**UNITED STATES DISTRICT COURT**
**EASTERN DISTRICT OF LOUISIANA**

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| **IN RE: XARELTO (RIVAROXABAN) PRODUCTS LIABILITY LITIGATION** | **MDL 2592** |
| | **SECTION L** |
| **THIS DOCUMENT RELATES TO:** | **JUDGE ELDON E. FALLON** |
| **Harriet Ibanez, et al. v. Janssen Research & Development, LLC f/k/a Johnson & Johnson Pharmaceutical Research & Development, LLC, et al.** ***Case No. 2:14-cv-02669*** | **MAG. JUDGE NORTH** |

**PLAINTIFFS' RESPONSE IN OPPOSITION TO DEFENDANTS' JOINT MOTION TO CERTIFY FOR INTERLOCUTORY APPEAL UNDER 28 U.S.C. §1292(b)**

## I. INTRODUCTION

Defendants seek summary judgments of dismissal as to Plaintiffs' failure-to-warn and design-defect claims, arguing they are preempted by federal law.[1] In addition, should this Court deny Defendants' motions, they seek certification of such a ruling for immediate interlocutory appeal under 28 U.S.C. §1292(b). However, in the event this Court adheres to its prior rulings and rejects Defendants' position that the claims in *Ibanez* are preempted as a matter of law, there is no justification for interlocutory appeal. Particularly with respect to the framing of a true legal issue which Defendants purport to have certified, the essential prerequisites set forth in 1292(b) clearly have not been satisfied.

## II. PROCEDURAL BACKGROUND

Defendants have moved for partial summary judgment on preemption on more than one occasion in the course of this litigation. This Court previously denied Defendants' FRCP 56

[1] Rec. Doc. Nos. 7653, 7660.

motions on preemption in the first three bellwether trials in this MDL – *Boudreaux*, *Orr*, and *Mingo*.[2] In doing so, Your Honor concluded that federal regulatory law did not foreclose either the pre-market design-defect claims or the pre-approval and post-approval failure-to-warn claims asserted by Plaintiffs in these cases. More importantly for present purposes, the Court reached its conclusions based on an analysis well-settled in the jurisprudence, as to which no substantial difference of opinion exists.

This Court specifically has ruled that the Defendants are not exempt from their state law duty to design a specific assay and/or antidote before sending Xarelto to the FDA for approval, and likewise are not exempt from their state law duty to warn and instruct physicians as to the availability of Neoplastin PT tests to measure the anticoagulative effects of Xarelto in patients.[3] The Court reasoned that Defendants were in a position to unilaterally update their Xarelto label after FDA approval, once made aware of the number of Xarelto users reporting major bleeding events while taking the drug.[4] The Court further observed that, pursuant to the authority of *Wyeth v. Levine*, 555 U.S. 555 (2009), Defendants seeking preemption are obliged to present "clear evidence" that the FDA would have rejected a Neoplastin PT instruction in Xarelto's label such as Plaintiffs have proposed.[5] As to the failure-to-warn claim, and based on the record presented, there likewise was no "clear evidence" that the FDA would have rejected warnings about U.S. subgroup data or a recall of the INRatio device used during clinical testing.[6]

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[2] Rec. Doc. Nos. 6196, 7110.
[3] Rec. Doc. 6196, at 6 (citing *Guidry v. Janssen Pharms., Inc.*, No. 15-4591, 2016 U.S. Dist. LEXIS 115447, at *48 (E.D. La. Aug. 29, 2016)); Rec. Doc. 7110, at 10, 12.
[4] *Id.*
[5] Rec. Doc. 6196, at 7-8; Rec. Doc. 7110, at 11-12.
[6] Rec. Doc. 7110, at 11.

Citing a similar paucity of evidence supporting the Defendants' affirmative defense of preemption, two different trial judges in the Xarelto mass tort proceedings in Pennsylvania state court did not differ with this Court in addressing these same issues.[7] Instead, both reached the same conclusion, namely, that Defendants' arguments that plaintiffs' claims are preempted could not be supported under the governing jurisprudence and the record of the cases at hand.

After the first three bellwethers trials in this MDL ultimately resulted in defense verdicts, Plaintiffs appealed those verdicts to the Fifth Circuit, and these appeals are now consolidated, briefed, and awaiting disposition. Notably, Defendants in these appeals have expressly raised for Fifth Circuit consideration the issue of federal preemption as an alternative ground for affirmance and dismissal.[8] Nonetheless, in now seeking a summary judgment dismissal of the claims in *Ibanez*, Defendants proceed with the admitted goal of requesting interlocutory Fifth Circuit review of yet another preemption ruling by this Court.[9]

The Court will recall that the PSC requested additional discovery in Ms. Ibanez's case, before these motions would be addressed, which included the discovery of all original encrypted FDA communications related to Xarelto and all Xarelto-related materials saved in the Global Regulatory Affairs Information Link ("GRAIL") database, a set of material first disclosed to the PSC in its effort to establish a proper foundational context for the label change communications.[10]

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[7] *Hartman v. Janssen Pharmaceuticals, Inc*., No. 160503416, Order of Oct. 2, 2017 (Control No. 17091098) (Order of Judge New denying Defendants' motion for summary judgment on preemption) [Attached hereto as Exhibit 1]; Hartman Trial Tr., 11/28/2017, Vol. 12, Afternoon Session, at 221:5-14 (Ruling by Judge Erdos that "The motion for compulsory nonsuit based on preemption continues to be denied . . . Clearly, there is some difference of opinion on this issue as it applies to initial FDA approval, so I'm guessing that probably the U.S. Supreme Court will have to look at that at some point, but that remains denied.") [Attached hereto as Exhibit 2].

