UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF PENNSYLVANIA

IN RE: TYLENOL (ACETAMINOPHEN) MARKETING, SALES PRACTICES, AND PRODUCTS LIABILITY LITIGATION	§ § § § § §	**MDL NO. 2436** **2:13-md-02436** **HON. LAWRENCE F. STENGEL**
This Document Relates to: Rana Terry, as Personal Representative and Administrator of the Estate of Denice Hayes, Deceased, Plaintiff, vs. McNEIL-PPC, Inc., McNeil Consumer Healthcare, and Johnson & Johnson, Inc., Defendants.	§ § § § § § § § § § § § § § §	Civil Action No. 2:12-cv-07263

M E M O R A N D U M

Stengel, J. **July 28, 2016**

This case is part of a Multidistrict Litigation (MDL) involving claims of liver damage from the use of Tylenol at or just above the recommended dosage.[1] This is the

[1] See Master Compl., 13-md-2436, Doc. No. 32. There are over two hundred other cases included in this MDL, along with several similar cases in New Jersey state court.

first "bellwether" case scheduled for trial.[2] The plaintiff plans to offer Dr. Laura Plunkett, Ph.D. as a general causation and regulatory expert. The defendants move to exclude certain parts of her testimony under Daubert. For the reasons stated below, I will deny their motion in part and grant it in part.[3]

I. LEGAL STANDARD

The admissibility of expert testimony is governed by Federal Rules of Evidence 702 and 703 as well as by Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579 (1993), and its progeny.[4] See In re Paoli RR Yard PCB Litigation (Paoli II), 35 F.3d 717, 735 (3d Cir. 1994). "Under the Federal Rules of Evidence, a trial judge acts as a 'gatekeeper' to ensure that 'any and all expert testimony or evidence is not only relevant, but also reliable.'" Pineda v. Ford Motor Co., 520 F.3d 237, 243 (3d Cir. 2008)(quoting Kannankeril v. Terminix Int'l, Inc., 128 F.3d 802, 806 (3d Cir. 1997)). The Third Circuit recognizes a "liberal policy of admissibility" regarding Rule 702. Pineda, 520 F.3d at 243 (quoting Kannankeril, 128 F.3d at 806); United States v. Schiff, 602 F.3d 152, 173 (3d Cir. 2010).[5]

[2] A "bellwether" case is a test case. "Bellwether" trials should produce representative verdicts and settlements. The parties can use these verdicts and settlements to gauge the strength of the common MDL claims to determine if a global resolution of the MDL is possible. See FEDERAL JUDICIAL CENTER, MANUAL FOR COMPLEX LITIGATION, FOURTH EDITION 360 (2004); DUKE LAW CENTER FOR JUDICIAL STUDIES, MDL STANDARDS AND BEST PRACTICES 16-21 (2014).

[3] In making my decision, I have reviewed all of the materials submitted as attachments to the parties' briefs, including those submitted during oral argument.

[4] Daubert held that the Federal Rules of Evidence, specifically Rule 702, controlled the issue of when experts were qualified. Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 587-88 (1993). It found that Rule 702 superseded the Court's prior precedent on the subject found in Frye v. United States, 54 App.D.C. 46, 47, 293 F. 1013, 1014 (1923). Id. at 587. Daubert went on to clarify what was required under Rule 702, as compared to Frye. See id. at 589-598.

[5] See also Holbrook v. Lykes Brothers Steamship Company, Inc., 80 F.3d 777, 780 (3d Cir. 1996); Zaprala v. USI Servs. Gp., Inc., No. 09–1238, 2013 WL 1148335, at *6 (E.D. Pa. Mar. 20, 2013)(quoting Pineda, 520 F.3d at 243).

"[B]ecause expert evidence is often more misleading than other evidence, Rule 403 gives a judge more power over experts than over lay witnesses." In re Paoli RR Yard PCB Litigation (Paoli II), 35 F.3d 717, 747 (3d Cir. 1994). However, "in order for a district court to exclude scientific evidence, there must be something particularly confusing about the scientific evidence at issue—something other than the general complexity of scientific evidence." Id.

a. Rule 702

Federal Rule of Evidence 702 has three major requirements: 1) the expert must be qualified; 2) the expert must testify about matters requiring scientific, technical, or specialized knowledge; and 3) the testimony must assist the trier of fact.[6] Pineda, 520 F.3d at 243 (citing Kannankeril, 128 F.3d at 806). 702's inquiry should be a "flexible one." Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 594 (1993).

i. Expert Must Be Qualified

An expert's qualifications may include education, provided it is in a field related to the one in which the expert intends to testify. Fedor v. Freightliner, Inc.,

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[6] Federal Rule of Evidence 702 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:
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> (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;
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> (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.

