc.*, No. FSTCV116009308S, 2014 WL 279655, at *1 (Conn. Super. Ct. Jan. 2, 2014).

In the preemption context, as discussed, the court must resolve any subsidiary issues of fact, perhaps at an evidentiary hearing. See *Merck Sharp & Dohme Corp. v. Albrecht*, supra, 139 S. Ct. 1680; *Ridings v. Maurice,* supra, slip op. at 3. At such a hearing, the defendant might have the burden of going forward in keeping with traditional summary judgment standards. In the present case, however, the court does not have to resolve any disputed, subsidiary fact issues.

A related factor is the claim that there is a presumption against preemption by federal statutes of state common law claims in this context.[8] That presumption would seem hard to apply in a case in which the issue is whether there is newly acquired information because this issue is essentially one of law. In such an instance, there is no need to assign a burden of proof and the court's only task is decide how the law applies in this context. However, to the extent that there can be a burden of proof on this issue, the court would agree that the presumption against preemption means that the defendants bear that burden. The question then becomes whether the defendants can rebut that presumption by showing that the plaintiff's proffer does not constitute newly acquired information. See *Roberto,* *11 n.19.

IV

The court must also address the plaintiff's improper briefing of this matter. The plaintiff's brief states that "[t]here are many examples of [relevant] 'newly acquired information' as that

---

[8]The majority opinion in *Wyeth v. Levine*, 555 U.S. 555 (2009), a case involving drug labeling, referred to the presumption against preemption and stated that "[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." (Internal quotation marks omitted.) Id., 565 & n.3. But a concurring Justice remarked that "this Court has never held that the presumption [against preemption] applies in an area—such as drug labeling—that has long been reserved for federal regulation." (Internal quotation marks omitted.) Id., 624 (Thomas, J., concurring in the judgment)

term is defined by Federal Regulations. As a chart reflecting the documents, and relevance of new information supporting a CBE label change is attached as Exhibit I, Plaintiff will comment on but a few representative examples here that reflect Defendants' acquisition of new information ...." (Pl. Amended Objection & Mem. of Law (Pl. Br.) (Entry # 116.00), pp.16-17 [footnote omitted.]) Exhibit I lists some forty items and also contains a column labeled "Significance" in which there is a one sentence explanation of the purported basis for labeling the item as newly acquired information. The plaintiff also attaches as exhibits a five page chart of "Labeling Permitted Under CBE" with an additional column entitled "Rationale/Support for Labeling Revision" (Pl. Ex. E) and a four page "Peer Reviewed and Scientific Literature List" with an additional column entitled "New Information based on Reanalysis of Existing Data or New Analysis of New Data." (Pl. Ex. L.). Finally, the plaintiff includes as an exhibit a declaration from Laura M. Plunkett, PhD, who concludes that there was relevant newly acquired information developed after 2010 and that BI's transmittals of safety data or analysis to the FDA do not constitute submissions for regulatory action purposes. (Pl. Ex. F, pp. 1-2.) The declaration refers to an attached sixty-four page expert report with thirty-nine pages of appendices and a thirteen page supplemental declaration, all of which contain opinions and arguments supporting her conclusions. The plaintiff's brief at most makes only passing mention of these supplemental materials.

The court will address the representative examples of newly acquired information that the plaintiff has briefed. But it is improper to expect the court, or the defendants, to address the laundry list of other examples contained in Exhibits E, I, and L and the opinions expressed in the supplemental declarations.

The court has previously advised the plaintiff's lawyers of the impropriety of briefing by

incorporating other argumentative exhibits created by counsel or counsel's experts.[9] Unfortunately, the plaintiff's lawyers have failed to heed the court's warning. The court will state again that placing a list of items and their purported significance in an exhibit without analysis in the brief, or the similar practice of referring, without full discussion, to substantive charts, memoranda, or declarations attached to the brief imposes undue burdens on the court and the defendants. For this reason, our appellate courts have deemed such points abandoned, both at the appellate level and in the trial court. See *Raynor v. Commissioner of Correction*, 117 Conn. App. 788, 796-97, 981 A.2d 517 (2009), cert. denied, 294 Conn. 926, 986 A.2d 1053 (2010) ("[R]eviewing courts are not required to review issues that have been improperly presented to th[e] court through an inadequate brief.... Analysis, rather than mere abstract assertion, is required in order to avoid abandoning an issue by failure to brief the issue properly.... Where a claim is asserted in the statement of issues but thereafter receives only cursory attention in the brief without discussion or citation of authorities, it is deemed to be abandoned.... These same principles apply to claims raised in the trial court...." [Internal quotation marks omitted.]) Further, the practice of incorporating other substantive materials by reference without permission of the judicial authority circumvents the page limits and the orderly process imposed by the rules of

