IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE: DIET DRUGS (PHENTERMINE/ FENFLURAMINE/DEXFENFLURAMINE) PRODUCTS LIABILITY LITIGATION	MDL NO. 1203
THIS DOCUMENT RELATES TO:	
JAMIE D. CHEEK v. WYETH, et al.	CIVIL ACTION NO. 11-20001
VALARIE FARMER v. WYETH PHARMACEUTICALS INC., et al.	CIVIL ACTION NO. 99-20593

MEMORANDUM IN SUPPORT OF SEPARATE PRETRIAL ORDER NO. 8933

Bartle, J. August 30, 2012

Plaintiffs Jamie D. Cheek and Valarie Farmer have each filed an action against defendant Wyeth, LLC ("Wyeth")[1] alleging that she suffers from primary pulmonary hypertension ("PPH")[2] as a result of ingestion of Wyeth's appetite-suppressant drugs fenfluramine, marketed as Pondimin, and dexfenfluramine, marketed as Redux ("Diet Drugs"). Before the court is the motion of Wyeth

1. Plaintiffs have also named as defendants various related corporate entities: (1) Pfizer, Inc.; (2) Wyeth-Ayerst International, Inc.; (3) Wyeth-Ayerst Pharmaceuticals, Inc.; (4) Wyeth-Ayerst Laboratories, Inc.; (5) Wyeth Pharmaceuticals, Inc; (6) Pfizer, Inc.; (7) American Home Products ("AHP") Corp.; and (8) AHP Subsidiary Holding Corporation. For purposes of this motion, we will refer to defendants simply as Wyeth.

2. PPH is also known as pulmonary arterial hypertension ("PAH").

to enjoin Ms. Cheek and Ms. Farmer from continuing with their lawsuits in the United States District for the District of South Carolina and the Court of Common Pleas of Philadelphia County respectively because of the bar under the provisions of the Diet Drug Nationwide Class Action Settlement Agreement ("Settlement Agreement") and PTO Nos. 1415 and 2383.[3] Wyeth has also moved to exclude the testimony of Ms. Cheek's medical experts on causation under Rules 702 and 403 of the Federal Rules of Evidence and Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993).

I.

It is undisputed that Jamie Cheek ingested Diet Drugs for approximately one year. She took the Diet Drug Fenfluramine from October 25, 1995 through June 17, 1996 and from September 11, 1996 to December 29, 1996. She also used the Diet Drug Dexfenfluramine from June 18, 1996 to July 15, 1996. On January 6, 2011, Ms. Cheek filed a lawsuit against Wyeth in the United States District Court for the District of South Carolina claiming, as noted above, that she was suffering from PPH caused by Diet Drugs. The action was transferred to this court for coordinated pretrial proceedings as part of the Diet Drug Multi-District Litigation ("MDL No. 1203").

During discovery, Ms. Cheek produced to Wyeth her complete medical records as well as expert reports by Stuart

---

3. See Cheek v. Wyeth, et al., No. 11-54 (D.S.C. Jan. 6, 2011); Farmer v. Wyeth Pharmaceuticals, Inc., et al., No. 01174 (Phila. C.P. July 13, 2011).

Rich, M.D. and Lewis Rubin, M.D. which exclude various known conditions as causing her PPH. These physicians opine that the onset of her PPH resulted from her use of Diet Drugs.

Plaintiff Valarie Farmer took the Diet Drug Pondimin for approximately three months in 1997. On June 29, 2011, she was diagnosed with PPH. Thereafter, on July 13, 2011, Ms. Farmer filed suit against Wyeth in the Court of Common Pleas of Philadelphia County alleging that her PPH resulted from her use of Diet Drugs. During discovery, Ms. Farmer produced her medical records and expert reports from Dr. Rubin and Harold Palevsky, M.D. Both determined that Ms. Farmer's PPH was caused by Diet Drugs. Jury selection is scheduled to begin in her case in the state court on September 27, 2012.