193 F. Supp. 2d 820, 827 (E.D. Pa. 2002). Overall, the court will consider both academic training and practical experience to determine if the expert has "more knowledge than the average lay person" on the subject. Id. at 827-28 (citing Waldorf v. Shuta, 142 F.3d 601, 627 (3d Cir. 1998)). "An expert may be generally qualified but may lack qualifications to testify outside his area of expertise." Calhoun v. Yamaha Motor Corp., U.S.A., 350 F.3d 316, 322 (3d Cir. 2003).

However, this does not mean that the "best qualified" expert must testify. "[W]itnesses may be competent to testify as experts even though they may not, in the court's eyes, be the 'best' qualified." Holbrook v. Lykes Bros. S.S. Co., Inc., 80 F.3d 777, 782 (3d Cir. 1995).[7] "Rule 702 and Daubert put their faith in an adversary system designed to expose flawed expertise." U.S. v. Mitchell, 365 F.3d 215, 244-45 (3d Cir. 2004)(citations omitted). "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." Id. at 244 (citations omitted).

ii. Expert's Methods Must be Reliable

This Circuit interprets the second factor as one of "reliability," i.e., the testimony is admissible so long as the process or technique the expert used in formulating the

[7] See also Keller v. Feasterville Family Health Care, 557 F. Supp. 2d 671, 675 (E.D. Pa. 2008)(Rice, J.).

opinion is reliable. Pineda, 520 F.3d at 244. An expert's opinion need not be correct, only reliable. See In re Paoli RR Yard PCB Litigation (Paoli II), 35 F.3d 717, 744 (3d Cir. 1994)("This does not mean that plaintiffs have to prove their case twice—they do not have to demonstrate to the judge by a preponderance of the evidence that the assessments of their experts are *correct*, they only have to demonstrate by a preponderance of evidence that their opinions are reliable." (emphasis in original)). "[A]n expert is permitted wide latitude to offer opinions, including those that are not based on firsthand knowledge or observation." Daubert, 509 U.S. at 592. "[I]t is the burden of the party offering the expert scientific testimony to demonstrate reliability by a preponderance of the evidence." In re TMI Litig., 193 F.3d 613, 705 (3d Cir. 1999)(citing Paoli II, 35 F.3d at 744).[8]

"Rule 702 grants the district judge the discretionary authority, reviewable for its abuse, to determine reliability in light of the particular facts and circumstances of the particular case." Kumho Tire Co., Ltd. v. Carmichael, 526 U.S. 137, 158 (1999). Judges considering this factor should look to whether a theory, technique, or opinion can be tested or has been subject to peer review or publication. Daubert, 509 U.S. at 593. "The fact of publication (or lack thereof) in a peer reviewed journal thus will be a relevant, though not dispositive, consideration in assessing the scientific validity of a particular technique or methodology on which an opinion is premised." Id. at 594. A court should also consider the known or potential rate of error involved in a scientific method. Id.

[8] See also FED. R. EVID. 702, Advisory Committee Note (2000 Amendments)("Under that Rule, the proponent has the burden of establishing that the pertinent admissibility requirements are met by a preponderance of the evidence." (citing Bourjaily v. United States, 483 U.S. 171 (1987)).

"Reliability" does not require that a technique or methodology be generally accepted by a scientific community. Id. See also id. at 597-98. However, "[w]idespread acceptance can be an important factor in ruling particular evidence admissible" while a minimally supported technique "may properly be viewed with skepticism." Id.

iii. Expert Must be Helpful

The third factor "is typically understood in terms of whether there is a sufficient 'fit' between the expert's testimony and the facts that the jury is being asked to consider." United States v. Schiff, 602 F.3d 152, 172-73 (3d Cir. 2010)(citing Daubert, 509 U.S. at 591). See also In re: TMI Litigation, 193 F.3d 613, 670 (3d Cir. 1999). This factor is about relevance. "Expert testimony which does not relate to any issue in the case is not relevant and, ergo, non-helpful." Daubert, 509 U.S. at 591 (quoting 3 Weinstein & Berger ¶ 702[02], p. 702–18). "Rule 702's 'helpfulness' standard requires a valid scientific connection to the pertinent inquiry as a precondition to admissibility." Id. at 591-92.

b. Rule 703

Under Federal Rule of Evidence 703, the data underlying the expert's opinion is the central focus. Rule 703 states:

> An expert may base an opinion on facts or data in the case that the expert has been made aware of or personally observed. If experts in the particular field would reasonably rely on those kinds of facts or data in forming an opinion on the subject, they need not be admissible for the opinion to be admitted. But if the facts or data would otherwise be inadmissible, the proponent of the opinion may disclose them to the jury only if their probative value in helping the jury evaluate the opinion substantially outweighs their prejudicial effect.