[8] *See In re Xarelto Prods. Liab. Litig.*, No. 17-30845, Brief of Defendants/Appellees/Conditional Cross-Appellants (5th Cir.) [ECF No. 00514505102].

[9] *See* Rec. Doc. 7660, at 1 n.1; Rec. Doc. 7653, at 1 n.1.

[10] Rec. Doc. Nos. 7962, 9211.

This additional discovery was obtained to create a more complete record in this case, and has proven relevant for the purposes of both preemption and the question of interlocutory appeal. The PSC respectfully submits that the record is now clear. Your Honor's prior rulings on preemption and the prospective ruling on the preemption motions herein, not only have been but now still may be predicated on the proper application of undisputed legal standards to the relevant facts of record. The "clear evidence" prerequisite of *Wyeth* now appears even further out of reach for Defendants in their effort to establish a defense of preemption as a matter of law.

Neither does it avail Defendants to cite differing outcomes in other district court decisions on preemption, since these rulings likewise cannot be characterized as being in substantial disagreement with the legal approaches to preemption found both in this Court's analysis and in reported case law. The decision in the Eliquis MDL on which they chiefly rely, does not stand in variance from the established legal analysis in preemption cases, but instead was decided on facts fundamentally different from the facts herein. This failure to demonstrate substantial discrepancy in the reported jurisprudence as to truly legal issues, must be considered fatal to the Defendants' professed strategy to use an additional ruling on preemption as a route to immediate appellate review.

## III. ARGUMENT

Pursuant to 28 U.S.C. §1292(b), an interlocutory order is permitted "[w]hen a district judge…shall be of the opinion (1) that such order involves a controlling question of law (2) as to which there is substantial ground for difference of opinion and (3) that an immediate appeal from the order may materially advance the ultimate termination of the litigation."[11] But the district court's opinion is then itself subjected to Fifth Circuit scrutiny, since the statute further provides

[11] *See In re Ichinose*, 946 F.2d 1169, 1177 (5th Cir. 1991).

that "[t]he Court of Appeals which would have jurisdiction of an appeal of such action may thereupon, in its discretion, permit an appeal to be taken from such order, if application is made to it within ten days after the entry of the order."[12] Accordingly, the Court of Appeals does not have jurisdiction to consider an order not otherwise appealable as a matter of right unless the district court certifies its order for interlocutory appeal and the court of appeals permits an appeal from the order.[13]

Such a statutory framework is consistent with the unambiguous stance in federal jurisprudence that litigation should not encompass piecemeal appeals.[14] Indeed, "[a]ny appeal under this section is necessarily a deviation from the ordinary policy of avoiding 'piecemeal appellate review of trial court decisions which do not terminate the litigation.'"[15] This is why a party moving to certify an issue for interlocutory appeal carries the three-fold burden specified in 1292(b).[16] Whatever the question at issue, courts are "fundamentally opposed to piecemeal litigation,"[17]in that such appeals interrupt the ordinary course of unfinished proceedings below, and engage the considerable resources of the appellate phase of litigation at a stage when not all

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[12] 28 U.S.C. §1292(b).

[13] *In re Am. Marine Holding Co.*, 14 F. 3d 276, 277 (5th Cir. 1994); *Burge v. Parish of St. Tammany*, 187 F.3d 452, 477 (5th Cir. 1999) (citing *Swint v. Chambers County Comm'n*, 514 U.S. 35, 46 (1995)).

[14] *See Switzerland Cheese Association, Inc. v. E. Horne's Market, Inc.*, 385 U.S. 23, 24 (1966) (citing *Baltimore Contractors, Inc. v. Bodinger*, 348 U.S. 176 (1955)); 28 U.S.C. §1291 (bestowing upon appellate courts "jurisdiction of appeals from all final decisions of the district courts").

[15] *Cardona v. General Motors Corp.*, 939 F. Supp. 351, 353 (3d Cir. 1996) (quoting *United States v. Hollywood Motor Car Co.*, 458 U.S. 263, 265 (1982)).

[16] *In re FEMA Formaldehyde Prods. Liab. Litig.*, No. MDL 07-1873, 2008 WL 4923035, at *2 (E.D. La. Nov. 13, 2009) (citing *In re Complaint of L.L.P. & D. Marine, Inc.*, Nos. 97-1668, 97-2992 & 97-3349, 1998 WL 66100, at *1 (E.D. La. Feb. 13, 1998)).

[17] *Southern U.S. Trade Ass'n*, No. CIV. A. 10-669, 2011 WL 2790182, at *2 (E.D. La. July 14, 2011) (citing *Henry v. Lake Charles Am. Press, LLC*, 556 F.3d 164, 170-71 (5th Cir. 2009) (quoting *Abney v. United States*, 431 U.S. 651, 656 (1977))).

claims and defenses have been fully developed and addressed on the merits. Accordingly, as this Court observed in the *Chinese-Manufactured Drywall Products Liability Litigation*, the Supreme Court directs that all three prerequisites of §1292(b) must be satisfied in order to warrant the statute's "exceptional" deviation from the "'basic policy of postponing appellate review'" until all issues are disposed of by final judgment.[18]

Notwithstanding these guidelines, Defendants broadly assert in *Ibanez* that "this litigation is ripe for appellate review" on the question of preemption.[19] While it is unclear what is meant by this reference to the "litigation," the "ripeness" of the Court's expected ruling denying preemption in *Ibanez* is far from the type of order as to which the essential criteria of §1292(b) can be satisfied. Neither is it true, as Defendants suggest, that rulings on preemption are by definition the type of rulings for which §1292(b) was designed to address. As with any issue raised in a case, the pertinent question is not simply whether preemption would be dispositive as to certain claims, but rather whether a district court's ruling on preemption gives rise to a substantial discrepancy in the case law on a truly legal, not factual, issue. If not, the appeal of the ruling must await finality of the entire case.