In support of its motions, Wyeth first argues that the opinions of plaintiffs' experts fail under the definition of PPH set forth in the Settlement Agreement because they do not exclude idiopathic, that is, unknown causes for plaintiffs' PPH. Wyeth further contends there is no reliable scientific or medical basis for an opinion that Diet Drugs caused Ms. Cheek's PPH when the PPH did not manifest itself until some eleven years after she ceased consumption of Diet Drugs. More specifically, it maintains that there is no reliable scientific evidence that Diet Drugs cause PPH after a latency period of five or more years.

We held a status conference with the attorneys for the parties, at which time they agreed that no evidentiary hearing was necessary and that the pending motions could be decided on

the record before the court. On August 23, 2012, this court held oral argument.

II.

This court has previously described the fatal disease known as PPH:

> PPH is a disease that affects pulmonary circulation. PPH is characterized by scarring and fibrosis of the pulmonary arteries which carry deoxygenated blood from the right side of the heart to the lungs. This scarring prevents the blood cells from effectively absorbing oxygen as they pass the alveoli in the lungs. Moreover, the scarring within the pulmonary arteries obstructs the flow of blood within the vessels, causing the blood pressure in the pulmonary arteries to rise. The right ventricle of the heart attempts to overcome the increasing resistance to the flow of blood through the pulmonary arteries by growing larger and more muscular. Ultimately, this dilatation and hypertrophy of the right ventricle will cause the heart to fail and result in the patient's death.
>
> PPH is a relentlessly progressive disease that leads to death in virtually all circumstances.

In re Diet Drugs Prods. Liab. Litig., 226 F.R.D. 498, 501 (E.D. Pa. 2005).

The Settlement Agreement, with limited exceptions, resolved the claims of those who used Wyeth's diet drugs known as Pondimin and Redux. Those who opted out of the settlement, of course, were not bound by its terms.[4] In addition, the PPH claims of persons who ingested Diet Drugs are excluded from the definition of settled claims. Settlement Agreement § VII.B.

---

4. Those opt-out provisions are not relevant for present purposes.

Such persons may sue Wyeth for PPH in the tort system.[5] Id. All other claims against Wyeth for Diet-Drug related injuries are subject to the release and bar provisions of the Settlement Agreement as set forth in PTO No. 1415:

> The court hereby bars and enjoins all class members who have not, or do not, timely and properly exercise an Initial, Intermediate, Back-End or Financial Insecurity Opt-Out right from asserting, and/or continuing to prosecute against [Wyeth] or any other Released Party any and all Settlement Claims which the class member had, has or may have in the future in any federal, state or territorial court.

PTO No. 1415 ¶ 7 (Aug. 8, 2000).

To avoid an injunction against proceeding with their PPH claims, plaintiffs must satisfy or at least come forward with evidence to satisfy a three-part definition of PPH under the Settlement Agreement. First, a plaintiff must produce evidence of one of three clinical findings:

(a) Mean pulmonary artery pressure by cardiac catheterization of ≥ 25 mm Hg at rest or ≥ 30 mm Hg with exercise with a normal pulmonary artery wedge pressure ≤ 15 mm Hg; or

(b) A peak systolic pulmonary artery pressure of ≥ 60 mm Hg at rest measured by Doppler echocardiogram utilizing standard procedures; or

(c) Administration of Flolan to the patient based on a diagnosis of PPH with cardiac catheterization not done due to

---

5. Under Section VII.B.4., "For purposes of any statute of limitations or similar time bar, the [Wyeth] Released Parties shall not assert that a Class Member actually had PPH unless and until the condition of the Class Member meets the definition of PPH set forth in Section I.46."

> increased risk in the face of severe right heart dysfunction[.]

