2013 PA Super 215

IN RE: REGLAN/METOCLOPRAMIDE LITIGATION,	IN THE SUPERIOR COURT OF PENNSYLVANIA
APPEAL OF: MORTON GROVE PHARMACEUTICALS INC., AND WOCKHARDT USA, LLC,	
Appellants	No. 83 EDA 2012

Appeal from the Order Entered November 18, 2011
In the Court of Common Pleas of Philadelphia County
Civil Division at No(s): January Term, 2010 No. 001997

BEFORE: STEVENS, P.J., BOWES, and PLATT,* JJ.

OPINION BY BOWES, J.: **FILED JULY 29, 2013**

Morton Grove Pharmaceuticals, Inc. and Wockhardt USA, LLC (collectively "Morton Grove") appeal from the trial court's November 18, 2011 order overruling their preliminary objections that were premised upon a position that certain of the counts in question were pre-empted under federal law. This appeal is one of four related appeals arising from mass tort litigation involving Plaintiffs, persons whom were allegedly injured after

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* Retired Senior Judge assigned to the Superior Court.

ingesting metoclopramide.[1] Common to each appeal are the issues of whether all claims against generic manufacturers are failure-to-warn claims indistinguishable from those held pre-empted by the United States Supreme Court's decision in ***PLIVA, Inc. v. Mensing***, 131 S.Ct. 2567 (2011), and whether the trial court thereby erred in not dismissing them. We have previously rejected the blanket pre-emption of all state-tort claims. We have ruled that pre-emption applies only to failure-to-warn claims against generic manufacturers that arose prior to the enactment of the Federal Drug Administration Amendments Act of 2007 ("FDAAA") and that are premised solely on the content of generic drug labels that conform to the label of the brand-name drug.

In the instant appeal, Morton Grove contends that it remains a generic manufacturer entitled to claim the benefit of ***Mensing*** pre-emption despite the Federal Drug Administration's ("FDA") designation of it as the reference listed drug ("RLD") holder for liquid syrup metoclopramide. Morton Grove premises jurisdiction to entertain this interlocutory appeal on the collateral order doctrine. We accept jurisdiction on that basis. After thorough review, we affirm.

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[1] The claims herein are representative of the claims of more than two thousand claims pending in the Court of Common Pleas of Philadelphia County. The preliminary objections were filed to their third amended master long form complaint.

The relevant facts are as follows. Morton Grove originally obtained permission to manufacture and sell liquid syrup metoclopramide by submitting an Abbreviated New Drug Application ("ANDA") to the FDA to obtain the right to sell a generic form of liquid metoclopramide. That document demonstrated that the syrup was equivalent in "active ingredients, safety, and efficacy" to the RLD. 21 U.S.C. § 355(j)(2)(A). Thereafter, the RLD holder discontinued marketing its drug, and the FDA withdrew approval. Under applicable regulations, the FDA was empowered to fill the void left by the withdrawn RLD by designating one of the generic manufacturers to serve as a substitute. The FDA designated Morton Grove as the RLD for liquid syrup metoclopramide. According to Morton Grove, despite its status as the RLD, it is merely a generic drug manufacturer which had no power to unilaterally alter its own labeling. ***See Mensing***, ***supra***.

Morton Grove filed preliminary objections to the master complaint, disputing that it had any special duties or responsibilities with regard to the label as a result of its designation by the FDA as the RLD holder. The trial court overruled the preliminary objections without prejudice to raising the same issue in a motion for summary judgment. Morton Grove's motion for reconsideration was denied, but the court granted its motion to certify the order as one involving "a controlling question of law as to which there is a substantial ground for difference of opinion" and for which "an immediate appeal . . . may materially advance the ultimate determination of the

matter." Order, 12/16/11, at 1 (quoting 42 Pa.C.S. § 702(b)). Morton Grove then filed both a timely petition for permission to appeal, which this Court denied by order of March 12, 2012. Morton also filed a direct appeal under Pa.R.A.P. 313. Plaintiffs moved to quash the appeal. By order of April 11, 2012, this Court denied the motion without prejudice to reassert the issue before this panel, which Plaintiffs have done.