### A. THE ISSUE WHETHER PLAINTIFFS' FAILURE-TO-WARN AND DESIGN DEFECT CLAIMS ARE PREEMPTED BY FEDERAL LAW IS NOT A CONTROLLING QUESTION OF LAW AS TO WHICH THERE IS SUBSTANTIAL GROUND FOR DIFFERENCE OF OPINION THAT WILL MATERIALLY ADVANCE THE ULTIMATE TERMINATION OF THE LITIGATION.

The preemption of less than all theories of liability herein, leaving other theories unaffected, does not present a controlling question of law or advance the ultimate termination of

[18] *In re Chinese-Manufactured Drywall Prods. Liab. Litig.*, No. 2:09-md-2047, Doc. 21322, at 7 (E.D. La. May 7, 2018) (Fallon, J.) (quoting *Coopers & Lybrand v. Livesay*, 437 U.S. 463, 475 (1978)).
[19] Rec. Doc. 9778-1, at 1.

the litigation. As stated *supra*, an interlocutory appeal first must involve a *controlling* question of law, i.e., an issue of law which potentially will have dispositive impact on the course of the litigation.[20] For this reason, "courts have found the issue of whether an interlocutory appeal involves a controlling question of law to be 'closely tied' to the requirement that the appeal will materially advance the ultimate termination of the litigation."[21]

In contrast, an interlocutory appeal from a denial of a motion for partial summary judgment based on a certain record or known set of facts, one addressed to less than all theories of liability, may not be readily characterized as one which would materially advance the ultimate termination of this litigation. Here, Defendants' motions do not address all of Plaintiffs' theories of liability. Defendants' motion for partial summary judgment primarily addresses Plaintiffs' theories related to warnings/instructions as to U.S. subgroup, PT testing, and INRatio information, but it does not address other failure to warn/instruct claims in the case. Since these would survive, therefore, any issue of law resolved by the motion is not "controlling" *vis-à-vis* the overall litigation. Defendants also address Plaintiffs' design-defect theories of liability on a specific assay and/or antidote, which remain a minor component of Plaintiffs' claims against Defendant in this litigation. Thus, there is little to favor Defendants' suggestion that any controlling question of law is presented by the current motion.

Defendants claim that "judicial economy necessitates that the parties receive guidance from the Fifth Circuit as to whether the defense of federal preemption can dispose of many or all of the claims in this MDL."[22] But Defendants' preemption argument in *Ibanez* must be viewed in the

[20] *Ryan v. Flowserve Corp.*, 444 F. Supp. 2d 718, 723 (N.D. Tex. 2006).
[21] *Id.* (citing Wright & Miller, supra, §3930 at 432; *see also* Nagel, *supra*, at 212 (courts have turned to the "materially advance" prong of §1292(b) in deciding whether an issue of law is controlling) (internal citations omitted)).
[22] Rec. Doc. 9778-1, at 1.

context of these entire proceedings. During this litigation writ large, Plaintiffs have presented various design-defect and failure-to-warn theories to factfinders depending on the circumstance presented by each case. Defendants now seek to address and dismiss only two of those failure-to-warn theories and design-defect theories through preemption.

An immediate appeal in this litigation therefore will not advance the ultimate termination of this MDL, since each individual Plaintiff in this litigation still may present other, equally meritorious failure-to-warn claims against Defendants. Likewise, in the first Philadelphia trial, Plaintiff Hartman did not rely on the PT testing claim presented in the MDL, and that jury found that the Defendants should pay punitive damages because they intentionally withheld important safety information about variability, the magnitude of the risk associated with concomitant use of aspirin, and U.S. sub-group data from the Xarelto label.[23] In the final analysis, no individual cases will be dismissed as a result of this Court's or the Court of Appeals' determination that only PT theory failure-to-instruct claims are preempted by federal law.[24]

Moreover, §1292(b) certification on Plaintiffs' design-defect claims would have little impact on this litigation. Plaintiffs' design-defect claims have not been a major component of this litigation. Indeed, the design-defect claims at issue have only been brought before a fact-finder in one MDL bellwether – *Mingo.*[25] Instead, Plaintiffs have predominately pursued their failure-to-warn theories against Defendants. As stated above, Defendants have not moved for certification

[23] On post-trial motions, the trial court found that the testimony of the Plaintiff's prescribing physician was insufficient to meet Indiana's proximate cause standard and granted a judgment notwithstanding the verdict. That ruling is currently on appeal.

[24] *See Seneca Res. Corp. v. Superior Driving Co.*, No. CIV.A. 05-250, 2006 WL 2568053, at *3 (E.D. La. Sept. 5, 2006) (an interlocutory appeal on a partial motion for summary judgment would still leave claims that will continue to trial regardless of the result of the interlocutory appeal).

[25] Plaintiffs dismissed their design-defect claims in the first and third MDL bellwethers – *Boudreaux* and *Orr*. *See* Rec. Docs. 6298, 6601.

for appellate review of all of Plaintiffs failure-to-warn theories of liability. The extraordinary remedy of §1292(b) is not intended to be so limited in scope. Thus, the certification of a portion of Plaintiffs' theories of liability would not materially advance this litigation. Rather, §1292(b) certification would only encourage piecemeal appellate review.

