UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

IN RE: XARELTO (RIVAROXABAN) PRODUCTS LIABILITY LITIGATION	*	MDL 2592
	*	SECTION L
THIS DOCUMENT RELATES TO ALL CASES	*	JUDGE ELDON E. FALLON
	*	MAG. JUDGE NORTH

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MEMORANDUM IN SUPPORT OF PLAINTIFFS' STEERINGN COMMITTEE'S MOTION TO COMPEL DISCOVERY

Pursuant to Federal Rule of Civil Procedure 37, the PSC respectfully moves to compel Defendants Janssen Pharmaceuticals, Inc., Janssen Research & Development, LLC, Janssen Ortho LLC, and Johnson & Johnson (collectively, "Defendants") to produce documents in response to Plaintiffs' Third Request for Production of Documents.

I. INTRODUCTION

This motion arises from Defendants' refusal to immediately produce documents related to the re-analysis of the Phase III clinical trial, ROCKET AF, conducted to obtain approval of the primary indication for Xarelto. Defendants touted the results of the ROCKET AF trial to the U.S. Food and Drug Administration ("FDA"), healthcare providers and the public as evidence of Xarelto's comparative efficacy and safety in relation to other anticoagulants, such as warfarin. Further, this trial formed the basis of FDA approval and the labeling of its primary indication.

Recently, the use of a recalled medical device during the study has called the results of this study into question and a re-analysis of the study has been completed and provided to Defendants. It is undisputed that the data and study that forms the basis of this re-analysis is

owned by Defendants and that the re-analysis report is within the possession, custody and control of the Defendants. Documents related to the re-analysis are highly material and their production in an expedited manner is critical given that the parties are beginning deposition discovery and that the first scheduled trial is just over one year away. If such production is delayed, Plaintiffs will be required to re-take many of these depositions as Plaintiffs have been deprived of relevant and material documents. Further, the delay of production is prejudicing the Plaintiffs' ability to work with their experts.

Plaintiffs seek to compel responsive documents regarding a re-analysis of the data in the ROCKET AF study triggered by a recall of the blood monitoring device used in the study. This information is highly relevant to Plaintiffs' claims because it concerns the integrity of the data underlying the ROCKET AF study on which Defendants' representations are based. The information is in Defendants' control, but Defendants refuse to produce it at this time, claiming that it has been submitted for publication in a peer-reviewed journal and is presently undergoing regulatory review.

There is no valid justification—peer review or otherwise—for delayed production of the information, especially with the protective order that is in place. Further, under the contract between the Defendants and the Duke Clinical Research Institute ("DCRI"), Defendants own all of the data from ROCKET AF and are able to produce this information. However, Defendants' position makes clear that their desire is to delay the production of this information, thereby prejudicing Plaintiffs' ability to conduct upcoming depositions which are on calendar.[1] Plaintiffs

[1] The Bayer Defendants' Objections and Responses indicate that responsive documents would be produced in the custodial file of Andrea Derix, among others. Ms. Derix is scheduled to be deposed in Amsterdam beginning March 1, 2016. The Janssen Defendants' Objections and Responses indicate that responsive documents would be produced in the custodial files of Christopher Nessel (February 16 -17), Sigmond Johnson (February 18-19) and Sanjay Jalota (March 3-4) among others. These three depositions are also set in New Jersey on the dates indicated.

are entitled to this evidence now and will suffer substantial prejudice from a delayed production because the Defendants will have the exclusive benefit of the data during upcoming depositions.

II. FACTUAL BACKGROUND

A. SIGNIFICANCE OF THE ROCKET AF STUDY AND CAUSE OF RE-ANALYSIS

The most widely prescribed indication for Xarelto is the prevention of strokes in patients with atrial fibrillation.[2] Approval of this indication hinged on the results of the phase III clinical trial named ROCKET AF, which compared the safety and efficacy of the then-current standard of care, warfarin, to Xarelto.[3] The ROCKET AF study is the centerpiece of the Defendants' Xarelto marketing campaign for the prevention of strokes in patients with atrial fibrillation and specifically for Defendants' disputed representation that such patients treated on Xarelto do not require blood monitoring.[4] Recent developments, including an FDA recall of a device used in the ROCKET AF study, have raised questions about the integrity of the results of ROCKET AF. Defendants report that they have engaged researchers at the Duke Clinical Research Institute to re-analyze the data.