FED. R. EVID. 703. The trial court must evaluate whether the data used by an expert is reasonably relied upon by experts in the field. See In re Paoli RR Yard PCB Litigation (Paoli II), 35 F.3d 717, 747-49 (3d Cir. 1994).

II. Dr. Laura Plunkett, Ph.D., DABT is a Qualified Expert[9]

Laura M. Plunkett, Ph.D. has advanced training as a pharmacologist and toxicologist.[10] She also has training in pharmacokinetics, the study of "the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body."[11] Dr. Plunkett has a Ph.D. in Pharmacology. She is board-certified as a Diplomate of the American Board of Toxicology (DABT). She was an Assistant Professor of Pharmacology and an Assistant Professor of Toxicology in the College of Medicine, at the University of Arkansas for Medical Sciences. She continues to give lectures on pharmacology, toxicology, and pharmacokinetics.

Between 1984 and 1986, she was a Pharmacology Research Associate Training (PRAT) fellow at the National Institute of General Medical Sciences in Bethesda, Maryland. Dr. Plunkett has written over forty (40) articles in the peer-reviewed literature

[9] The information about Dr. Plunkett's qualifications can be found in her expert report (Doc. No. 112, Ex. A, 1-3), in her Curriculum Vitae (Doc. No. 122, Ex. A, 41-78), and her deposition (Doc. No. 112, Ex. B). The defendants do not challenge Dr. Plunkett's qualifications; however, an overview of her credentials is helpful in explaining my rulings.

[10] Pharmacology is the study of how substances interact with living organisms to produce a change in function. Alfred G. Gilman, et al., eds., Goodman & Gilman's The Pharmacological Basis of Therapeutics, 6th ed. 1980. Toxicology is the study of the adverse effects of xenobiotics, or chemicals, on living organisms. It is the study of symptoms, mechanisms, treatments and detection of poisoning, especially the poisoning of people. Curtis D. Klaassen, ed., Casarett & Doull's Toxicology: The Basic Science of Poisons, 7th ed., 2008.

[11] See American Heritage Dictionary (2007). See also Mosby's Medical Dictionary, 8th ed. (2009)(defining pharmacokinetics as the "study of the actions of a drug in the body, which can, in many respects, be envisioned as the actions of the body on an administered drug, it includes the studies of mechanism of drug absorption, distribution, metabolism, and excretion; onset of action; duration of effect; biotransformation, and effects of excretion of the metabolites of the drug.").

on issues related to pharmacology, toxicology, and pharmacokinetics. Most of these articles involve animal/pre-clinical studies, human studies, and *in vitro* studies. She has served as an expert witness in over forty trials, the majority of which involve drug products liability.[12]

Dr. Plunkett has over twenty years of experience as a regulatory consultant. Between 1989 and 1997, she was employed as a manager for ENVIRON Corporation, where she served as a consultant to pharmaceutical companies in areas of pharmacology, toxicology, human health risk assessment, and regulatory strategy. Since 1997, Dr. Plunkett has been a private consultant to pharmaceutical companies, which are in the process of developing and marketing FDA-regulated pharmaceutical products. Her consultations focus on issues related to pharmacology, toxicology, pharmacokinetics, human health risk assessment, and FDA regulatory compliance.

III. An Overview of Dr. Plunkett's Opinions

In formulating her opinions, Dr. Plunkett undertook an exhaustive review of the scientific data and regulatory opinions and issues pertaining to acetaminophen, including internal documents from the defendants, scientific literature, labeling, expert depositions, and other regulatory documents.