While the PSC has long been aware of the intention of Defendants to seek an interlocutory appeal on preemption in *Ibanez*, it has always been, and remains, the position of the PSC, and Mrs. Ibanez that such an appeal would be extremely difficult to justify. That has proven to be the case, in view of the argument and authority presented in this motion. Defendants cite the Court's certification of an interlocutory appeal on the question of jurisdiction over certain defendants in the Chinese-Manufactured Drywall Products Liability Litigation, where such an appeal was considered necessary to avoid a "long and costly process of serial trials"[26] The same cannot be said in this matter. The Court's expected ruling on preemption will address only some, not all, of the theories of liability being presented in both *Ibanez* and the MDL at large.

Further, it again is important to note that certification of an interlocutory order under 28 U.S.C. §1292(b) is not the only path Defendants have to appellate review of their preemption defense. In each of the three bellwether cases in the MDL, this Court denied Defendants' preemption motions, and in the pending appeals by Plaintiffs in these cases, Defendants have raised federal preemption as an alternative ground for affirmance of the judgments in their favor. Whether in these cases or in others, Defendants have appellate rights available to them from a final judgment.[27] Defendants' belief that it is "unlikely"[28] the Fifth Circuit in the pending appeals will address the question of preemption is a prediction, nothing more and nothing less. It should not

[26] Rec. Doc. 9778-1, at 3.
[27] See fn. 8 *supra*.
[28] Rec. Doc. 9778-1, at 2.

be readily accepted as truth by this Court, much less weighed in consideration whether interlocutory review of the preemption question at this stage of the proceedings in this case is justified.

### B. NO SUBSTANTIAL GROUND FOR DIFFERENCE OF OPINION ON A QUESTION OF LAW IS DEMONSTRATED HEREIN, AS EVIDENCED BY DEFENDANTS' OWN RELIANCE ON THE LEGAL STANDARD ARTICULATED IN *WYETH*.

Defendants have not identified a true question of law as to which there is a substantial ground for difference of opinion in their pursuit of rulings from this Court on preemption. Their failure to do so is critical, in light of the strict requirements of §1292(b). Indeed, "[p]arties must clear a high bar when attempting to show that a question involves a substantial ground for difference of opinion."[29] District courts, for example, have found a substantial ground for difference of opinion:

> (1) [if] a trial court rules in a manner which appears contrary to the rulings of all Courts of Appeals which have reached the issue, (2) if the circuits are in dispute on the question and the Court of Appeals of the circuit has not spoken on the point, (3) if complicated questions arise under foreign law, or (4) if novel and difficult questions of first impression are presented.[30]

None of these illustrations applies to a prospective ruling of this Court in *Ibanez,* assuming it tracks the analysis reflected in Your Honor's prior rulings on preemption in the MDL bellwether cases. Defendants may disagree, perhaps vigorously disagree, with the <u>outcome</u> in cases where preemption is denied, but their right to challenge outcome already is preserved on appeal under our system. To take advantage of the narrowly-defined process of 1292(b), mere disagreement

[29] *Consumer Fin. Prot. Bureau v. Frederick J. Hanna & Assoc., P.C.*, 165 F. Supp. 3d 1330, 1335 (N.D. Ga. 2015).
[30] *Ryan*, 444 F. Supp. 2d at 723-24 (quoting 4 Am.Jur.2d *Appellate Review* §128 (2005)) (brackets added).

with outcome is not enough. It is for this reason that Courts have reminded litigants that "[a]n interlocutory appeal is 'exceptional' and 'does not lie simply to determine the correctness of a judgment.'"[31] Such an appeal is not a vehicle to question the correctness of a district court's ruling or to obtain a second, more favorable opinion."[32] What must be shown under §1292(b), then, is a substantial discrepancy in different rulings on a dispositive legal question. The exceptional process offered by the statute is decidedly not available "simply because…counsel disagrees on applicable precedent…. Nor does a party's claim that a district court has ruled incorrectly demonstrate a substantial disagreement" in the jurisprudence in deciding the same legal issues.[33]

Here, there simply is no "genuine doubt as to the correct legal standard to be applied."[34] Governing Supreme Court and related precedent make clear that federal law did not invariably bar Defendants from complying with their obligation under Louisiana law to update their label. Brand-name manufacturers, like Defendants, remain the master of their labels at all times, and thus are afforded clear pathways to make appropriate changes to their labels, without FDA approval. This has been, and remains, the law when preemption is raised in defense of state law claims involving prescription drugs.

Manufacturers of brand-name drugs, like Xarelto, are permitted to make changes under the FDA's Changes Being Effected ("CBE") regulations and related agency guidance, to "add or strengthen a contradiction, warning, precaution, or adverse reaction" or "an instruction about

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[31] *In re Chinese-Manufactured Drywall Prods. Liab. Litig.*, No. 2:09-md-2047, Doc. 21322, at 7 (E.D. La. May 7, 2018) (Fallon, J.) (citing *Chauvin v. State Farm Mut. Auto. Ins. Co.*, Nos. 06-7145 & 06-8769, 2007 WL 4365387, at *2 (E.D. La. Dec. 11, 2007) (quoting *Clark-Dietz & Assocs.-Eng'rs, Inc. v. Basic Const. Co.*, 702 F.2d 67, 68, 69 (5th Cir. 1983))).

[32] *Ryan*, 444 Supp. 2d at 722 (citing *McFarlin v. Conseco Serv., LLC*, 381 F.3d 1251, 1256 (11th Cir. 2004) (quoting S.Rep. No. 85–2434 (1958), reprinted in U.S.C.C.A.N. at 5260–61)).

[33] *Id.* at 724 (internal citations omitted).