Settlement Agreement § I.46.a(1). A plaintiff must also come forward with the following medical records:

> (a) Echocardiogram demonstrating no primary cardiac disease including, but not limited to, shunts, valvular disease (other than tricuspid or pulmonary valvular insufficiency as a result of PPH or trivial, clinically insignificant left-sided valvular regurgitation), and congenital heart disease (other than patent foramen ovale); and
>
> (b) Left ventricular dysfunction defined as LVEF < 40% defined by MUGA, Echocardiogram or cardiac catheterization; and
>
> (c) Pulmonary function tests demonstrating the absence of obstructive lung disease (FEV_1/FVC > 50% of predicted) and the absence of greater than mild restrictive lung disease (total lung capacity > 60% of predicted at rest); and
>
> (d) Perfusion lung scan ruling out pulmonary embolism; and
>
> (e) If, but only if, the lung scan is indeterminate or high probability, a pulmonary angiogram or a high resolution angio computed tomography scan demonstrating absence of thromboembolic disease[.]

Id. at § I.46.a(2). Finally, a plaintiff must have evidence that:

> Conditions known to cause pulmonary hypertension including connective tissue disease known to be causally related to pulmonary hypertension, toxin induced lung disease known to be causally related to pulmonary hypertension, portal hypertension, significant obstructive sleep apnea, interstitial fibrosis (such as silicosis, asbestosis, and granulomatous disease) defined as greater than mild patchy

> interstitial lung disease, and familial causes, have been ruled out by a Board-Certified Cardiologist or Board-Certified Pulmonologist as the cause of the person's pulmonary hypertension.[6]

Id. at § I.46.a(3).

Under PTO No. 2383 and PTO No. 3699, a putative PPH plaintiff must initially meet the threshold definition of PPH as set forth in the Settlement Agreement or at least raise a genuine dispute of material fact in this regard. See PTO No. 3699 at 4 (July 6, 2004); PTO No. 2383 at 3 (Feb. 26, 2002). If Wyeth disputes a plaintiff's diagnosis of PPH, it may file a motion to enjoin the plaintiff from proceeding with his or her tort action pursuant to PTO No. 1415. Id. at 6. Wyeth must use its "best efforts" to file such a motion within 60 days of receipt of the plaintiff's medical records. Id. This court then compares the plaintiff's medical records with a checklist based on the definition of PPH in Section I.46 of the Settlement Agreement, as set forth above. Id. at 7. Such analysis "[i]n most if not all instances ... will not be unduly time consuming." Id. at 8. If plaintiff has not met his or her burden, the court will prohibit the plaintiff from proceeding with a PPH tort claim.[7] Id.

---

6. The definition of PPH is different for a diagnosis made after an individual's death. Such differences are not relevant to the instant motion.

7. "The denial of a motion to enforce PTO 1415 pursuant to this Order shall not have any preclusive effect and shall not be admissible in the litigation of such claims. Similarly, such denial shall not preclude [Wyeth] or any other Released Party from challenging, in this Court or in the underlying action, the existence of facts that purportedly qualify the Class Member to

(continued...)

Wyeth does not contest that Ms. Cheek and Ms. Farmer have met the criteria set forth in the first two parts of the PPH definition. See Settlement Agreement, § I.46.a(1)-(2). It is also undisputed that the medical experts retained by Ms. Cheek and Ms. Farmer have excluded the other known causes of PPH including those enumerated in the third part of the PPH definition. See id. at § I.46.a(3).

Wyeth asserts, however, that the experts have not excluded "idiopathic" pulmonary hypertension ("IPAH"). IPAH is pulmonary hypertension which results from an unknown cause. According to Wyeth, approximately 300 to 600 Americans develop IPAH each year. Wyeth maintains that to move forward with their actions plaintiffs "must present reliable evidence that their PPH was caused by diet drugs, rather than idiopathic PAH." Such "reliable evidence," Wyeth contends, does not exist because IPAH is "indistinguishable" from Diet-Drug-induced PPH and, as a result, "[t]here is no clinical test that can distinguish between pulmonary hypertension resulting from distant diet drug use as opposed to IPAH."

