IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

SANOFI-AVENTIS U.S. LLC, SANOFI-AVENTIS DEUTSCHLAND GMBH, and SANOFI WINTHROP INDUSTRIE,

Plaintiffs,

v.

MERCK SHARP & DOHME CORP.,

Defendant.

Civil Acton No. 16-812-RGA

MEMORANDUM ORDER

I. BACKGROUND

Pending before the Court are Plaintiffs' Motion to Exclude the Testimony of Dr. John McLean (D.I. 252) and Plaintiffs' Motion to Exclude the Testimony of Dr. Rodolfo Pinal (D.I. 253). The issues have been fully briefed. (D.I. 252, 253, 266, 269, 274, 276). For the reasons stated herein, Plaintiffs' Motion to Exclude the Testimony of Dr. John McLean (D.I. 253) is **DENIED** without prejudice, and Plaintiffs' Motion to Exclude the Testimony of Dr. Rodolfo Pinal (D.I. 253) is **DENIED** without prejudice.

II. LEGAL STANDARD

Federal Rule of Evidence 702 sets out the requirements for expert witness testimony and states:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if: (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue; (b) the testimony is based on sufficient facts or data; (c) the testimony is the product of reliable principles and

methods; and (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702. The Third Circuit has explained:

> Rule 702 embodies a trilogy of restrictions on expert testimony: qualification, reliability and fit. Qualification refers to the requirement that the witness possess specialized expertise. We have interpreted this requirement liberally, holding that "a broad range of knowledge, skills, and training qualify an expert." Secondly, the testimony must be reliable; it "must be based on the 'methods and procedures of science' rather than on 'subjective belief or unsupported speculation'; the expert must have 'good grounds' for his o[r] her belief. In sum, *Daubert* holds that an inquiry into the reliability of scientific evidence under Rule 702 requires a determination as to its scientific validity." Finally, Rule 702 requires that the expert testimony must fit the issues in the case. In other words, the expert's testimony must be relevant for the purposes of the case and must assist the trier of fact. The Supreme Court explained in *Daubert* that "Rule 702's 'helpfulness' standard requires a valid scientific connection to the pertinent inquiry as a precondition to admissibility."
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> By means of a so-called "*Daubert* hearing," the district court acts as a gatekeeper, preventing opinion testimony that does not meet the requirements of qualification, reliability and fit from reaching the jury. *See Daubert* ("Faced with a proffer of expert scientific testimony, then, the trial judge must determine at the outset, pursuant to Rule 104(a) [of the Federal Rules of Evidence] whether the expert is proposing to testify to (1) scientific knowledge that (2) will assist the trier of fact to understand or determine a fact in issue.").

Schneider ex rel. Estate of Schneider v. Fried, 320 F.3d 396, 404-05 (3d Cir. 2003) (footnote and internal citations omitted).[1]

III. ANALYSIS

A. Dr. McLean's Testimony

Plaintiffs wish to exclude two aspects of Dr. McLean's testimony. The first is Dr. McLean's rebuttal infringement testimony that relies on a construction of polysorbate 20 that limits polysorbate 20 to a particular chemical entity. The second is Dr. McLean's reliance on the

[1] The Court of Appeals wrote under an earlier version of Rule 702, but the recent amendments to it were not intended to make any substantive change.

Escherichia coli Metabolome Database of small molecule metabolites found or produced by *E. coli* strain K-12, MG1655.

The parties' dispute regarding Dr. McLean's polysorbate 20 testimony appears to turn on whether the Court's claim construction for "polysorbate 20" from the *Eli Lilly* litigation is limited to a specific chemical entity that has 20 ethylene oxide units. (D.I. 252, p. 8; D.I. 266, p. 1). I think this issue is best addressed after trial in view of whatever evidence the parties present at trial.

The parties also disagree as to whether Dr. McLean's use of the Database will provide reliable testimony. Dr. McLean plans to rely on the Database to argue that the trace amounts of polysorbate 20 detected by Plaintiffs' expert in Merck's product could have been attributable to other materials used in the manufacture of Merck's product. (D.I. 252, p. 15; D.I. 266, p. 13). Plaintiffs maintain that Dr. McLean's testimony does not pass muster under Rule 702.