[34] *Southern U.S. Trade Ass'n*, 2011 WL 2790182, at *2.

dosage and administration that is intended to increase the safe use of the drug product" without prior approval from the FDA.[35] Labeling changes under the CBE process are based on "newly acquired information," which is not limited to new data, but also includes "new analyses of previously submitted data."[36] As the Court in *Wyeth* explained, the CBE regulation "accounts for the fact that risk information accumulates over time and that the same data may take on a different meaning in light of subsequent developments."[37] In *Wyeth*, at least 20 adverse event reports over the time period since 1967 were deemed sufficient to justify a CBE warning change.[38] Under the regulation, as quoted in the Supreme Court's opinion, if a manufacturer "'conducts a new analysis of data showing risks of a different type or of a greater severity or frequency than did reports previously submitted to the FDA, the sponsor meets the requirement for 'newly acquired information.'"[39]

*Wyeth* remains the highest governing case authority on preemption in the context of claims against the manufacturers of brand-name drugs; and in it, characterizing "impossibility preemption" as a "demanding" defense, the Supreme Court unambiguously held that the CBE regulation negates such preemption "absent clear evidence that the FDA would not have approved a change."[40]

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[35] *Wyeth*, 555 U.S. at 568; *In re Xarelto*, 2017 U.S. Dist. LEXIS 56629, at *10-11 (citing *Wyeth*, 555 U.S. at 568); *In re Xarelto*, 2017 U.S. Dist. LEXIS 56630 (citing *Wyeth*, 555 U.S. at 568); *In re Xarelto*, 2017 U.S. Dist. LEXIS 114338, at *14 (citing *Wyeth*, 555 U.S. at 568).
[36] *Id.* at 569; *In re Xarelto*, 2017 U.S. Dist. LEXIS 56629, at *10-11 (citing *Wyeth*, 555 U.S. at 569); *In re Xarelto*, 2017 U.S. Dist. LEXIS 56630, at *9-10 (citing *Wyeth*, 555 U.S. at 569); *In re Xarelto*, 2017 U.S. Dist. LEXIS 114338, at *14-15 (citing *Wyeth*, 555 U.S. at 569).
[37] *Wyeth*, 555 U.S. at 569.
[38] *Id.* at 569-70 (noting that Wyeth "could have analyzed" these adverse event reports, which opportunity alone was sufficient to trigger a CBE warning).
[39] *Id.*
[40] *Id.* at 568.

Adhering to such authority, Your Honor properly has recognized the demanding standard required of Defendant manufacturers in efforts to establish a preemption defense, by denying Defendants' summary judgments motions in *Boudreaux, Orr,* and *Mingo.* In these bellwether trials, the Court considered all the evidence and facts of record as to each case, and concluded that in each case the Defendants had not provided "clear evidence" that they were prohibited from updating their label under the CBE regulation after they became aware of the number of its consumers claiming they experienced a major bleeding event while taking Xarelto.[41] Now the Court has an even more complete record before it, based on additional discovery since this Court's prior rulings; and this record further confirms that Defendants have failed to provide "clear evidence" that the FDA would have even challenged, much less foreclosed, the labeling proposed by the Plaintiffs in the Warnings Section of the Xarelto label. The Court has been given no reason to alter either its decision or, importantly, its application of the legal standard in *Wyeth.*

Critically, the Defendants are unable to present any opinion by another court that disagrees with this Court's adherence to the legal framework of a preemption analysis. This is indisputably true in regard to other Xarelto litigation. Both of the Philadelphia County judges who have considered the preemption arguments of the Defendants have reached the same conclusion as this Court. Applying the *Wyeth* standards, they have found no basis for preemption. Hence, rather than demonstrate matters as to which there is a substantial ground for difference of opinion, the Defendants must acknowledge that the Xarelto decisions in federal and state court stand in unison. These rulings not only cement the correctness of this Court's ruling, but they serve to illustrate that there are no grounds for satisfying an essential criteria of 1292(b).

[41] Rec. Doc. 6196, at 7-9; Rec. Doc. 7110, at 10.

### C. DEFENDANTS' RELIANCE ON DECISIONS IN THE ELIQUIS MDL HIGHLIGHTS FACTUAL DIFFERENCES IN CASE OUTCOME, NOT A SUBSTANTIAL DISCREPANCY IN THE RESOLUTION OF THE SAME, CONTROLLING LAW.

This Court has recognized that, for 1292(b) purposes, "the issue for appeal must involve a question of *law* – not fact."[42] "A question which requires a factual as well as legal decision is simply not suitable to trigger the exceptional process for interlocutory review."[43] "Thus, it is the resolution of a legal issue presented which must give rise to a substantial disagreement among jurists; and this issue must be easily discernable and capable of being addressed independent of dispositive factual issues. A litigant seeking 1292(b) review should not oblige the court of appeals to go 'hunting through the record' to see whether 'a genuine issue of material fact may be lurking there.'"[44]

Defendants claim that federal district courts are split on "[w]hether accumulating adverse event reports regarding a known risk that is disclosed in the medication's labeling can constitute 'newly acquired information' under FDA's CBE regulation, 21 C.F.R. § 313.70(c)(6)(iii)."[45] They chiefly rely on a pair of decisions rendered by a single judge in the Southern District of New York in *Utts I and II* on whether adverse event reports constituted newly acquired information requires this Court to grant their requested interlocutory appeal.[46] But, even pretermitting whether