---

[9] *Roberto,* *15 n. 26 ("the plaintiff, in particular, has submitted numerous supplemental materials, such as a four page chart listing examples of newly acquired information (Pl. Supp. Br. in Opp. to Defs. Motion for Summary Judgment, Entry # 278.00, Ex. Q), an eight page, single spaced document entitled "Preemption Considerations," which was submitted but not marked at oral argument, and a Motion to Supplement the Record, consisting of a ten page memorandum of law and 219 pages of exhibits filed on August 23, 2019 (Entry # 332.00.) These supplemental filings circumvent the court's page limitations, unfairly create uncertainty for the defendants as to how to respond, and pose an undue burden on the court in its attempt to finalize a decision. Out of an abundance of caution, however, the court has considered these materials as well.")

court. See Practice Book § 4-6.[10] Accordingly, the court will not consider the matters contained in Exhibits E, I, and L and the supplemental declarations unless the plaintiff analyzes them in his brief.[11]

V

A final procedural matter concerns the plaintiff's attempt to raise claims unrelated to blood plasma concentration and blood monitoring. The plaintiff has designated this case as a Group A case under Case Management Order (CMO) 23. CMO 23 provides: "Group A cases are those in which the only failure to warn claim involves plasma concentration and/or blood monitoring or assessment." See *Connecticut Pradaxa Litigation*, HHD -CV13-5036974, Entry # 292.00, p. 1. Contrary to this directive, the plaintiff lists "Pradaxa's 'local effect' on the Gastrointestinal Tract" in his brief and other patient characteristics such as GERD, gastritis, esophagitis, and the presence of legions in his attached chart as conditions allegedly requiring more warnings in the label. (Pl. Br., p. 27; Pl. Ex. E, pp. 3-4.) But because there is no indication that these conditions are related to blood plasma concentrations or the absence of blood monitoring or assessment, these claims are not properly before the court. For this reason and because, as explained above, the plaintiff has not briefed them adequately, the court will not consider these claims further.[12]

---

[10]Section 4-6 provides in pertinent part: "The text of any trial brief or any other brief concerning a motion in any case shall not exceed thirty-five pages without permission of the judicial authority."

[11]The defendants have understandably produced their own charts to respond to the plaintiff's extra-briefing arguments. (Defs. Exs. A, B.) For consistency, the court has not relied on or even substantively reviewed the defendants' charts.

[12]The plaintiff's reference to "Amiodarone as a P-gp inhibitor" as a risk factor specific to the plaintiff apparently does refer to a claim linked to plasma concentration but, because the

V

The court now turns to analysis on the merits of what the plaintiff claims was newly acquired information on plasma concentration and monitoring. As discussed, the court will examine the claims that the plaintiff has a) actually briefed, rather than those just mentioned in passing or included only in exhibits, b) properly raised in a Group A case, and c) not already presented in *Roberto.*[13]

1. Schumacher emails, Patent Application, and other documents purportedly showing an optimal range of Pradaxa levels

The first claim in the plaintiff's brief is that various items reveal "Boehringer's consistent scientific reanalysis of the RE-LY data showing that more Pradaxa is *not* better, all of which occurred after Pradaxa's US approval." (Emphasis in original) (Pl. Brief, p. 18.) The plaintiff

---

plaintiff merely provides a citation to several sources without any further analysis in the brief, the court considers the claim abandoned. (Pl. Br., p. 27).