Morton Grove presents one issue for our consideration:

> Does the FDA's unilateral designation of Morton Grove's ANDA product as a RLD impose additional duties or obligations different from those of any ANDA [, i.e., generic] holder, and enable plaintiffs to assert unique state-law claims against Morton Grove solely on the basis of the RLD designation?

Morton Grove's brief at 3-4.

We refer to our related opinions at Nos. 81 and 82 EDA 2012, which contain the legal basis for our exercise of collateral order jurisdiction. In addition, we held therein that ***Mensing*** does not confer upon generic drug manufacturers blanket pre-emption of all state-law tort claims. Our resolution of issues involving Morton Grove's status will determine whether it can avail itself of ***Mensing*** pre-emption at all.

In reviewing the trial court's order overruling preliminary objections, we apply the same standard as the trial court. ***See De Lage Landen Services, Inc. v. Urban Partnership, LLC***, 903 A.2d 586, 589 (Pa.Super. 2006). "All material facts set forth in the complaint as well as all inferences reasonably deducible therefrom are admitted as true for the purpose of this

review. The question presented by the demurrer is whether, on the facts averred, the law says with certainty that no recovery is possible." ***Soto v. Nabisco, Inc.***, 32 A.3d 787, 790 (Pa.Super. 2011). Any doubt is resolved by refusing to sustain the demurrer. ***Insurance Adjustment Bureau, Inc. v. Allstate Ins. Co.***, 905 A.2d 462, 468 (Pa. 2006); ***Butler v. Charles Powers Estate***, 29 A.3d 35 (Pa.Super. 2011) (*reversed on other grounds by* ***Butler v. Charles Powers Estate ex rel Warren***, 65 A.3d 885 (Pa. 2013)).

The issue, as framed by Morton Grove, is one involving interpretation of federal law. It maintains that despite its status as the RLD holder for liquid syrup metoclopramide, it remained a generic manufacturer of an ANDA-approved product, and that it had no ability to use the Changes Being Effected ("CBE") process to modify its warnings label. Thus, it claims, under the ***Mensing*** rationale, that it cannot be liable under state tort law for failure to change its label.

Plaintiffs counter that the successor RLD is the same as the name-brand manufacturer for purposes of FDA regulations. They argue that the FDA's designation of Morton Grove as a successor RLD places that entity in the "shoes of the pioneer manufacturer," with the authority and the duty to update warnings on the drug's label. Appellees' brief at 34. To hold otherwise, Plaintiffs contend, would result in a finding that no entity had the ability to use the CBE process to change the RLD label. ***Id***.

In support of that contention, Plaintiffs direct our attention to the fact that the ***Mensing*** Court excluded RLDs from its definition of generic drugs and used the designation "name-brand" and "listed" interchangeably. Further, Plaintiffs reason that since the RLD labeling is the standard that generic drug manufacturers must meet, Morton Grove, as the RLD, has the same authority to use Changes Being Effected ("CBE") regulations to change the label that a name-brand manufacturer RLD possesses. Thus, Plaintiffs contend that Morton Grove is not entitled to the benefit of ***Mensing*** pre-emption.

We note that a generic manufacturer's inability to unilaterally change the warning label on its generic drug is the foundation for the ***Mensing*** Court's pre-emption holding. In pre-empting state tort claims based on generic drug manufacturers' failure to provide adequate warning labels for generic metoclopramide, the ***Mensing*** Court reasoned as follows. A generic drug manufacturer is responsible under federal law for ensuring that its warning label is identical to that of the brand name's label, and a generic manufacturer cannot unilaterally change its label to attach a stronger warning if required by state law. Under that scenario, a state failure-to-warn cause of action against the generic cannot be pursued because it is impossible for generic drug manufacturers to comply with both federal and state law. That rationale does not support a finding of impossibility pre-

emption herein if Morton Grove, as the RLD holder, had the same ability as the RLD to use CBE regulations to change its label.