While an expert can surely opine that the cause of any injury is unknown, it is at least questionable whether an expert can ever really exclude an unknown cause since by definition it is unknown. The Court of Appeals in Heller v. Shaw Industries, Inc., cautioned that an expert is not required under Daubert "to rule out all alternative possible causes of [a person's]

---

7. (...continued)
assert a claim based on PPH." PTO No. 2383 at 8.

illness."[8] 167 F.3d 146, 156 (3d Cir. 1998). It then quoted Professor Capra, the Reporter to the Advisory Committee on the Federal Rules of Evidence:

> [T]o require the experts to rule out categorically all other possible causes for an injury would mean that few experts would ever be able to testify....
>
> ... Obvious alternative causes need to be ruled out. All possible causes, however, cannot be and need not be eliminated before an expert's testimony will be admitted.

Id.; see also In re Asbestos Prods. Liab. Litig., No. 09-69123, 2010 WL 4676563, at *4 (E.D. Pa. Nov. 15, 2010). In any event, evidence excluding idiopathic or unknown causes of PPH is not required under the plain meaning of the Settlement Agreement. The definition of PPH set forth in the Settlement Agreement dictates that those who wish to proceed with a tort claim based on PPH must produce evidence excluding certain "[c]onditions known to cause pulmonary hypertension." Settlement Agreement, at § I.46.a(3) (emphasis added). As discussed above, IPAH is by definition a diagnosis of pulmonary hypertension which arises from an unknown cause. Any interpretation of the Settlement Agreement to require exclusion of conditions unknown, that is, an idiopathic cause or diagnosis, would be "inconsistent with [a] common sense" reading of the Agreement and therefore cannot be adopted by this court. See, e.g., Disabled in Action of Pa. v.

---

8. As an MDL court sitting within the Third Circuit, we apply the law as set forth by our Court of Appeals. See In re Korean Airlines Disaster, 829 F.2d 1171, 1174 (D.C. Cir. 1987); In re Automotive Refinishing Paint, 229 F.R.D. 482, 486-87 (E.D. Pa. 2005).

Se. Pa. Transp. Auth., 539 F.3d 199, 210 (3d Cir. 2008). Under the undisputed facts before us, both Jamie Cheek and Valerie Farmer have satisfied the multi-part definition of PPH as written into Section I.46 of the Settlement Agreement.

III.

Whether Diet Drugs caused the PPH from which the plaintiffs suffer is a separate issue.[9] Each must prove, in addition to the criteria of the Settlement Agreement, that her use of Diet Drugs precipitated the onset of her PPH. As to Valerie Farmer, her lawsuit has never been before this court for pretrial proceedings as part of MDL 1203. It has proceeded and will be tried in the Court of Common Pleas of Philadelphia County where the test for the reliability of an expert's testimony will be determined not under Daubert, but under the Frye test. See, e.g., Commonwealth v. Nazarovitch, 436 A.2d 170, 172 (Pa. 1981) (citing Frye v. United States, 293 F. 1013 (D.C. 1923)). It is for the state court to decide on the admissibility of the medical opinions of plaintiff's experts and if admissible for the jury to make a finding on causation.

The Cheek case, on the other hand, was transferred here for pretrial proceedings as part of MDL 1203 but will be returned for trial to the transferor court, the United States District

---

9. PTO No. 2383, ¶ 14, provides, "A ruling on a motion to enforce PTO 1415 shall not be deemed an adjudication on the merits of any element of the Class Member's claims against AHP or any other Released Party. Further, nothing in this Order shall effect the right of AHP or any Released Party to conduct discovery relating to a Class Member's claim of PPH or otherwise, as permitted by applicable law."