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[42] *Ryan*, 444 F. Supp. 2d at 722 (citing *Clark-Dietz*, 702 F. 2d at 69 (holding that "fact-review" issues are inappropriate for §1292 review)).
[43] *Speizman Knitting Mach. Co. v. Terrot Strickmaschinen GmBH*, 505 F. Supp. 200, 202 (D.N.C. 1981) (citing *Johnson v. Alldredge*, 488 F. 2d 820, 822 (3rd. Cir. 1973), *cert. denied sub nom. Cronrath v. Johnson*, 419 U.S. 882 (1974)); *see also Brooks v. Farm Fresh, Inc.*, 759 F. Supp. 1185, 1198 (E.D. Va. 1991) (where question of law is grounded in specific facts of the case, and cannot be divorced from those facts, they fail to present a narrow question of pure law), *vacated, Shaffer v. Farm Fresh, Inc.*, 966 F. 2d 142 (4th Cir. 1992).
[44] *Ryan*, 444 F. Supp. 2d at 722 (citing *Ahrenholz v. Bd of Trustees of the Univ. of Illinois*, 219 F. 3d 674, 676 (7th Cir. 2000)).
[45] Rec. Doc. 9778-1, at 7.
[46] *Id.* at 10-11.

decisions in one case by one other district judge would suffice to establish the legal issue discrepancy required under 1292(b), Defendants' reliance on *Utts* is misplaced. That Court, though critical of adverse event reports generally as a source of "newly acquired information," proceeded to actually consider and weigh the adverse reports on Eliquis before concluding that, as a matter of content, they failed to trigger the Defendants' obligation to modify the Eliquis label under the CBE regulations. This is an evidence-based determination and not a purely legal one. Again, '[t]he 'substantial ground' for difference of opinion must be about a purely legal issue, not a factual one or 'the application of settled law to fact'"[47] [emphasis added].

> [A] party may argue that there is a substantial ground for difference of opinion based on the divergent application of a legal standard. But the mere fact that "settled law might be applied differently" is insufficient to show that there is substantial ground for difference of opinion. Instead, a party seeking to pursue an interlocutory appeal must show that "other courts have substantially differed in applying the standard." If the application of the same legal standard to similar facts has led to divergent outcomes, then the legal standard may have to be further redefined or clarified.[48]

The district court in *Utts* did not adopt a legal analysis substantially different from this Court's own. Rather, it applied the legal standard established in *Wyeth* to case-specific facts. It was a fact-based, case-specific record which drove the preemption analysis in *Utts* and which explains the preemption outcome. *Utts* involved the NOAC Eliquis, which is manufactured by Bristol-Myers Squibb Company and Pfizer Inc.[49] Plaintiffs asserted that the Eliquis label did not adequately warn of the risk of excessive bleeding.[50] Based on the pleadings alone, that court dismissed Plaintiffs' failure-to-warn claims as preempted, but also permitted Plaintiffs the

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[47] *Consumer Fin. Prot. Bureau*, 165 F. Supp. 3d at 1335 (citing *McFarlin*, 381 F.3d at 1258).
[48] *Southern U.S. Trade Ass'n*, 2011 WL 2790182, at *2-5 (citations omitted).
[49] *See Utts v. Bristol-Myers Squibb Co.*, 226 F. Supp. 3d 166 (S.D.N.Y. 2016) ("*Utts I*"); *Utts v. Bristol-Myers Squibb Co.*, 251 F. Supp. 3d 644 (S.D.N.Y. 2017) ("*Utts II*").
[50] *Id.*

opportunity to amend their complaint.[51] In *Utts II*, the court then determined that the nine reports, studies, and articles which Plaintiffs relied on in their amended pleading did not constitute "newly acquired information" as defined under the CBE regulation.[52] But Plaintiffs in *Utts* relied heavily on the Institute for Safe Medical Practices ("ISMP") QuarterWatch Report, which analyzed adverse drug reports, to support their claim that the defendants acquired new information which disclosed the incidence of bleeding in patients using Eliquis;[53]and this same ISMP report, compared three NOACs (Xarelto, Pradaxa, and Eliquis),[54] averred that Eliquis "'showed the strongest safety profile from several perspectives' and "had the best adverse safety profile by several measures.'"[55] In fact, the report indicated that Eliquis had "the fewest deaths, and the lowest percentage of deaths."[56]

That a district court would elect to discount such evidence in determining whether it was the kind of "newly acquired information" required by the CBE regulation, is hardly equivalent to the necessary proof of a substantially discrepant legal conclusion. Nor does it follow that the decision in *Utts* to discount the evidentiary weight of the adverse event reports as to Eliquis stands in conflict with Your Honor's prospective analysis herein.

The Defendant manufacturers of Xarelto received post-approval a staggering number of reports of serious incidents of bleeding by patients taking the drug. An alarming number of these

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[51] *Id.* Other judges in the Southern District of New York, applying the same standards set by the Supreme Court in *Wyeth*, have ruled in a manner consistent with your Honor. *See, e.g., Sullivan v. Aventis, Inc.*, No. 14cv-2939, 2015 WL 4879112, at *6 (S.D.N.Y. Aug. 13, 2015) ("[T]here is no federal law that prevents a manufacturer from complying with its state-law duty by strengthening a brand-name drug's warning label (pre or post-approval).").
[52] *Utts II*, 251 F. Supp. 3d at 662-63.
[53] *Id.* at 663.
[54] *Id.*
[55] *Id.*
[56] *Id.*

involved patients dying from bleeding caused by Xarelto. In 2012, the first full year during which Xarelto was on the market, the ISMP ranked Xarelto tenth in terms of direct Serious Adverse Event ("SAE") reports to the FDA.[57] There were 2,081 SAE reports in 2012, 151 of which involved death.[58] During the same period, there were only 861 SAE reports for warfarin, and only 56 of those involved death.[59] The ISMP concluded that these figures constituted an "important safety signal,"[60] defined as "evidence of sufficient weight to justify an alert to the public and the scientific community, and to warrant further investigation."[61] While this report was not published until October 2013 – and therefore clearly constitutes newly available information – Defendants would have received information about each SAE report as the reports were made, and were obligated to monitor them. The trend even continued; and, from 2012 through 2015, Xarelto-related adverse events were the most frequently reported among all pharmaceuticals sold in the U.S. market, with 81% involving bleeding events.[62] In addition, data from Defendants' post-marketing surveillance program identified numerous instances of patients with elevated PT results who experienced bleeding complications.[63] The Defendants nonetheless refused to change their label to warn of the magnitude of the risk learned from this newly acquired data.