[13]The plaintiff filed a supplemental brief containing a three page list of exhibits that "have not previously been brought to the Court's attention in the preemption context and/or with regard to newly acquired information." (Entry # 122.00, p. 2.) Examination of this list reveals only one item – the October, 2019 testimony of Dr. Maureen Oakes – that was not available at the time of briefing in *Roberto.* The supplemental brief also identifies nine "arguments in the objection/memorandum of law" – apparently in *Roberto* – "[that] have been modified ...." (Entry # 122.00, p. 4.) This list contains only two items that were not available at the time of the *Roberto* briefing – the testimony of Dr. Oakes and the new Third Circuit case of *In re Avandia Marketing, Sales & Product Liability Litigation*, supra, 2019 WL 6873681. It is not clear why, in their *Roberto* briefs, the plaintiff's lawyers did not present the long list of exhibits and arguments that they concede existed at the time, especially given the multiple opportunities the court gave the plaintiff to brief the matter. See note 9 supra. It is hardly an efficient use of judicial resources, or those of the parties, to have to redo the same massive project in order to give the plaintiff's lawyers yet another bite of the apple. At oral argument, the plaintiff's lawyers apologized to the court because they had "not done as good of job as we believe we're capable of in communicating to the Court some of these issues." (2/13/20 Tr., p. 34.) While the court appreciates the apology, it did not address the court's primary concern about the inefficiency and now bifurcated nature of the plaintiff's presentation.

cites an internal email from a Dr. Helmut Schumacher, a BI scientist, stating that "a plasma level between 30 and 150 appears to be optimal regarding both, prevention of ischemic strokes and avoidance of bleeds." (Pl. Ex. 610, p. 7.) The plaintiff also cites: an analysis performed by Thorsten Lehr of BI (Pl. Ex. 47), a December 2011 draft of the Reilly-Lehr paper (Pl. Ex. 183),[14] a 2016 paper by James Reiffel, a 2013 patent application that BI allegedly filed (Pl. Ex. 3115), and BI's 2011 Clinical Overview Statement (Pl. Ex. 149.)

These exhibits, either individually or collectively, do not establish newly acquired information. There are several concerns about some of the exhibits individually. First, as stated in *Roberto,* the court cannot recognize the statement from a single scientist, such as Dr. Schumacher or Dr. Lehr, as constituting newly acquired information, at least until that statement becomes part of a peer-reviewed article or finds other forms of corroboration. *Roberto,* *16, 19. Second, the court has expressed reluctance to rely on a draft of an article, such as the Reilly article, especially when the final version differs. *Roberto,* *16, 20.[15] Third, the 2016 Reiffel paper postdates the 2014 bleed in this case and thus does not constitute information available to BI that could have led to a timely change in the label. See *McGrath v. Bayer HealthCare Pharmaceuticals Inc.*, supra, 393 F. Supp. 3d 166.

The plaintiff claims that the patent application "includes ranges within those identified by all other scientists identified here." (Pl. Br., p. 17 n.76.) In a footnote, the plaintiff quotes the

---

[14]P. Reilly & T. Lehr, "The Effect of Dabigatran Plasma Concentrations and Patient Characteristics on the Frequency of Ischemic Stroke and Major Bleeding in Atrial Fibrillation Patients," Journal of the American College of Cardiology (Feb. 2014) (hereinafter the Reilly paper).

[15]The Schumacher statement was part of an "exploratory analysis" that was consistent with the 2011 Reilly draft. (Pl. Ex. 610, p. 8; Pl. Br., p. 17-18.)

application as stating: "Surprisingly it has been found that a dabigatran plasma concentration of 40 ng/mL to 110 ng/mL, preferably 49 ng/mL to 102 ng/mL, particularly preferred 80 ng/mL to 90 ng/mL, provides an optimal therapeutal efficacy, e.g. an optimum of stroke prevention, in conjunction with a significantly reduced major bleeding risk compared to Warfarin treatment or compared to standard dabigatran treatment ... The present invention solves the problems stated above." (Pl. Br., p. 6 n.24.)[16] As the plaintiff notes, however, BI withdrew the application shortly after the plaintiff's bleed. BI stated the following in an August, 2014 submission to the FDA: "An initial review concluded that these analyses were of sufficient importance to file a patent application for a dose adjustment approach by trough concentration. However, all patent applications have been withdrawn and/or abandoned, including in Europe and the United States. No patent rights were ever granted for this approach." (Def. Reply Br., Ex. 7, Bates Nos. 5200-00001, 5200-069.) Although BI did not withdraw the patent application until after the plaintiff's May, 2014 bleeding event, the court cannot consider a pending application to have the finality and reliability necessary to constitute newly acquired information. One court has stated: "[b]ecause the claims in the pending patent applications have not yet been 'allowed' by the [Patent and Trademark Office], they are subject to being modified, amended, added to or deleted during the patent prosecution process. A decision construing those claims at this stage would not be final ...." *Simonton Building Products, Inc. v. Johnson*, 553 F. Supp. 2d 642, 650 (N.D.W. Va. 2008). Stated differently, a pending patent application, especially one later withdrawn, resembles a draft