Plaintiffs first note that the Database contains data from a different strain of *E. coli* than the one used in Merck's product. (D.I. 252, p. 15). Defendant responds that the metabolites present in the K-12 strain of *E. coli* are comparable to the metabolites present in the *E. coli* strain used in Merck's product because the genomes of the two *E. coli* strains are 99% homologous. (D.I. 266, p. 15). Defendant also offers a study finding many metabolic characteristics to be conserved across an *E. coli* strain and a yeast, and Dr. McLean's assertion that, "it is unlikely that the small molecules and metabolites of the two strains would be qualitatively different." (*Id.* pp. 14-15). Defendant has failed to provide evidence of any association between the metabolites and metabolic pathways at issue here and the homologous portions of the *E. coli* genomes. Since Defendant may be able to produce evidence of such associations, however, I cannot presently say that the Database is unreliable because it contains data from a different strain of *E. coli* than the one used in Merck's product.

Plaintiffs also maintain that the MS Search tool that Dr. McLean used is unreliable because it is based on a peak matching algorithm that Defendant has not shown to be reliable. (D.I. 252, p. 17). Defendant has not provided evidence of error rates or peer review for the peak matching algorithm, or user guides or instruction manuals for the MS Search Tool. (*Id.*). Nor has Defendant pointed to any standards or methodology used by the MS Search Tool that would allow Plaintiffs to evaluate the scientific accuracy of the tool or corroborate Dr. McLean's results. (*Id.* pp. 17-18). Defendant responds that the Database has been cited over 100 times by independent research groups in peer-reviewed publications, and cites a peer-reviewed article describing how the Database had been updated as of 2015. (D.I. 266, p. 16). Though Defendant's arguments generally suggest that the data contained in the Database is accurate, they do not address whether Dr. McLean's methods or the MS Search Tool are reliable.

Though I am presently dubious that Dr. McLean's testing of the Database has produced reliable results relevant to this case, I will be in a better position to judge the reliability of Dr. McLean's testimony on a full record made at trial. While I acknowledge the "gate-keeper" function of a federal trial judge, it is not so important that it be done pretrial when the trial is a bench trial. *See In re Salem*, 465 F.3d 767, 777 (7th Cir. 2006); *United States v. Brown*, 415 F.3d 1257, 1269-70 (11th Cir. 2005); *Warner Chilcott Labs. v. Impax Labs., Inc.*, 2012 WL 1551709, *23-24 (D.N.J. Apr. 30, 2012). Live testimony and cross-examination are much more likely to result in a correct decision from me about whether the experts are giving appropriate scientific testimony. Thus, while I am denying the motion for now, each side may make (and, indeed, in order to preserve the issue, must make) objections at appropriate times. I expect that Defendant will lay an appropriate foundation for this expert and his challenged testimony as part of its case. Failure to make a timely appropriate objection will result in the objection being waived. The Court

will only consider evidence actually adduced at trial (whether through cross-examination or testimony from other witnesses) in ruling on any renewed motion. Therefore, I will deny without prejudice Plaintiffs' motion to exclude Dr. McLean's opinions regarding polysorbate 20 and results of his analysis of data in the Database.

B. Dr. Pinal's Testimony

Plaintiffs wish to preclude Dr. Pinal from relying on consumer complaints made to Sanofi and to the FDA through the MedWatch program about the prior Lantus product to support a motivation to combine prior art references to overcome the problems of turbidity and aggregation in the prior Lantus product. (D.I. 253, p. 6). The issue is whether an expert may rely on confidential, non-prior art documents[2] to establish an inherent property to support a motivation to combine.

Defendant argues, "Once a product is in 'public use,' all of the features of that product, regardless of whether they are openly visible, are considered to be in the prior art." (D.I. 269, p. 3 (citing *New Railhead Mfg. LLC v. Vermerr Mfg. Co.*, 298 F.3d 1113, 1119 (Fed. Cir. 2002))). Features that are not publicly known may nonetheless be prior art. (*Id.* (citing *Egbert v. Lippman*, 104 U.S. 333, 336 (1881))). According to Defendant, turbidity is an inherent feature in the Lantus product that need not be publicly known to be in the prior art. (*Id.* pp. 4-5). Dr. Pinal relied on consumer complaints merely to "demonstrate[e] the properties of Sanofi's original LANTUS product." (*Id.* p. 4). Dr. Pinal opines that the consumer complaints "simply support [his] opinion that a POSA would have been aware of the aggregation problem in the prior art LANTUS product because it precisely is characteristic of that product that is readily observed when the product is used." (*Id.* pp. 4-5). In other words, because turbidity is an inherent property of the original Lantus