As anticoagulants thin the blood to reduce the incidence of clots and strokes, they can also increase the risk of major bleeding events.[5] This balance between efficacy and safety is commonly referred to as the "therapeutic range," which in the case of warfarin is measured by the International Normalized Ratio ("INR").[6] The therapeutic range for warfarin patients treated

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[2] Compl. ¶¶ 49, 50, 83 (May 29, 2015), No. 2:14-md-02592, Doc. No. 923.
[3] *Id.* at ¶¶ 55-56.
[4] *See* https://www.xarelto-us.com/atrial-fibrillation ("In a clinical study of more than 14,000 people [ROCKET AF], treatment with XARELTO® was proven to lower your chance of having a stroke due to AFib not caused by a heart valve problem. XARELTO® is an anticoagulant blood thinner that works by helping to keep blood clots from forming."). The site contains a hyperlink to the ROCKET AF study for readers to download it for free.
[5] *See* Manesh R. Patel, et al. *Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation*, 365 NEW ENG. J. OF MED. 883, 888 (2011), attached as Exhibit A.
[6] *Id*. at 884.

for the prevention of strokes due to atrial fibrillation is an INR between 2 and 3.[7] The ROCKET AF investigators[8] were advised to 1) measure the INR of the warfarin patients at least once per month; and 2) adjust the dose in warfarin-treated patients to maintain the INR in the therapeutic range of 2 to 3. At the end of the trial, the number of strokes and bleeds experienced by the INR-monitored warfarin patients were compared to those experienced by the Xarelto patients to generate the ROCKET AF results.[9]

The double-blind design of the clinical trial required all ROCKET AF investigators to use the same point-of-care ("POC") device to measure the INR levels in all of the warfarin patients, which was called INRatio, manufactured by Hemosense, Inc.[10] This device's measurements guided the decisions of ROCKET AF investigators to maintain, decrease or increase the dosage of warfarin in all warfarin treated patients.

In December 2014, the FDA issued a Class I recall of the INRatio POC device, stating that the device "may provide an INR result that is lower than expected result obtained using a laboratory INR method."[11] A lower INR value would result in the over anti-coagulation of the patients in the warfarin arm of ROCKET AF thereby increasing the number of bleeds on warfarin. This improper over anti-coagulation would render the results of the study unreliable as the comparison to the number of bleeds in the Xarelto arm would be invalidated. In other words, the use of the recalled medical device may invalidate the study that forms the basis for approval of Xarelto and could potentially lead to a withdrawal of the indication.

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[7] *See id.* at 886.
[8] These investigators include the hundreds of doctors responsible for the treatment of the 14,000 ROCKET AF patients.
[9] *Id*. at 886-90.
[10] *See id*. at 884.
[11] http://www.fda.gov/MedicalDevices/Safety/ListofRecalls/ucm429496.htm, attached as Exhibit B.

According to a December 7, 2015, statement released by the ROCKET AF executive committee, this recall prompted a "secondary analysis of the phase III trial (ROCKET AF) of the oral anticoagulant rivaroxaban."[12] In subsequent media reports, ROCKET AF principal investigator Dr. Manesh Patel stated that the results of the secondary analysis had "been made available to the FDA, European Medicines Agency, and the drug's manufacturers, Janssen and Bayer."[13] Under Defendants' contract with DCRI, Defendants own all of the data from ROCKET AF: "All clinical data, including case report forms and other relevant information and findings generated as a result of conducting the Research Activities and/or Study, (all of the foregoing to be referred to collectively as "Clinical Data") shall be promptly and fully disclosed to COMPANY, *shall constitute COMPANY's property, and shall be freely usable by COMPANY*." [14] Thus, Defendants are able to produce this information.