Court for the District of South Carolina. See 28 U.S.C. § 1407. Wyeth argues that under Daubert there is no reliable medical or scientific evidence that Diet Drugs can cause an individual to develop PPH eleven years after a patient discontinues use of the drugs, as occurred here with Ms. Cheek. It asserts that there are no epidemiological studies measuring the risk of developing PPH more than five years after an individual has ceased taking Diet Drugs. Wyeth submits that the only such study regarding PPH is the 1996 International Primary Pulmonary Hypertension Study ("IPPHS"). While Wyeth concedes that the IPPHS found that Diet Drugs can cause PPH, it asserts that the IPPHS demonstrates that the risk of developing PPH was no longer statistically significant for patients one year after they discontinued taking Diet Drugs. Wyeth reasons that without any epidemiological study, Ms. Cheeks lacks sufficient scientific evidence to proceed with her lawsuit.

The IPPHS considered 95 patients with PPH in France, Belgium, the United Kingdom, and the Netherlands and compared them with 335 control patients. The study confirmed that Diet Drugs cause PPH and calculated the relative risk, or "odds ratio," of developing PPH for Diet Drug users. Relative risk has been explained as:

> The ratio of the risk of disease or death among people exposed to an agent to the risk among the unexposed. For instance, if 10% of all people exposed to a chemical develop a disease, compared with 5% of people who are not exposed, the disease occurs twice as frequently among the exposed people. The relative risk is 10%/5% = 2. A relative risk

> of 1 indicated no association between exposure and disease.

Fed. Judicial Ctr., Reference Manual on Scientific Evidence 395 (3d ed. 2011).

Overall, the IPPHS determined that individuals who had ingested Diet Drugs had a relative risk of 6.3, meaning that they were 630% more likely to develop PPH than individuals who had not ingested Diet Drugs. The relative risk for recent users was 10.1. In contrast, the study reported that those individuals who had ceased use of Diet Drugs more than one year earlier had a relative risk of 2.4. The study also revealed that the relative risk sharply increased with duration of exposure. While individuals who used Diet Drugs for three months or less had a relative risk of 1.8, those who had used Diet Drugs for longer than three months had a relative risk of 23.1. The study concluded "[t]he risk of primary pulmonary hypertension seems to increase steadily with the quantity of appetite suppressants used, but there has been very little experience with their long-term use in Europe." It acknowledged that "[h]ow fenfluramine and dexfenfluramine may lead to pulmonary hypertension is unknown."

Wyeth asserts that the 2.4 odds ratio did not reach statistical significance because the confidence interval included 1.0. A confidence interval is "a range of possible values calculated from the results of a study.... The width of the confidence interval reflects random error." Reference Manual on Scientific Evidence at 389. "Where the confidence interval

contains a relative risk of 1.0, the results of the study are not statistically significant. Id. The confidence interval for the odds ratio for past users in the IPPHS study ranged from 0.7 to 8.2. Therefore, because the boundaries of the confidence interval encompass a relative risk of 1.0, Wyeth asserts that the study is not statistically significant. See id.

Wyeth also relies on the expert opinion of Mitchell Levine, M.D. Dr. Levine is a Professor of Medicine at McMaster University in Ontario, Canada and an Adjunct Professor at the University of Michigan School of Public Health. He is board-certified in the field of internal medicine and specializes in epidemiology and pharmacology, although not board-certified in cardiology or pulmonology. In his expert report, Dr. Levine stated: "I am of the opinion to a reasonable degree of medical and scientific certainty that there is statistically significant scientific support for an association between diet drug exposure and the development of PPH only in patients when symptoms begin within one year after the discontinuation of diet drug use."