[16]Unfortunately, the plaintiff fails to provide a page cite within the patent application. The court has had to comb through a highly technical, ten page, single-spaced, two column document to verify the plaintiff's claim. (Pl. Ex. 3115, p. 4.)

opinion that does not necessarily represent a tested, final conclusion.[17]

The most reliable component of the plaintiff's package is BI's 2011 Clinical Overview Statement. The plaintiff appears to rely on statements to the effect that the European label "will refer to 200 ng/mL to be associated with an increased risk of bleeding: ' ... dabigatran concentrations above 200 ng/ml measured at trough after 150 mg twice daily dosing (10-16 hours after the previous dose), are associated with an increased risk of bleeding.'" (Pl. Br., pp. 18-19; Pl. Ex. 149, p. 4.) In addition, one of the few pieces of truly new, albeit largely undisputed, information that the plaintiff offers is the October, 2019 testimony of Dr. Maureen Oakes of BI that a clinical overview statement can, when appropriate, become the basis for a CBE label change. (Pl. Ex. A, pp. 629-30.)

The 2011 clinical statement itself, however, is not new. The court extensively reviewed the 2011 statement in *Roberto*. *Roberto,* *17-*18. The court discussed the fact that, prior to Pradaxa's approval, the FDA already had its own study showing the following: '"There is a significant relationship between dabigatran exposures and incidence of bleeding events (major bleeding or life-threatening bleeding). The probability of a life-threatening bleed ... increases with increasing dabigatran concentration. Going from the 10th to 90th percentile of observed pre-dose

---

[17]The plaintiff claims that he relies on documents that were of the "same type and nature" as those used by the defendants to support a 2011 CBE Pradaxa label change. (Pl. Br., pp. 1-2.) The plaintiff then cites BI's own Company Core Data Sheet and its Clinical Overview Statement. (Pl. Br., p. 2 n.4.) At oral argument, the plaintiff added more generally that a CBE label change submission can draw support from an unpublished internal study. The court agrees with the latter proposition. The fact that a study is internal and unpublished, as long as it is final, does not prevent it from containing newly acquired information. The court disagrees, however, that the plaintiff has relied only on the same type of information contained in the defendants' CBE papers. There is no indication that the CBE application relied on matters such as preliminary drafts or a withdrawn patent application, as the plaintiff has here.

dabigatran concentrations (22.9 ng/mL to 238.3 ng/mL) in RE-LY, the probability of a life-threatening bleed within 1 year in a typical patient is predicted to increase from 0.27% to 1.82%.'" *Roberto*, *18 (quoting 2010 FDA Clinical Pharmacology Review (Def. Ex. 2 herein, p. 9.)) As the court also suggested, a graph relied on by the FDA shows that, as dabigatran trough concentrations go up with the 150 mg dose, the probability of a life-threatening bleed rises as well and that, at 200 ng/ml, the probability of such a bleed is well over 1%. Id. (citing 2010 FDA Clinical Pharmacology Review (Def. Ex. 2 herein, p. 61.) (See also Def. Reply Br., Ex. 14 (Sept. 20, 2010 FDA Efficacy Review), Bates p. 5788-00055).[18] The court also noted that the final draft of the Reilly paper relied on the premise that "'currently it is unknown whether there is a single concentration range where the balance between thromboembolic events and bleeding events is optimal for all AF patients'" and concluded that "[t]here is no single plasma concentration range that provides optimal benefit risk for all patients." *Roberto,* *18 (quoting Pl. Ex. 3247, pp. 2, 8.) The court concluded that the information in the 2011 clinical statement was in essence "previously submitted to the [FDA]" and that there was neither a "basis nor a need for a warning in the United States that blood plasma concentrations above a specific level pose additional dangers for all patients." *Roberto,* *18 (citing *Dolin v. GlaxoSmithKline LLC*, 901 F.3d 803, 816 (7th Cir. 2018), cert. denied, 139 S. Ct. 2636 (2019) ("The [2011] article contained the same figures as GSK's 2006 analysis, which GSK submitted to the FDA. There is no basis to conclude that this was a new analysis or that it was 'not previously submitted to the Agency.'")). See also *In re Lipitor (Atorvastatin Calcium) Marketing, Sales Practices & Product Liability Litigation,*