Dr. Plunkett's opinions discuss two key questions: 1) whether the defendants' actions were in line with what a reasonable drug manufacturer would or should do, and 2) whether the defendants' actions or inactions may have led to Ms. Hayes' death. These

[12] See L. Plunkett Expert Report, May 2, 2014 at 55-58 ("List of Trial and Deposition Testimony for Laura M. Plunkett, Ph.D., DABT")(Doc. No. 112, Ex. A); L. Plunkett Dep., Apr. 24, 2015 at 684-91 (Doc. No. 112, Ex. B).

opinions can help the jury determine whether the defendants appropriately warned of the risk of the acetaminophen-induced acute liver failure and/or designed Extra Strength Tylenol in a way that meets the reasonable expectations of a consumer.[13]

IV. Defendants' Daubert Challenge to Dr. Plunkett

The defendants move to exclude the following testimony and opinions by Dr. Laura Plunkett:

1) Whether or not McNeil is a "responsible drug company" and/or had improper corporate motives, as well as her personal opinions about what McNeil knew, and/or should have known and when;

2) Opinions that "fasting," malnutrition, and alcohol intake can deplete glutathione (an antioxidant) stores in the liver and "influence" the dose of acetaminophen—the active ingredient in Tylenol—needed to reach the threshold for toxicity;

3) Opinions that acetaminophen causes acute liver failure when taken "at or near" the recommended dose;

4) Opinions that the maximum dosage of Tylenol should be lowered, additional warnings should be added to the label (including a warning that has been explicitly rejected by the FDA), and its availability as an over-the-counter product should be limited;

5) Opinions that only a very small percentage of acute liver failure are reported as adverse events; and

6) Personal criticisms of the FDA's regulatory process.

[13] See, e.g., Casrell v. Altec Indus., Inc., 335 So.2d 128, 131-34 (Ala. 1976); Atkins v. Am. Motors Corp., 335 So.2d 134, 137-43 (Ala. 1976); Gurley By and Through Gurley v. Am. Honda Motor Co., Inc., 505 So.2d 358, 361 (Ala. 1987); Beam v. Tramco, Inc., 655 So.2d 979, 981 (Ala. 1995)(citing Casrell v. Altec Industries, Inc., 335 So.2d 128, 133 (Ala. 1976); Entrekin v. Atlantic Richfield Co., 519 So.2d 447 (Ala. 1987)).

a. Dr. Plunkett's Methodology in Formulating Opinions about Industry Standards is Reliable

The defendants argue the Dr. Plunkett's opinions about what a "responsible drug company would or would not do" are based on unreliable methodology. The defendants imply that her methodology is unsound because it is not defined in a scientific manner.

Though Dr. Plunkett's background could be defined as "scientific," her opinions about industry standards are not "scientific;" they do not require the use of a scientific method like would be used in conducting an experiment.[14] When an opinion is not scientific, an expert's personal experience and expertise are often more important to the reliability analysis than a specific rubric of factors. See Betterbox Commcns. Ltd. v, BB Techs., Inc., 300 F.3d 325, 329 (3d Cir. 2002)("[I]n cases not involving scientific testimony, '[t]he factors identified in Daubert may or may not be pertinent in assessing reliability, depending on the nature of the issue, the expert's particular expertise, and the subject of his testimony.' In such cases…'the relevant reliability concerns may focus upon personal knowledge or experience.'")(quoting Kumho Tire Co. v. Carmichael, 526 U.S. 137, 150 (1999)).

As the defendants themselves admit, Dr. Plunkett considered all applicable regulations, relied on her understanding of the industry (as informed by her training and experience), reviewed internal company documents outlining the company's principles and credos, reviewed pertinent trade association documents, and read relevant peer-

[14] See Kumho Tire Co., Ltd. v. Carmichael, 526 U.S. 137, 150 (1999)("[T]here are many different kinds of experts, and many different kinds of expertise.").

reviewed literature. These methods are an acceptable way to offer an opinion about industry standards.[15]

b. Dr. Plunkett's Opinions about Corporate Motives and Knowledge are Admissible

The defendants move to exclude Dr. Plunkett's opinions about what the defendants' motives or knowledge were; they claim these opinions invade the province of the jury. I agree that it is the jury, which ultimately gets to decide what the defendants' intent was.[16] To the extent Dr. Plunkett testifies about what the defendants intended by their actions, her testimony will be excluded.

However, I do not see Dr. Plunkett's opinions as going this far. She states what the defendants knew about risks of acetaminophen-induced liver failure based on internal documents or depositions by defense witnesses she reviewed. Her opinions are not based on speculation or inference. She offers these opinions to show how the defendants' actions differed from what a reasonable drug manufacturer should or would have done. In context, her statements about what the defendants knew or did not know would be

[15] See Kannankeril, 128 F.3d at 806 ("In order for the expert testimony to be 'reliable,' we have required that the testimony be based on the 'methods and procedures of science,' rather than on 'subjective belief or unsupported speculation.'")(citing Paoli, 35 F.3d at 744); Holbrook v. Lykes Bros. S.S. Co., Inc., 80 F.3d 777, 784 (3d Cir. 1995)("The reliability requirement, however, should not be applied too strictly."); id. ("If the expert has 'good grounds' for the testimony, the scientific evidence is deemed sufficiently reliable.").