[2] Defendant acknowledges that the complaints to Sanofi and to the FDA through the MedWatch program are not prior art. (D.I. 269, p. 2 ("[Dr. Pinal] does not opine that the consumer complaints are prior art.")).

product, Defendant may rely on non-prior art evidence to support a POSA's knowledge of the inherent property. (*See id.* p. 4). As support for its inherency argument, Defendant also offers the Lantus label, which instructs users to discard vials if the solution contained therein was not "clear, colorless, and free of particles." (*Id.* p. 8). Defendant also offers an unsupported paragraph from Dr. Pinal's reply expert report stating that formulations of insulin glargine were prone to aggregation, that the air in the Lantus vials would create the potential to aggregate, and that the low pH of Lantus would lead a POSA to believe there would be increased rates of aggregation. (*Id.* p. 7 (citing D.I. 271-2 at 94)).

Plaintiffs assert that a problem in the prior art must actually be known for it to provide a motivation to combine references. (D.I. 274, p. 2 (citing *Novartis Pharm. Corp. v. Par Pharm., Inc.*, 48 F. Supp. 3d 733, 758 (D. Del. 2014) ("There can be no motivation to combine prior art references to solve a problem that no one knows exists."))). According to Plaintiffs, "The prior art must show that a POSA would have known that the prior Lantus product had a vulnerability to turbidity that required additional stabilization and Merck should not be permitted to rely on non-public information to make that showing." (D.I. 274, p. 3). Regardless, Plaintiffs argue, turbidity is not an inherent property of the original Lantus product. (*Id.* p. 5). As support, Plaintiffs offer an internal Sanofi analysis demonstrating that consumers complained of turbidity or aggregation on average in approximately one out of every 10,000 vials. (*Id.* (citing D.I. 275-4 at 4)). Since turbidity was "a rare occasion" and "a low probability event" that "did not flow naturally from the prior Lantus product," Plaintiffs argue that turbidity is not an inherent property of the original Lantus product. (*Id.*).

Inherency is most commonly used to supply a limitation missing from a reference in an anticipation argument. To rely on inherency in an obviousness analysis, a party must meet a high

standard—"the limitation at issue necessarily must be present, or the natural result of the combination of elements explicitly disclosed by the prior art." *Par Pharm., Inc. v. TWi Pharm., Inc.*, 773 F.3d 1186, 1195-96 (Fed. Cir. 2014). "The mere fact that a certain thing may result from a given set of circumstances is not sufficient to render the result inherent." *Millennium Pharm., Inc. v. Sandoz Inc.*, 862 F.3d 1356, 1367 (Fed. Cir. 2017) (citations omitted).

Defendant offers the complaints to Sanofi and to the FDA under the MedWatch program as additional evidence that turbidity and aggregation are inherent properties of the original Lantus product. Absent proof that turbidity and aggregation are inherent properties of the original Lantus product, I find the complaints irrelevant. I conclude that Defendant has failed so far to prove by clear and convincing evidence that turbidity or aggregation is an inherent property of the original Lantus product. Dr. Pinal's unsupported testimony is insufficient to sustain a finding that turbidity or aggregation is an inherent property of the original Lantus product, especially in light of Sanofi's internal analysis suggesting that turbidity and aggregation were low probability events in the original Lantus product. I also note that if turbidity and aggregation were inherent properties in the original Lantus formulation, one might expect prior art references to have identified them as problems to be solved.

Though the evidence cited in the papers does not establish that turbidity and aggregation are inherent properties of the original Lantus product, the evidence presented at trial may support a finding that turbidity and aggregation are inherent properties of the original Lantus product. In that case, the complaints may become relevant. Thus, while I am denying the motion for now, each side may make (and, indeed, in order to preserve the issue, must make) objections at appropriate times. I expect that Defendant will lay an appropriate foundation for this expert and his challenged testimony as part of its case. Failure to make a timely appropriate objection will

result in the objection being waived. The Court will only consider evidence actually adduced at trial (whether through cross-examination or testimony from other witnesses) in ruling on any renewed motion. Therefore, I will deny without prejudice Plaintiffs' motion to exclude Dr. Pinal's opinions.

IV. CONCLUSION

For the reasons stated above, Plaintiffs' Motion to Exclude the Testimony of Dr. John McLean (D.I. 253) is **DENIED** without prejudice. Plaintiffs' Motion to Exclude the Testimony of Dr. Rodolfo Pinal (D.I. 253) is **DENIED** without prejudice.

IT IS SO ORDERED.

Entered this 29 day of May, 2018.

United States District Judge