[18]In their reply brief, the defendants cite another study purportedly supporting a similar proposition. There is, however, no agreement of the parties or clear showing in the defendants' papers that the defendants submitted this study to the FDA. (Def. Reply Br., p. 11.)

185 F. Supp. 3d 761, 769 (D.S.C. 2016) ("any claim that a drug label should be changed based solely on information previously submitted to the FDA is preempted because the CBE regulation cannot be used to make a label change based on such information.")

The court adheres to the conclusion that the 2011 Clinical Overview Statement does not contain newly acquired information concerning unacceptably high Pradaxa plasma concentration levels. Even when one adds the other components in the plaintiff's compilation, the items collectively do not establish with sufficient reliability any "risks of a different type or of greater severity or frequency than ... reports previously submitted to FDA" so as to constitute newly acquired information. (Internal quotation marks omitted.) *Wyeth v. Levine,* 555 U.S. 555, 569 (2009) (quoting 73 Fed. Reg. 49607.)

2. Potential Mid to Long-Term Strategy for Monitoring

The plaintiff next relies on a 2012 presentation made by Dr. Klaus Dugi, BI's chief medical officer, to BI's leadership team entitled "Potential Mid to Long Term Strategy for Pradaxa in SPAF [stroke prevention in atrial fibrillation patients]." (Pl. Ex. 40.) Dugi proposed: "a strategy of a one time initial measurement (perhaps repeatedly annually and in some instances such as moderate renal impairment in shorter intervals) and titration of the Pradaxa dose to achieve an exposure in an individual patient that has been demonstrated in RE-LY to provide the best benefit risk ratio of preventing ischemic strokes with as little increase in bleeding risk ...." (Pl. Ex. 40, p. 2.). The plaintiff also states that this information served as a basis for the 2013 patent application.

An examination of the Dugi presentation reveals that it was a proposal that neither BI nor any other entity accepted. The court actually reviewed the Dugi presentation in *Roberto* and

concluded that it was "preliminary in nature and [examines] only potential strategies." *Roberto*, *20 (citing *Uits v. Bristol-Myers Squibb Co.*, supra, 251 F. Supp.3d 669.) What the court did not state or even know at the time of the *Roberto* decision was that BI did not adopt the Dugi strategy because the "scientific data would not support such a concept."[19]

To be sure, the fact that a company's leadership rejects a proposal should not foreclose the proposal from constituting newly acquired information, as long as the proposal achieves some sort of acceptance that would reveal its reliability. The plaintiff attempts to meet that standard by claiming that the Dugi study served as a basis for the 2013 patent application. The plaintiff's brief contains no analysis of what language in the ten page, single spaced, double column patent application supports the Dugi proposal. And, as mentioned, BI withdrew the application. Accordingly, the court cannot conclude that the proposal for monitoring bears sufficient scientific

---

[19]Questioning of Dr. Dugi at a deposition proceeded as follows:
Q. "Okay. There are some folks at the company who have suggested that one of the ways to ensure safe use of the product of Pradaxa is to monitor for blood plasma concentration levels either -- in multiple potential ways, either through the Hemoclot or aPTT and other -- ECT, for example, right? So there have been folks who have discussed this at the company over the years, that there should be regular or periodic or scheduled monitoring, right?
MR. IMBROSCIO: Object to the form, compound, vague.
A. I think it's always important to look for opportunities to further increase the risk/benefit profile of a product. And I was actually one of the colleagues wanting to look at, is this a way where we can further improve on the benefit/risk profile of patient treatment. Unfortunately, I had to find out that this scientific data would not support such a concept.
Q. "Okay. Okay. It's -- you're referring to your mid- to long-term strategy for Pradaxa -- potential strategy for Pradaxa?
2 A. "I'm not sure which --
3 Q. "Okay. So -- one second. You said that you found out that this -- the scientific data would not support such a concept. And you're talking about monitoring potentially, right?
8 A. "That was an idea.
9 Q. "Okay.
10 A. "To see whether we could further improve the benefit/risk. But, unfortunately, the data didn't support the concept."
(Def. Reply Br., Ex. 8, pp. 253-55.)

validity to constitute newly acquired information.