Thus, our resolution of the issue of whether impossibility pre-emption applies to Morton Grove hinges on whether that entity, as the RLD holder, had the ability under federal law to change or update its label. In essence, Morton Grove maintains that its status as an ANDA generic drug manufacturer governs what it is permitted to do under the FDA's regulations and that its subsequent designation in 2006 as the RLD holder does not enhance either its duties or obligations. It alleges that Plaintiffs "failed to cite a single statutory or regulatory authority that imposes any new or additional responsibilities upon a generic manufacturer whose product or formulation is subsequently and unilaterally designated by FDA as RLD." Appellant's brief at 7.

We begin our analysis of this issue with an examination of federal regulations defining an RLD. The term "reference listed drug" is "the listed drug identified by the FDA . . . upon which an applicant relies in seeking approval of its abbreviated application." 21 CFR 314.3(b). An RLD is different from a "listed drug," a term that refers to all drugs that are approved and listed in the FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations." ***Id***. The FDA further explains that the RLD

> is an approved drug product to which new generic versions are compared to show that they are bioequivalent. A drug company seeking approval to market a generic equivalent must refer to the Reference Listed Drug in its Abbreviated New Drug

> Application (ANDA). By designating a single reference listed drug as the standard to which all generic versions must be shown to be bioequivalent, the FDA hopes to avoid possible significant variations among generic drugs and their brand name counterpart.

U.S. Food & Drug Admin., *Drugs@FDA Glossary of Terms*. ***See*** http://www.fda.gov/Drugs/informationondrugs/ucm079436.htm. That same FDA glossary defines a "brand name drug" as "a drug marketed under a proprietary, trademark-protected name." ***Id***. A generic drug is defined as follows:

> A generic drug is the same as a brand name drug in dosage, safety, strength, how it is taken, quality, performance, and intended use. Before approving a generic drug product, FDA requires many rigorous tests and procedures to assure that the generic drug can be substituted for the brand name drug. The FDA bases evaluations of substitutability, or "therapeutic equivalence," of generic drugs on scientific evaluations. By law, a generic drug product must contain the identical amounts of the same active ingredient(s) as the brand name product. Drug products evaluated as "therapeutically equivalent" can be expected to have equal effect and no difference when substituted for the brand name product.

Id.

In both ***Wyeth v. Levine***, 555 U.S. 555 (2009) and ***Mensing***, ***supra***, perhaps for the sake of clarity, the Supreme Court spoke in broad terms of "manufacturers," both brand-name and generic manufacturers. The ***Wyeth*** Court observed that although the FDCA and FDA regulations have been amended, "it has remained a central premise of the federal drug regulation that the manufacturer bears responsibility for the content of its label at all time. It is charged both with crafting an adequate label and with ensuring

that its warnings remain adequate as long as the drug is on the market." ***Wyeth***, 555 U.S. at 571. The "manufacturer" in that case was Wyeth, the brand-name manufacturer which was also the designated RLD. The Court rejected Wyeth's impossibility pre-emption defense, finding it to be empowered by an FDA regulation governing the CBE process to make certain changes to its label before receiving the agency's approval.

The labeling regulations at issue in ***Wyeth*** did not contain the terms "brand name" and "generic." Rather, the regulations refer to the "applicant" seeking to change the label to "add or strengthen a contraindication, warning, precaution or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product" and who could make the labeling change upon filing its supplemental application with the FDA. 21 CFR §§ 314.70(c)(6)(iii)(A), (C). ***Wyeth***, 555 U.S. at 568. An "applicant" is defined as "any person who submits an application or abbreviated application or an amendment or supplement to them under this part to obtain FDA approval of a new drug or an antibiotic drug and any person who owns an approved application or abbreviated application." 21 CFR § 314.3. An application is one described under § 314.50 as a new drug application ("NDA") or submitted under section 505(b)(1)(A) (ANDA). ***Id***. In ***Wyeth***, the name-brand manufacturer was both the NDA applicant and the RLD holder, and the Court held that it had the power to utilize the CBE process to

change its label. The ***Wyeth*** Court did not specifically state, however, whether that authority stemmed from Wyeth's status as a brand-name manufacturer that filed the NDA or as the RLD holder.