In response, Ms. Cheek offers the opinions of Dr. Rich and Dr. Rubin. In his declaration dated July 26, 2012, Dr. Rich opines that the IPPHS was not created to study the latency of Diet-Drug-induced PPH. Dr. Rich was a principal investigator for and a co-author of the IPPHS study. He posits that Wyeth's position "is a distortion of the results" of the IPPHS. In addition, Dr. Rich references several subsequent case studies which support his opinion that Diet Drugs can cause PPH more than ten years after ingestion. While he acknowledges that the risk

of developing PPH declines with the passage of time, it is his medical opinion that there is no known cut-off applicable in all cases and that the duration and quantity of a person's Diet Drug use can extend the latency period. Finally, contrary to the opinion of Dr. Levine, Dr. Rich opines that Ms. Cheek's Diet Drug ingestion caused her PPH. In his deposition, Dr. Rubin similarly explained that his opinion was based on not only on the IPPHS, but on medical literature, clinical studies, and a differential diagnosis in reaching his conclusion.

A transferee court presiding over a multi-district litigation may exercise authority over all pretrial proceedings. See In re Patenaude, 210 F.3d 135, 144 (3d Cir. 2000). A motion in limine to exclude an expert opinion under Daubert is certainly within the jurisdiction of this court. See, e.g., In re Diet Drugs Prods. Liab. Litig., No. 12-1203, 2001 WL 454586 (E.D. Pa. Feb. 1, 2001); In re Diet Drugs Prods. Liab. Litig., No. 12-1203, 2000 WL 962545 (E.D. Pa. June 28, 2000).

The court has a "gatekeeping" function in connection with expert testimony. See Gen. Electric Co., et al. v. Joiner, 522 U.S. 136, 142 (1997); see also Daubert, 509 U.S. at 589. Rule 702 of the Federal Rules of Evidence provides:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the

> principles and methods reliably to the facts of the case.

As our Court of Appeals has repeatedly noted, Rule 702 embodies three requirements: qualification, reliability, and fit. Pineda v. Ford Motor Co., 520 F.3d 237, 244 (3d Cir. 2008). Wyeth does not question the credentials of Ms. Cheek's experts or the fit of their opinions. Instead, it challenges Ms. Cheek's experts only as to reliability.

To determine reliability, we focus not on the expert's conclusion but on whether that conclusion is "based on the methods and procedures of science rather than on subjective belief or unsupported speculation." Schneider v. Fried, 320 F.3d 396, 404 (3d Cir. 2003) (internal quotation marks omitted). Our analysis may include such factors as:

> (1) whether a method consists of a testable hypothesis; (2) whether the method has been subject to peer review; (3) the known or potential rate of error; (4) the existence and maintenance of standards controlling the technique's operation; (5) whether the method is generally accepted; (6) the relationship of the technique to methods which have been established to be reliable; (7) the qualifications of the expert witness testifying based on the methodology; and (8) the non-judicial uses to which the method has been put.

Pineda, 520 F.3d at 247-48.

"[T]he test of reliability is flexible" and this court possesses a broad latitude in determining reliability. Kumho Tire Co. v. Carmichael, 526 U.S. 137, 141-42 (1999). To be reliable under Daubert, a party need not prove that his or her

expert's opinion is "correct." In re Paoli R.R. Yard PCB Litig., 35 F.3d 717, 744 (3d Cir. 1994). Instead:

> As long as an expert's scientific testimony rests upon good grounds, based on what is known, it should be tested by the adversary process-competing expert testimony and active cross-examination-rather than excluded from jurors' scrutiny for fear that they will not grasp its complexities or satisfactorily weigh its inadequacies.

United States v. Mitchell, 365 F.3d 215, 244 (3d Cir. 2004) (quoting Ruiz-Troche v. Pepsi Cola Bottling Co., 161 F.3d 77, 85 (1st Cir. 1998)).

Daubert does not require that an expert opinion regarding causation be based on statistical evidence in order to be reliable. Matrixx Initiatives, Inc. v. Siracusano, 131 S. Ct. 1309, 1319 (2011). In fact, many courts have recognized that medical professionals often base their opinions on data other than statistical evidence from controlled clinical trials or epidemiological studies. Id. at 1320. Our Court of Appeals has stated, "we do not believe that a medical expert must always cite published studies on general causation in order to reliably conclude that a particular object caused a particular illness." Heller, 167 F.3d at 155. It explained:

> To so hold would doom from the outset all cases in which the state of research on the specific ailment or on the alleged causal agent was in its early stages, and would effectively resurrect a Frye-like bright-line standard, not by requiring that a methodology be "generally accepted," but by excluding expert testimony not backed by published (and presumably peer-reviewed) studies.