3. The Reilly Paper

The court discussed the Reilly paper extensively in *Roberto*. The court stated that it could not rely on preliminary discussions or earlier drafts of the paper because they "do not provide reliable evidence of new risks." *Roberto,* *16. And the court reasoned that the final, published Reilly paper, which concluded that "[t]here is no single plasma concentration range that provides optimal benefit risk for all patients," does not "identify any specific plasma concentration levels that pose 'risks of a different type or greater severity or frequency than previously included in submissions to the FDA.'" *Roberto,* *17.

The plaintiff offers two new points. First, he claims that, under Connecticut law, the knowledge and statements of employees, such as Dr. Reilly, are imputable to the company. Assuming that proposition were true, it would not change the result here.[20] Even if one presumes that BI endorsed the preliminary drafts of the Reilly paper, those drafts remained preliminary and did not reflect the company's final position as stated in the final version of the article. That position remained that "[t]here is no single plasma concentration range that provides optimal benefit risk for all patients."

Second, the plaintiff contends that the Reilly paper supports the newly discovered claim that "patients do not get statistically significantly more stroke prevention once their Pradaxa level

---

[20]The first case that the plaintiff cites, however, states a very different proposition. See *Village Mortgage Co. v. Veneziano*, 175 Conn. App. 59, 75 n.6, 167 A.3d 430, cert. denied, 327 Conn. 957, 172 A.3d 205 (2017) ("The general rule is that knowledge of an agent will not ordinarily be imputed to his principal where the agent is acting adversely to the latter's interest." [internal quotation marks omitted.])

is over approximately 50 ng/ml." (Pl. Br., p. 5.) It is hard to verify this contention because the plaintiff never cites to a specific page in the text of the article. In any event, prior to approval, the FDA already knew that there was a "rapid decrease in probability of stroke from a concentration of zero through approximately 70 ng/ml, with only a *gradual* reduction in risk at higher concentrations." (Emphasis added.) (Def. Ex. 27 (Oct. 19, 2010 FDA Center for Drug Evaluation and Research approval of Pradaxa 110 mg strength), p. 6.) The FDA also stated in this context that the "parameter describing the relationship between dabigatran concentration and ischemic stroke was of *marginal significance* but was included in the final model." (Emphasis added.) (Def. Ex. 2 (April 19, 2010 Office of Clinical Pharmacology: Pharmacometric Review, p. 9 of 15), p. 58). See also Pl. Ex. B (BI 2011 CBE Application to the FDA), Bates p. 0002017405 (based in part on "assessment of the spontaneous fatal cases associated with bleeding reported since market authorization," the "slope of the stroke-concentration relationship is relatively flat at high concentrations. Any subgroup with higher exposure will tend to have *minimal change* in the probability of stroke with increase or decrease in dose.") (Emphasis added.)[21] Thus, to the extent that the plaintiff correctly interprets the Reilly article as finding no significant stroke prevention benefit at higher doses, that finding does not differ from the FDA's information, which found only a "gradual" or "minimal" stroke reduction benefit at higher concentrations without finding statistical significance. Thus, the Reilly study does not "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);

---

[21]In their reply brief, the defendants cite an additional preapproval study purportedly supporting a similar proposition. Once again, however, there is no agreement of the parties or clear showing in the defendants' papers that the defendants submitted this study to the FDA. (Def. Reply Br., p. 5 n.5.)

note 5 supra.[22]