Although the conclusion reached in *Utts* had more to do with drug-specific information in that matter than with legal principle, the case is, ironically, instructive for a different reason. There the plaintiffs observed, and neither the district judge nor the defendants appeared to have disputed,

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[57] *See* Exhibit 3, QuarterWatch Report 2012 Q4, 10/7/13 ("QuarterWatch Report"), at 10.
[58] *Id.*
[59] *Id.*
[60] *Id.*
[61] *Id.* at 8.
[62] *See* Exhibit 4, Expert Report of Cindy Leissinger, M.D. ("Lessinger Report"), at 17 (citing data sources).
[63] *See* Exhibit 5, Declaration of Suzanne Parisian, M.D. ("Parisian Declaration"), at ¶ 20.

that "real-world signal data from Xarelto was….found to have a much high[er] incidence of adverse events than reported in the clinical studies."[64] The court noted that this "says nothing about how the real world performance of Eliquis compares to the clinical data disclosed by the defendants to the FDA," and added that "[t]he table and the description from the ISMP report do not suggest – nor do the plaintiffs allege – that the real-world signal data for Eliquis shows a greater severity or frequency of bleeding events or deaths than previously disclosed in Eliquis' submission to the FDA."[65] In other words, the Eliquis case is actually confirmation that a drug's post-approval performance is relevant in the preemption context when failure to warn claims are at issue; and it likewise is critical herein that Xarelto was only shown pre-approval to be "non-inferior" to warfarin, but post-approval was the subject of more than double the number of SAEs and almost triple the number of deaths than warfarin. Indeed, the same independent watchdog group referred to in *Utts* noted that the reports for Xarelto – unlike the reports for Eliquis – were sufficient to create an "important safety signal" that "justif[ied] an alert to the public and the scientific community" and "further investigation."[66]

Plaintiffs both in *Ibanez* and in this MDL strongly disagree with the conclusion reached in *Utts*, but an outcome based on the sufficiency of case-specific evidence is of no avail to Defendants' argument for interlocutory appeal. Understandably enough, Defendants seek this opportunity in the Xarelto MDL to highlight a different, and favorable, preemption outcome involving the manufacturer of a competing drug, Eliquis. But market concerns, though characterized as legal concerns, are irrelevant under 1292(b). *Utts* does not satisfy the needed proof of a substantially different handling of a purely legal issue, so much as a fact-driven

[64] *Utts II*, 251 F. Supp. 3d at 664.
[65] *Id.* at 665.
[66] *See* Exhibit 3, QuarterWatch Report, at 10.

difference in outcome, and a different weighing of adverse event report evidence relevant to the CBE regulation.

Defendants also claim that federal district courts are split on "[w]hether FDA's decision to strike language from a medication's proposed labeling is 'clear evidence'…that the FDA would not have approved a unilateral change adding language to the same effect back into the labeling."[67] They insist that there is "clear evidence" the FDA would not have approved language on PT-related information and U.S. subgroup data because the FDA previously rejected such language.[68] However, Defendants again conflate purely legal questions with questions addressed to the weight or value of specific, relevant evidence. Any alleged conflict as to whether the FDA would have approved language in the Xarelto label is grounded in fact, not law. Indeed, the supporting cases that Defendants cite address this question pursuant to the same legal standard, i.e., the "clear evidence" test from *Wyeth*.[69]

Defendants further claim that district courts are split on "[w]hether federal law preempts Plaintiffs' design-defect claims."[70] Yet this Court, taking guidance from *Guidry v. Janssen Pharm., Inc.*, makes clear that *Wyeth's* mandate applies to design-defect claims.[71] As Plaintiffs argued in their previous briefing on preemption and now reiterate here, federal law did not prevent Defendants from pursuing safer alternative designs prior to FDA approval, including an anti-Factor Xa assay or reversal agent/antidote and other courts have agreed with this legal principle.[72]

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[67] Rec. Doc. 9778-1, at 7.
[68] *Id.* at 11-13.
[69] *Id.* at 13 n. 6.
[70] *Id.* at 13.
[71] *In re: Xarelto Prod. Liab. Litig.*, MDL No. 2592, 2017 WL 3188456, at *6 (E.D.La. July 21, 2017), *citing, Guidry, supra.*
[72] *See Young v. Bristol-Myers Squibb Co.*, No. 4:16-CV-00108-DMB-JMV, 2017 U.S. Dist. LEXIS 24730, *17-18 n.3 (N.D. Miss. 2017) (citing *Guidry v. Janssen Pharms., Inc.*, 206 F. Supp. 3d 1187, 1208 (E.D. La. 2016)). Similarly, defendants have offered no evidence that the

Defendants rely on *PLIVA, Inc. v. Mensing*, 564 U.S. 604 (2011) and *Mutual Pharmaceutical Co. v. Bartlett*, 133 S. Ct. 2466 (2013) when arguing that Plaintiffs' design-defect claims are preempted unless Defendants could have "unilaterally" changed the design of Xarelto without seeking the FDA's approval.[73] But the legal analysis on unilateral changes set forth in *Mensing* and *Bartlett* is directed to generic manufacturers, which are more limited in their abilities to make independent changes to their labels in comparison to branded manufacturers such as Defendants. While *Mensing* and *Bartlett* therefore should be distinguished and not given much weight by this Court, it may be true that other federal district courts have found that pre-approval design-defect claims are preempted,[74] while others have not.[75] Nonetheless, Defendants also must satisfy the other two prerequisites for §1292(b) certification, and cannot do so.