Id.

Medical experts are entitled to rely on a differential diagnosis. A differential diagnosis is a process by which a physician rules out alternative causes through review of a patient's medical histories and records, physical examination of the patient, laboratory testing, study of relevant medical literature, and other techniques. See Heller, 167 F.3d at 156; Paoli, 35 F.3d at 758-59. Such technique is generally accepted in the medical community. Heller, 167 F.3d at 156. Our Court of Appeals agrees that opinions based on differential diagnoses should not be excluded under Daubert unless the physician failed to utilize the diagnostic techniques normally relied upon in the medical community or failed to explain why another likely cause did not bring about the plaintiff's illness. Paoli, 35 F.3d at 760.

Ms. Cheek's experts properly rely on the conclusion of the IPPHS that Diet Drugs can cause PPH. Wyeth, we reiterate, does not dispute that point. As discussed above, that study established that the risk of developing PPH increased 630% after ingestion of Diet Drugs. The study need not address the exact circumstances under which Ms. Cheek developed PPH in order to support Dr. Rich and Dr. Rubin's opinions.[10] Contrary to Wyeth's assertions, the IPPHS does not establish that an individual

---

10. In his declaration dated July 26, 2012, Dr. Rich also points out that there has never been a controlled study measuring relative risk for many other known causes of PPH, such as connective tissue disease, portal hypertension, and the human immunodeficiency virus ("HIV"). Nonetheless, medical experts do not dispute that these conditions can lead to the development of PPH.

cannot develop PPH more than five years after ingestion ends. That study was simply not designed to examine latency. Instead, it included only seven past users and none had ceased use of the drugs for more than five years.

In addition to the IPPHS, plaintiff's experts rely on differential diagnoses made after review of Ms. Cheek's medical records. A differential diagnosis is a reliable method of demonstrating causation under Daubert because such a method "consists of a testable hypothesis," has been peer reviewed, and is generally accepted. See Heller, 167 F.3d at 156; Paoli, 35 F.3d at 758-59. In their diagnoses, Dr. Rich and Dr. Rubin have excluded all other known causes of PPH. They need not exclude unknown or idiopathic causes of PPH in order for their differential diagnoses to be a reliable basis for their opinions. See In re Asbestos, 2010 WL 4676563, at *4. According to Wyeth, an idiopathic origin accounts for only one to two cases of PPH per million people annually. To bolster their differential diagnoses, Dr. Rich and Dr. Rubin also point out that development of PPH after a period of latency is biologically plausible. There are many other causes of the disease that have significant latency periods. For example, PPH caused by connective tissue disease can lay dormant for a period of up to twenty-seven years. Similarly, the latency period for the development of PPH due to a genetic mutation or birth defect is often decades.

Dr. Rich and Dr. Rubin also rely on a large number of case reports which have been published in peer-reviewed journals. In one such study published in 2006 in the American Journal of

Respiratory and Critical Care Medicine, "Pulmonary Arterial Hypertension in France: Results from a National Registry," 43% of patients who had ingested appetite-suppressant drugs such as the Diet Drugs experienced a delay of more than five years between their last intake of the drugs and the onset of symptoms of PPH. Similarly, a case study published in the European Respiratory Journal, "Pulmonary Arterial Hypertension Associated with Fenfluramine Exposure: Report of 109 Cases" found the median time between Diet Drug exposure and onset of PPH symptoms to be 4.5 years and reported latency periods of greater than ten years. These case studies can help establish that an expert's opinion is reliable. See Wolfe v. McNeil-PPC, Inc., et al., No. 07-348, 2011 WL 1673805, at *5 (E.D. Pa. May 4, 2011). Case studies are particularly relevant when dealing with rare or newly-discovered diseases, which often have not been the subject of an epidemiological study. See Reference Manual on Scientific Evidence at 474-75. PPH, fortunately, is a rare disease, and it has not been the subject of any epidemiological study on latency.