4. Miscellaneous Medical Literature

The plaintiff states that "[t]here have also been multiple publications in the peer-reviewed medical literature evaluating new data and performing new analysis of existing data showing Pradaxa risks of a different type or of greater severity or frequency than were known pre-approval." (Pl. Br., p. 25.) But the plaintiff only discusses two of these articles in his brief, and even then relegates the discussion of them to a footnote. (Pl. Br., p. 6 n.26.) The first is a "Commentary" published in the British Journal of Clinical Pharmacology principally written by Dr. Paul Chin and entitled "Perspective on dabigatran etexilate dosing: why not follow standard pharmacological principles?" (Pl. Ex. 3067.) The commentary proposes that "[a]s a result of the very strong relationship between dabigatran plasma concentrations and anticoagulant effects, monitoring of anticoagulant effects could assist in the management of patients at higher risk of thrombotic episodes and/or haemorrhage." It suggests that the range of 50-300 ug (equivalent to ng/ml) "might be considered a starting point for discussion regarding the desirable limits of exposure" and that the "slightly narrower range" of 75-240 ug "might be considered a useful target range." (Pl. Ex. 3067, p. 2.) It adds that "[l]aboratories should be encouraged to set up Ecarin Clotting Test (ECT) or Hemoclot Thrombin Time (TT) assays because of the extremely strong linear relationship with dabigatran concentrations." (Pl. Ex. 3067, p. 5.) The commentary

---

[22]The defendants present what appears to be a synopsis of the Reilly paper in a Periodic Safety Update Report dated May 14, 2014. (Def. Reply Br., Ex. 18, pp. 1, 47-51.) Even assuming that the defendants presented this report to the FDA, they would presumably have done so after the plaintiff's May 3, 2014 bleed. Thus the Reilly paper itself, unlike some of its underlying concepts, does not constitute information "previously included in submissions to FDA" in this case.

concludes that "[s]uch an approach lends itself to further clinical trials." (Pl. Ex. 3067, p.5.)

Although the commentary does not contain any new data, the plaintiff asserts that it represents a "new analysis." (Pl. Br., p. 6 n.26.) However, without any new data, the commentary's rather tentative statement of a therapeutic range and its conclusion that its proposal for monitoring "lends itself to further clinical trials" do not establish newly acquired information with any reliability. See *Sabol v. Bayer Healthcare Pharmaceuticals, Inc.*, supra, 2020 WL 705170, *13 ("the authors here draw only a tentative, at best, suggestion of a causal relationship between the brain signals and the gadolinium retention."); *McGrath v. Bayer HealthCare Pharmaceuticals, Inc.*, supra, 393 F. Supp. 3d 169 (study concluding that "further studies are required" was "inconclusive" and "would not justify a unilateral label change"); *Utts v. Bristol-Myers Squibb Co.*, supra, 251 F. Supp. 3d 669 (rejecting articles that "merely express a desire for further investigation into NOAC [novel oral anticoagulant] dosing regimens or reversal agents"). The article presents a proposal rather than making a finding. Further, its recommendation that monitoring with the ECT or TT test "could assist" the management of AF patients is essentially no stronger than what the Pradaxa label already stated in the year before the plaintiff's bleed: "The degree of anticoagulant activity can also be assessed by the ecarin clotting time (ECT) .... In the RE-LY trial, the median (10^{th} to 90^{th} percentile) trough ECT in patients receiving the 150 mg dose was 63 (44 to 103) seconds." (Pl. Ex. 94, § 12.2 (Dec. 2013); Def. Reply Br., Ex. 33, § 12.2 (Apr. 2014)). Given the inconclusive nature of the commentary and what the Pradaxa label already stated by 2013, it is simply unclear what change to the label the Chin commentary would have permitted the defendants to make. The court concludes that the

Chin commentary does not constitute newly acquired information.[23]

VI

The court grants the defendants' motion for summary judgment.

It is so ordered.

Schuman, J.

Carl J. Schuman
Judge, Superior Court

Notice sent: 3/13/20
- OCR

[23]The second piece noted by the plaintiff in his section on medical literature is the 2016 article principally authored by Dr. James A. Reiffel from the American Heart Journal entitled "NOAC monitoring, reversal agents, and post-approval safety and effectiveness evaluations: A cardiac safety research consortium think tank." (Pl. Ex. 3246.) As stated above, because the publication of this article took place after the plaintiff's 2014 bleed, it cannot constitute newly acquired information in this case.