[16] See, e.g., Robinson v. Hartzell Propeller Inc., 326 F. Supp. 2d 631, 648 (E.D. Pa. 2004)("[T]he question of intent is a classic jury question and not one for experts.")(quoting In re Diet Drugs Prods Liab. Litig., 2000 WL 876900, at *9 (E.D. Pa. June 20, 2000)); Bethlehem Area School Dist. v. Zhou, 2011 WL 4471304, at *2 (E.D. Pa. Sept. 27, 2011)(same); In re Rezulin Prods. Liab. Litig., 309 F. Supp. 2d 531, 546 (S.D. N.Y. 2004)("[O]pinions of these witnesses on the intent, motives or states of mind of corporations, regulatory agencies and others have no basis in any relevant body of knowledge or expertise.").

appropriate. These opinions will help the jury understand how the defendants' actions may have fallen short of the duties required of them.

c. Dr. Plunkett's Opinions about Whether "Fasting," Malnutrition, and Alcohol Intake can Increase Risks of Acetaminophen-induced Acute Liver Failure are Admissible

The defendants take issue with Dr. Plunkett's methodology as unsound or undefined regarding her opinions on hepatotoxicity. I see nothing unreliable about Dr. Plunkett's explanations on how the liver processes toxins. She is a toxicologist who specializes in studying how the body processes drugs. She has reviewed the relevant medical literature and interpreted it based on her knowledge of toxicology, pharmacology, and pharmacokinetics.[17] In drawing this conclusion, she used the Bradford-Hill method—a set of nine guidelines to evaluate scientific data to determine causation.[18] See In re Seroquel Products Liability Litigation, No. 6:06–md–1769–Orl–22DAB, 2009 WL 3806435, at *5 (M.D. Fla. Jun. 23, 2009). This is a generally accepted

[17] The defendants point out several flaws in the articles on which Dr. Plunkett relies. The articles themselves are from peer-reviewed publications and appear to be reliable sources. Any deficiencies the literature may have are best addressed during cross-examination. They relate more to the strength of the opinion than to its admissibility.

[18] The Bradford-Hill methods, enunciated by Sir Austin Bradford Hill in a 1965 speech before the Royal Society of Medicine, includes a collection of "nine different viewpoints" from which to "study association before we cry causation." Hill, A.B., The Environment and Disease: Association or Causation?, PROC. R. SOC. MED. 58(5):295–99 (May 1965). These nine guidelines are: 1) the strength of the association; 2) consistency of the association; 3) specificity or whether there are multiple causes of a condition; 4) the temporal relationship between a condition followed the exposure to the agent; 5) biological gradient or the existence of a dose-response relationship; 6) how plausible the association is biologically; 7) whether the association is "coherent" with (i.e., does not seriously conflict with) generally known facts of the natural history and biology of the disease; 8) does experimentation--removing the causative agent—improve the condition; and 9) analogy. Id. See also In re Seroquel Products Liability Litigation, No. 6:06–md–1769–Orl–22DAB, 2009 WL 3806435, at *5, n. 5 (M.D. Fla. Jun. 23, 2009).

methodology. Id. I see nothing improper about her methodology. I see nothing unreliable about these methods.[19]

Furthermore, her explanation of how the body metabolizes acetaminophen—a dose-dependent toxin—would be helpful to the jury. Her testimony explains how fasting, malnutrition, and/or alcohol consumption may affect the processing of acetaminophen.[20] This evidence is highly probative of how likely it is that acetaminophen can cause liver damage at or just above the recommended dose. This evidence can only be provided through expert testimony. It may also help the jury understand the way in which acetaminophen and its by-products can affect the body and the liver.[21]

Dr. Plunkett's testimony about the relationship between fasting, malnutrition, and/or alcohol consumption and acetaminophen-induced ALF is admissible.[22]

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[19] See, e.g., Kumho Tire Co. v. Carmichael, 526 U.S. 137, 150 (1999); Betterbox Commcns. Ltd. v, BB Techs., Inc., 300 F.3d 325, 329 (3d Cir. 2002).