B. PLAINTIFFS' DOCUMENT REQUEST AND DEFENDANTS' RESPONSE

On December 4, 2015, the Plaintiffs' Steering Committee served their Third Request for Production of Documents on Defendants. Therein, Plaintiffs' Request No. 1 sought the production of documents related to the FDA's recall of the device used in Rocket AF, due to the possibility that the recall undermined the validity of the original results.[15] In its response to Request No.1, Defendants refused to produce responsive documents because the re-analysis of the test results "has been submitted to a peer-reviewed journal for publication" and "the peer-review process could well result in further analysis, correction and/or revisions to the

[12] https://www.dcri.org/research/news/2015-news-archives/rocket-af-secondary-analysis, attached as Exhibit C.
[13] http://www.medpagetoday.com/Cardiology/CardioBrief/55218?comment=true, attached as Exhibit D.
[14] *See* Research Funding Agreement, ¶ 9 attached as Exhibit E. (Emphasis added.)
[15] Documents and information concerning the recall and the reanalysis of ROCKET AF also were covered by Plaintiffs' First Requests for Production of Documents, and Defendants had a duty to produce such information in accordance with the duty to supplement under Federal Rule of Civil Procedure 26(e).

conclusions in the reanalysis."[16] Defendants state that they "will not produce responsive documents until the peer review process is complete and the reanalysis is final so as to prevent misinterpretation of the yet-to-be finalized results. At that time, Defendants will produce responsive documents."[17]

III. ARGUMENT

Under Federal Rule of Civil Procedure 37(a), a party seeking discovery may move for an order compelling production if a party fails to produce documents requested under Rule 34. The Federal Rules grant the district court broad discretion in ruling on discovery matters such as a motion to compel. *Crosby v. La. Health Serv. & Indem. Co.*, 647 F.3d 258, 261 (5th Cir. 2011)

Federal courts have an established policy of liberal discovery. Fed. R. Civ. P. 26(b); *Hickman v. Taylor,* 329 U.S. 495, 507 (1947); *Dollar v. Long Mfg. N.C., Inc.* 561 F.2d 613, 616 (5th Cir. 1977); *Intralox, L.L.C. v. Habasit Belting, Inc.*, 2004 WL 2999097, at *3 (E.D. La. Dec. 23, 2004). As amended, effective December 1, 2015, Rule 26(b)(1) permits broad discovery of "any nonprivileged matter that is relevant to any party's claim or defense and proportional to the needs of the case." Rule 26(b)(1).[18] The term "relevant" in Rule 26 is "construed broadly to encompass any matter that bears on, or that reasonably could lead to other matter that could bear

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[16] Defendants Janssen Pharmaceuticals, Inc., Janssen Research & Development, LLC, Janssen Ortho LLC And Johnson & Johnson's Responses To Plaintiffs' Third Request For Production Of Documents, p.7 (Jan. 4, 2016), attached as Exhibit F.

[17] *Id*.

[18] Rule 26(b)(1), as amended in 2015, states in full:

> Scope in General. Unless otherwise limited by court order, the scope of discovery is as follows: Parties may obtain discovery regarding any nonprivileged matter that is relevant to any party's claim or defense and proportional to the needs of the case, considering the importance of the issues at stake in the action, the amount in controversy, the parties' relative access to relevant information, the parties' resources, the importance of the discovery in resolving the issues, and whether the burden or expense of the proposed discovery outweighs its likely benefit. Information within this scope of discovery need not be admissible in evidence to be discoverable.

Fed. R. Civ. P. 26.

on, any issue that is or may be in the case." *Oppenheimer Fund, Inc. v. Sanders*, 437 U.S. 340, 351 (1978).

Here, Defendants do not attempt to base their refusal on an enumerated and recognized exception under Rule 26. Defendants have not asserted privilege or any valid assertion of undue burden, cumulativeness, or availability of the evidence through more accessible means. *See* FRCP 26(b)(2)(C). Nor have Defendants asserted that these documents are not relevant to Plaintiffs' claims. Instead, they effectively say that "now is not a good time."