In ***Mensing***, none of the generic defendants was also the RLD holder. In concluding that the generic defendants did not have the power to unilaterally change the label, the Court did not address the issue before us: whether a generic holder which is subsequently designated as the RLD can unilaterally change its label. We note, however, that the ***Mensing*** Court referred to RLD holders and brand-name manufacturers interchangeably in its opinion. In fact, the ***Mensing*** Court inserted the language "the brand-name" when quoting regulations employing the term "listed drug," ***Mensing*** at 2575 (quoting 21 CFR 314.150(b)(10)), although it also noted that an RLD is "typically a brand-name drug." ***Mensing***, ***supra*** at 2574 n.2.

Morton Grove directs our attention to two federal district court cases where the courts dismissed failure-to-warn claims against an RLD/generic manufacturer based upon pre-emption. In ***Cooper v. Wyeth, Inc.***, 2010 U.S. Dist. LEXIS 29209 *24 (M.D. La. 2012), the court concluded that the FDA considered RLDs to be synonymous with NDA applicants based upon its definition of a listed drug as "a version of the drug that was previously approved under a new drug application (NDA)." (quoting 72 Fed.Reg. 39629-01). We find that definition to be in conflict with aforementioned

definitions of an RLD. Furthermore, since we have RLDs such as Morton Grove that were not approved via an NDA, that definition is suspect.

Nor are we persuaded by the court's decision in ***Esposito v. Xanodyne Pharm., Inc.*** (***In re Darvocet, Darvon and Propoxyphene Prods. Liability Litig.***), 2012 U.S. Dist. LEXIS 30593 (E.D. Ky. Mar. 5, 2012). Therein, the plaintiffs asserted that Mylan and other generic manufacturers were not protected by ***Mensing*** because they were the RLD holders for certain propoxyphene products. The defendants relied upon an FDA publication that they maintained indicated that the FDA, not the RLD holder, controlled label changes if the NDA holder has removed its product from the market for reasons other than safety or effectiveness.

The article was entitled, "Determination That Brethine (Terbutaline Sulfate) Injection Was Not Withdrawn from Sale for Reasons of Safety or Effectiveness, 72 Fed. Reg. 39,629 (July 12, 2007). The defendants cited it for the proposition that where an NDA manufacturer withdraws its drug and a generic manufacturer is designated as the RLD holder, only the FDA can revise labeling. The actual language relied upon was, "If the FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise [Abbreviated New Drug Application] applicants to submit such labeling." No one disputes that the FDA has the power to order that labels be revised. The question is whether

the successor generic RLD can utilize the CBE process. That question was not posed or answered.

The court dismissed the claims since the plaintiffs did not provide any authority to support their contention that when a generic drug manufacturer becomes an RLD holder, it is thereby empowered to independently change the drug's warning label. After reviewing that decision, we find no support for the interpretation.

We, unlike the United States Supreme Court in ***Wyeth*** and ***Mensing***, do not have the benefit of the FDA's interpretation of its own regulations. In our examination of the regulations regarding the CBE process, we find no indication that only brand-name manufacturers that obtained NDA approval, rather than RLDs generally, can utilize the process. If the CBE process is available only to the original NDA/RLD holder, there would be no need to designate a successor RLD in a situation where the original RLD withdraws its drug. Generic manufacturers could continue to file ANDAs demonstrating that their proposed generic drugs are equivalent to that of the obsolete NDA/RLD, but no manufacturer would bear any responsibility for the content of the label or the continued safety and efficacy of the drug. The purpose for designating a successor RLD is to have a standard to which subsequent ANDAs must correspond. This includes labeling.

Herein, we have a generic RLD seeking to avoid liability under the ***Mensing*** rationale. The burden of proving the basis for the pre-emption

defense rests with Morton Grove, and it has not established with the requisite certainty that it was impossible to modify its label.

Order affirmed.

Judge Platt files a Concurring and Dissenting Opinion.

Judgment Entered.

Prothonotary

Date: 7/29/2013