We further note that Dr. Rubin and Dr. Rich have impressive credentials. Dr. Rich is a board-certified internist and cardiologist who currently serves as a Clinical Professor of Medicine at the University of Chicago. He has studied PPH for over 30 years and has authored most of the leading publications regarding this fatal disease. In addition, Dr. Rich served as a principal investigator for the IPPHS study and co-authored the article describing the results of that study in the New England Journal of Medicine. Dr. Rubin is presently Emeritus Professor

of Medicine at the University of California in San Diego. He is board-certified in pulmonary disease and critical care medicine. Like Dr. Rich, he has devoted most of his career to the study of PPH and has authored hundreds of peer-reviewed articles and book chapters pertaining to the disease. Dr. Rubin also worked on the IPPHS study. Together with Dr. Rich, he wrote a textbook on PPH that is considered the authoritative manuscript on the disease and is cited in Section I.46 of the Settlement Agreement - a document which Wyeth had a hand in drafting. See L.J. Rubin & S. Rich, Primary Pulmonary Hypertension (1997).

Finally, the methods of Ms. Cheek's experts have general acceptance in the medical community. As recently as 2009, the Journal of the American College of Cardiology published the Dana Point Classification for PPH. That classification system identified Diet Drugs as a "definite" risk factor for PPH and included Diet-Drug-induced PPH as a diagnosis for any patient with PPH who did not have a family history of PPH or other known risk factor, without regard to latency. The differential diagnoses conducted by Dr. Rich and Dr. Rubin are in line with this classification system and are the same method used by physicians who deal with PPH, including Ms. Cheek's own treating physicians.

When viewed in totality, the IPPHS coupled with the differential diagnoses performed by these experts, the case reports on which they rely, their credentials, the peer review and publication of their methods, and the general acceptance of their methodology in the medical community demonstrate that the

opinions of Dr. Rich and Dr. Rubin are reliable under Daubert. While Wyeth points to various statements of Dr. Rich and Dr. Rubin which one might argue show some inconsistency on the issue of latency, these statements simply go to their credibility and do not undermine the reliability of their methodology in determining causation. See In re Unisys Savings Plan Litig., 173 F.3d 145, 166 (3d Cir. 1999). The testimony of Dr. Rich and Dr. Rubin will be of assistance to the trier of fact. See Fed. R. Evid. 702.

The court, of course, expresses no view on whether Ms. Cheek's ingestion of Diet Drugs caused her PPH when her symptoms did not appear until eleven years after she stopped taking those drugs. That is a matter for the jury to decide after hearing from the experts on both sides and considering all other relevant evidence.

IV.

Accordingly, the motion of Wyeth to enjoin Ms. Farmer and Ms. Cheek under PTO Nos. 1415 and 2383 from proceeding with their respective lawsuits will be denied. The motion of Wyeth to

exclude the testimony of Dr. Rubin and Dr. Rich in Cheek under Rule 702 of the Federal Rules of Evidence will also be denied.[11]

11. In 2003, Wyeth moved in Smith v. Wyeth-Ayerst Laboratories Co., 278 F. Supp. 2d 684 (W.D.N.C. 2003), the transferor court, to bar Dr. Rich, plaintiff Smith's PPH expert, from testifying on the ground that his methodology on the issue of latency was not reliable under Daubert. Wyeth waited to make its motion until after pretrial proceedings had concluded and this MDL court had returned it to the Western District of North Carolina for trial. As in this case, that court ruled against Wyeth. See id. There, the plaintiff used Diet Drugs for a total of 8.5 months and developed PPH approximately three years after her last use of the drugs. Id. at 689.