To the extent that Defendants' concern is the potential misinterpretation of scientific data that has been submitted for peer review, that concern does not find support in the Federal Rules of Civil Procedure. Courts have compelled the production of ongoing research data even from third parties. In *In re Prempro Products Liability Litigation*, the defendant moved to compel the non-parties National Institute of Health and the Fred Hutchinson Cancer Center to produce data related to ongoing research on the drug at issue in the case. The court granted this motion, notwithstanding the fact that the research was ongoing and was being conducted by third-party.[19] The concern about the potential impact on publication was alleviated by compelling production under the terms of a confidentiality order. *See also Smith v. Dow Chem. Co.*, 173 F.R.D. 54, 58 (W.D.N.Y. 1997) (compelling production of documents from defendant relating to ongoing study concerning the health effects of exposure to vinyl chloride); *see also AGA Med. Corp. v. W.L. Gore & Assocs., Inc.*, No. CIV. 10-3734 JNE/JSM, 2011 WL 11023511, at *27 (D. Minn. Oct. 19, 2011) (compelling production of ongoing clinical studies). Defendants also will have the ability, and duty, to supplement their production under Rule 26(e)

[19] *In Re Prempro Prods. Liab. Litig.*, No. 4:03-CV-1507-WRW (E.D. Ark. Jan. 6, 2005), Order Re: Rulings from Dec. 10, 2004 Hr'g, attached as Exhibit G.

if additional information becomes available as a result of the reported peer-review process. This, too, alleviates Defendants' concern about possible misinterpretation of the data.

Moreover, confidentiality treatment can be afforded under the Court's Protective Order.[20] For example, in the Vioxx litigation, the Superior Court of New Jersey was confronted with a similar situation.[21] The defendant, Merck & Company, was conducting follow-up studies of the drug at issue, and the studies produced interim data that Plaintiffs sought to obtain. Notwithstanding the data's "interim" status, the court ordered the defendant to produce the data, under the terms of the protective order.[22] Defendants' concerns in the instant matter can likewise be alleviated by producing the requested data in accordance with the Court's protective order.

The efficacy and safety results of the ROCKET AF study represent the foundation of Defendants' marketing and warnings concerning Xarelto's risk of major bleeding events. Plaintiffs dispute Defendants' interpretation of the original ROCKET AF results, on which Defendants rely heavily in representing the safety of Xarelto to prescribers and patients in terms of its risk of major bleeding events – the primary injury alleged in this MDL. As such, the data that forms the basis of the reanalysis and the reanalysis solicited by Defendants are directly relevant to Plaintiffs' claims and should be produced without delay.

Any additional delay in production will result in irreparable prejudice to Plaintiffs. Currently, Plaintiffs are preparing for depositions of Defendants' employees with direct knowledge of ROCKET AF, the INRatio device and likely direct involvement in the secondary analysis. Further, Plaintiffs also are conferring with experts and developing trial strategy, and

[20] Pre-trial Order No. 12, ¶¶ 6-7, *In Re Xarelto (Rivaroxaban) Products Liability Litigation*, MDL No. 2592 (E.D. La. May 4, 2015) (affording confidential treatment to qualifying information concerning drug development and personal information), attached as Exhibit H.
[21] *In Re Vioxx Litig.*, Amended Order Regarding Production of Interim Data From The Approve Follow Up Studies, C.A. 619 (Sup. Ct. N.J., Mar. 10, 2006), attached as Exhibit I.
[22] *Id.*

the Defendants' exclusive control of this secondary analysis puts Plaintiffs at a disadvantage. The prejudice that will accrue to Plaintiffs now is too great to allow Defendants to produce this information at some later time.

IV. CONCLUSION

For the foregoing reasons, Plaintiffs respectfully request that the Court grant Plaintiffs' Motion to Compel and enter an Order compelling Defendants to promptly produce the documents requested in the Third Request for Production of Documents.

DATE: January 11, 2016

Respectfully submitted,

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