[20] In this same line of thinking, Dr. Plunkett also discusses possible effects of bariatric surgery (i.e., gastric bypass surgery) on the body's absorption of acetaminophen. She does so in the context of explaining that other causal factors may affect the way acetaminophen is absorbed into the body and processed by the liver. She cites a 2014 article about the possible increased risk patients who underwent gastric bypass surgery may have for acetaminophen-induced liver injury. See Plunkett Supp. Report, Feb. 13, 2015 at ¶ 64 (citing Holt, E. W., S. DeMartini, and T. J. Davern, Acute Liver Failure Due to Acetaminophen Poisoning in Patients With Prior Weight Loss Surgery: A Case Series, J. Clin. Gastroenterol., 2014). The decedent underwent gastric bypass surgery the year before she died, several years before this article was published. Dr. Plunkett may offer this information in the context of explaining that all risk factors about acetaminophen may not be known. However, she cannot offer this evidence for notice of bariatric surgery as a risk factor because the article in question—the only one she cites—was published after the decedent's death.

[21] The defendants argue that her opinions about alcohol consumption are not relevant to this case. While alcohol was likely not a factor contributing to the decedent's death, Dr. Plunkett's testimony about alcohol's effect on the liver may still be relevant to explaining how the body processes toxins, such as acetaminophen. Jurors are more likely familiar with the fact that alcohol and acetaminophen can cause damage to the liver. Dr. Plunkett's testimony about alcohol may help them to better understand how acetaminophen itself can damage the liver. For this reason, I will allow this testimony. The defendants, of course, may cross-examine Dr. Plunkett about this point

[22] Specifically, they take issue with her inability to definitively state what constitutes "fasting" or "malnutrition" and her perceived inability to explain how much alcohol combined with acetaminophen would cause liver failure. Dr. Plunkett explains that fasting, malnutrition, and alcohol may affect different people in different ways. Any criticisms the defendants may have of these opinions are best addressed on cross-examination. They go to the weight of the

d. Dr. Plunkett's Opinions about the Risk of Liver Injury "at or near" the Recommended Dose are Admissible

The defendants argue that Dr. Plunkett cannot offer these opinions because she is not an expert in liver diseases nor has she published anything about acetaminophen. I am not persuaded that this disqualifies her testimony. She is a pharmacologist and toxicologist. It is generally known and accepted that acetaminophen is a dose-dependent toxin. Dr. Plunkett is qualified to offer an opinion about how acetaminophen may affect the liver.[23]

The defendants claim that Dr. Plunkett is not qualified to offer opinions about the adequacy of the Tylenol label, especially because she was not retained for this reason. They claim her testimony on this issue should be excluded because she is not a medical

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opinions, not their admissibility. See, e.g., FED. R. EVID. 702 (Advisory Committee Notes); Daubert, 509 U.S. at 596 ("Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are traditional and appropriate means of attacking shaky but admissible evidence."); Keller v. Feasterville Family Health Care, 557 F. Supp. 2d 671, 674 (E.D. Pa. 2008); Taylor v. Danek Medical, Inc., No. Civ. A. 95-7232, 1999 WL 310647, at *2 (E.D. Pa. May 10, 1999).

[23] The defendants' criticisms of Dr. Plunkett's inability to cite randomized clinical trials or case control studies are more appropriate for cross-examination. Dr. Plunkett explains why such studies are unavailable—that they raise ethical concerns about fasting human subjects to establish causation to acetaminophen-induced ALF. See L. Plunkett Dep., Apr. 24, 2015 at 511, 562-69, 708-10 (Doc. No. 112, Ex. B). I am not persuaded by the defendants' argument. See In re Levaquin Products Liab. Litig., No. MDL 08-1943 JRT, 2010 WL 8400514, at *4 (D. Minn. Nov. 8, 2010)("When courts allow expert testimony premised on animal studies, it is because human studies cannot be done for ethical reasons, or there is a reasonable basis to believe that the results from the animal studies can be reliably extrapolated to humans….Though courts should be cautious in presuming that findings derived from animal studies are applicable to humans, the applicability of animal studies is often appropriately explored during cross-examination.")(citations omitted). See also J. Brent Dep., Jun. 6, 2014 at 24 (Doc. No. 151, Ex. 14)(under seal)(defendants' expert testifying: "Q. Right. To actually test the boundaries specifically to see how much acetaminophen it takes to cause acute liver failure in a human being would be unethical; true? A. As a randomized clinical trial would be unethical."); Memorandum Denying Defendants' Daubert motion for Neil Kaplowitz, M.D., Jul. 26, 2016, at *10-17 (Doc. No. 232); Memorandum Denying Defendants' Daubert motion for Timothy Davern, M.D., Jul. 26, 2016, at *10-19 (Doc. No. 234)(explaining why epidemiological or case-controlled studies may not be available for this case).