Courts do not justify interlocutory appeals where the case cited to prove a legal issue disagreement "did not alter the standard nor was the application substantially different simply because the result was different."[76] If the different results were guided by the facts and evidence

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FDA would have exercised its authority to prohibit defendants from creating and submitting such a design for approval.") (emphasis omitted); *Trahan v. Sandoz, Inc.*, No. 3:13-CV-350-J- 34 MCR, 2015 U.S. Dist. LEXIS 66869, 2015 WL 2365502, at *6 (M.D. Fla. Mar. 26, 2015) ("[I]n her Amended Complaint Trahan arguably states a claim that Sandoz breached its duty to design a reasonably safe product when it initially selected the defective glass, prior to FDA approval. Complying with its state law duty of care at that time was not 'impossible' in the absence of any federal law requiring Sandoz to utilize the allegedly defective glass container.") (emphasis omitted); *Sullivan v. Aventis, Inc.*, No. 14-dv-2939, 2015 U.S. Dist. LEXIS 107360, 2015 WL 4879112, at *6 (S.D.N.Y. Aug. 13, 2015) ("[C]ounsel has cited no federal law that restricts a brand-name drug manufacturer from designing a reasonably safe product *prior* to FDA approval.") (emphasis in original)).

[73] *Id.* at 14.
[74] *See Yates v. Ortho-McNeil-Janssen*, 808 F. 3d 2801 (6th Cir. 2015). Plaintiffs note that this Sixth Circuit decision has been criticized by Defendants' own cited case law, *Brazil v. Janssen Research & Dev. LLC.*, No. 15-cv-0204, 2016 U.S. Dist. LEXIS 137695 *54-55 (N.D. Ga. Mar. 24, 2016).
[75] *See* footnote 72 *supra.*
[76] *Southern U.S. Trade Ass'n*, 2011 WL 2790182, at *2-5.

in a specific case, interlocutory appeal is not available. Federal preemption rulings by district courts, in the final analysis, are based on both law and fact. To merely cite different outcomes in such rulings is insufficient. A pure "question of law" must be demonstrated as to which a "substantial" ground for differing opinions also is shown. The cases cited by Defendants were based on weighing factual evidence, as opposed to adoption of a fundamentally different framework for legal analysis under *Wyeth*.

The same proposition is illustrated in the case of *AMA Disc., Inc. v. Seneca Specialty Ins. Co.*, 697 F. App'x 354 (5th Cir. 1997). There, the parties did not challenge a legal standard, but rather the application that standard to the facts of the case. The Fifth Circuit thus observed that "the parties to this appeal do not actually challenge what law applies to the issue the district court found decisive…. The parties merely dispute whether the district court accurately applied this standard when it held that Seneca had a duty to defend its insured."[77] On the basis of this independent determination, the Court declined to accept §1292(b) certification, because 'the 'controlling question of law' is one as to which there is no current 'substantial ground for difference of opinion.'"[78]

Facts are hard things; and Defendants may rightly complain that the facts in *Utts* relevant to Eliquis radically differ from the facts attendant to Xarelto. But, assuming this Court denies Defendants' motions for summary judgment based on its prior reasoning and the facts now of record, nothing in the *Utts* decisions or other decisions cited by Defendants, presents a purely legal issue determinative of outcome, much less one reflective of a substantial discrepancy in the law.

[77] *AMA Disc, Inc.*, 697 F. App'x at 355.
[78] *Id.*

## IV. CONCLUSION

None of the three essential prerequisites for certification of an interlocutory appeal have been satisfied; and the law is clear that it is Defendants' burden to establish all three. While Plaintiff agrees that an enormous amount of time and effort is required to take each of the cases in this MDL to trial, piecemeal appellate review will not reduce this burden, and, likewise, the termination of this entire litigation will not be materially advanced by certifying this Court's expected preemption order for interlocutory appeal. In the final analysis, Defendants cannot identify a purely legal question as to which the case law on preemption is in substantial disagreement. Mere differences in case outcomes turning on facts presented, do not suffice in addressing this important prerequisite.[79] The proper appellate course for Defendants, therefore, is the one already available to them pursuant to ordinary proceedings, when a given case is disposed of with finality and not before.

For the reasons set forth above, an immediate appeal under 28 U.S.C. §1292(b) is not warranted in this case. Defendants' Joint Motion to Certify for Interlocutory Appeal Under 28 U.S.C. §1292(b) should be denied.

Dated: June 14, 2018

Respectfully submitted,

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[79] If this Court is nonetheless inclined to certify an interlocutory appeal, Plaintiff respectfully asks for the opportunity to submit for consideration an appropriately tailored statement of the legal issue to be reviewed.

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**CERTIFICATE OF SERVICE**

I hereby certify that on June 14, 2018 a copy of the above and foregoing Plaintiffs' Response In Opposition to Defendants' Joint Motion to Certify for Interlocutory Appeal Under 28 U.S.C. §1292(b) has contemporaneously with or before filing been served on all parties or their attorneys in a manner authorized by FRCP 5(b)(2), Local Rule 5.1 of the Eastern District of Louisiana and via MDL Centrality, which will send notice of electronic filing in accordance with the procedures established in MDL 2592 pursuant to Pre-Trial Order No. 17.

*/s/ Gerald E. Meunier*
**Gerald E. Meunier**