doctor and uses unreliable methodology.[24] Dr. Plunkett's testimony about the Tylenol label are made in reference to her opinions as a regulatory expert—about what actions she believes the defendants should have taken to fulfill their legal duties as a drug manufacturer. She is qualified to offer such as opinion.[25] See In re Seroquel Products Liab. Litig., No. 6:06-MD-1769-ORL-22D, 2009 WL 3806436, at *10-11 (M.D. Fla. July 20, 2009)(finding that Dr. Plunkett is qualified to offer opinions about labeling and efficacy of warnings); Newman by & through Newman v. McNeil Consumer Healthcare, No. 10 C 1541, 2013 WL 9936293, at *5 (N.D. Ill. Mar. 29, 2013)("Dr. Plunkett is qualified and has a reliable foundation for her opinions concerning the OTC status and labeling of Motrin products.").

The defendants also claim that Dr. Plunkett cannot offer general causation testimony because her methodology is unreliable and she can't offer a specific dose at which liver failure would actually occur. Dr. Plunkett opines that the maximum daily dose of four grams (the dosage on the Tylenol label at the time of the decedent's death) was too high and posed a risk of acetaminophen-induced acute liver failure to the decedent.[26] She explains that she cannot offer an exact dose which is risky because each

[24] The defendants also argue that Dr. Plunkett's opinions about the recommended dose are not helpful because Dr. Plunkett is vague about the seriousness and type of liver injury that acetaminophen may cause. They fault her for using "acute liver injury" and "hepatotoxicity" interchangeably, though they are distinct. I would hope that Dr. Plunkett is careful with the wording she uses during her testimony, but I don't see her lack of precision being enough to exclude her testimony. This argument is more relevant to weight than to admissibility.

[25] While Dr. Plunkett may offer an opinion that the defendants should have offered stronger warnings, she cannot offer an opinion that the label itself was inadequate or that the defendants "failed to warn" consumers. That is an inference or conclusion only the jury can draw.

[26] The defendants' arguments about alleged flaws in the articles Dr. Plunkett used to support this opinion go to the weight of her opinion, not its admissibility. These points are best raised on cross-examination, not in a Daubert challenge.

person's body processes acetaminophen differently. However, she explains that there was enough information to show that the maximum daily dose posed a risk to consumers, thereby triggering the defendants' duty to lower the dose or include a stronger warning.[27] She again used the Bradford-Hill method in drawing this conclusion.[28] See In re Seroquel Products Liability Litigation, No. 6:06–md–1769–Orl–22DAB, 2009 WL 3806435, at *5 (M.D. Fla. Jun. 23, 2009). I see nothing improper about her methodology. Dr. Plunkett may offer opinions related to general causation on the issue of dose.[29] See id. at *14

Among these references, Dr. Plunkett cites Larson, A.M., et al., Acetaminophen-induced acute liver failure: results of a United States multicenter, prospective study, Hepatology, 2005 Dec.: 42(6): 1364-1372. The defendants filed a separate motion to exclude the use of this article. See Motion to Exclude Opinion Testimony of Laura Plunkett based on Supplemental Data, Jan. 29, 2016 (Doc. No. 193). I denied that motion. See Memorandum and Order Denying Defendants' Motion to Exclude Plaintiff's Expert Testimony Based on Larson Article/ALFSG Data, Jul. 14, 2016 (Doc. No. 224, 225). I see nothing improper with how Dr. Plunkett has used the Larson article—along with other evidence—in rendering her opinion.

[27] For this reason, I see nothing improper about Dr. Plunkett's reliance on the FDA Acetaminophen Hepatotoxicity Working Group's 2008 recommendations in forming her opinions. Nor do I see anything improper about her reliance on the August 25, 2004 FDA Letter to McNeil about the risk of liver injury in doubling the maximum dose for several days. The defendants' argument to this effect confuses what is required of the defendants. They are not required to warn of possible risks when causation has 100% definitely been proven. They are instead required to prevent a known risk. Dr. Plunkett's simply recognizes that a risk of liver injury at recommended doses was shown to be possible. She opines that the amount of information available about this risk triggered the defendants' duty to act to prevent consumer injury. The FDA Letter is also relevant because it offers evidence that the defendants were on notice of possible safety risks; this information is used by Dr. Plunkett in forming her opinion about whether the defendants' actions were reasonable under the circumstances.

[28] The Bradford-Hill methods, enunciated by Sir Austin Bradford Hill in a 1965 speech before the Royal Society of Medicine, includes a collection of "nine different viewpoints" from which to "study association before we cry causation." Hill, A.B., The Environment and Disease: Association or Causation?, PROC. R. SOC. MED., 58(5):295–99 (May, 1965). These nine guidelines are: 1) the strength of the association; 2) consistency of the association; 3) specificity or whether there are multiple causes of a condition; 4) the temporal relationship between a condition followed the exposure to the agent; 5) biological gradient or the existence of a dose-response relationship; 6) how plausible the association is biologically; 7) whether the association is "coherent" with (i.e., does not seriously conflict with) generally known facts of the natural history and biology of the disease; 8) does experimentation--removing the causative agent—improve the condition; and 9) analogy. Id. See also In re Seroquel Products Liability Litigation, No. 6:06–md–1769–Orl–22DAB, 2009 WL 3806435, at *5, n. 5 (M.D. Fla. Jun. 23, 2009).

[29] The defendants take issue with the fact that Dr. Plunkett cannot offer a specific dose at which acetaminophen actually caused liver failure or damage. This concern relates to the strength of her opinion, not its admissibility. It is best raised on cross-examination. See In re Seroquel Products Liability Litigation, No. 6:06–md–1769–Orl–22DAB, 2009 WL 3806435, at *3, *6 (M.D. Fla. Jun. 23, 2009)(admitting Dr. Plunkett's general causation testimony though she cannot offer the exact mechanism by which adverse effects occur).

(admitting Dr. Plunkett's testimony about general causation in drug products liability action); In re: Gadolinium-Based Contrast Agents Prod. Liab. Litig., 2010 WL 1796334, at *14 (N.D. Ohio May 4, 2010)(same).

e. Dr. Plunkett's Opinions about Adverse Event Reporting Are Admissible

The defendants argue that Dr. Plunkett's opinions about adverse event reporting should be excluded as unreliable. They again claim Dr. Plunkett should have used a "scientific method" in reaching her conclusions. The defendants are splitting hairs. In her explanation about why adverse event reports (AERs) should raise concerns for drug manufacturers, Dr. Plunkett explains that AERs are often underreported. She references peer-reviewed studies and FDA materials that support this opinion. This opinion comes from her experience and other sources discussing this issue. Any flaws in her reasoning should be addressed on cross-examination.[30]

f. Dr. Plunkett's Criticisms of the FDA's regulation of Monograph and/or NDA Drugs and Opinions About Whether Acetaminophen is GRASE Will Be Excluded

In my decision on the defendants' Motion in Limine #11, I found that criticisms of the FDA's regulatory process of monograph drugs should be excluded as irrelevant to the parties' case-in-chief.[31] In another Daubert motion, I determined that expert opinions

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[30] See, e.g., FED. R. EVID. 702 (Advisory Committee Notes); Daubert, 509 U.S. at 596 ("Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are traditional and appropriate means of attacking shaky but admissible evidence."); Keller v. Feasterville Family Health Care, 557 F. Supp. 2d 671, 674 (E.D. Pa. 2008); Taylor v. Danek Medical, Inc., No. Civ. A. 95-7232, 1999 WL 310647, at *2 (E.D. Pa. May 10, 1999).

[31] See Memorandum on Defendants' Motions in Limine (MIL 11), Apr. 19, 2016 at 36-37 (Doc. No. 336)(denying defendants' motion but explaining that information was most likely relevant on rebuttal only).

about whether Tylenol was considered Generally Recognized as Safe and Effective (GRASE) by the FDA will be excluded because they involve a legal determination.[32] Dr. Plunkett's opinions about the adequacy of the monograph system would only become relevant if the defendants raised the defense that compliance with FDA regulations absolved them of liability. For this reason, Dr. Plunkett's opinions about the efficacy of the current monograph system will be excluded. They would not be helpful to the jury and could lead to confusion about the legal duties of the defendants in this case. If evidence is presented which would make this information probative, I am willing to revisit this ruling.

V. CONCLUSION

For the foregoing reasons, I will **GRANT** the defendants' motion as it pertains to Dr. Plunkett's opinions about whether acetaminophen is considered GRASE or whether the current monograph system is effective. I will **DENY** the defendants' motion as to all other arguments. Dr. Plunkett's testimony on all other topics is admissible, as explained above.[33]

An appropriate Order follows.

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[32] See Memorandum Granting in Part and Denying in Part Defendants' Daubert motion to exclude Testimony of Gerald Rachanow, Jul. 27, 2016 (Doc. No. 241).

[33] Dr. Plunkett's testimony should also be in line with my rulings on the parties' motions in limine. See Memorandum on Defendants' Motions in Limine, Apr. 19, 2016 (Doc. No. 210, 211); Memorandum on Plaintiff's Motions in Limine, Jun. 3, 2016 (Doc. No. 222, 223).