UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: PROTON-PUMP INHIBITOR PRODUCTS LIABILITY LITIGATION	**2:17-MD-2789 (CCC) (LDW) (MDL 2789) and all member and related cases**
This Document Relates to: All Actions	**Judge Claire C. Cecchi**

REPORT & RECOMMENDATION OF SPECIAL MASTER ELLEN K. REISMAN REGARDING *DAUBERT* MOTIONS

TABLE OF CONTENTS

I. INTRODUCTION

The Judicial Panel on Multidistrict Litigation ("JPML") established this MDL 2789 proceeding in August 2017 to consolidate claims alleging personal injury and wrongful death resulting from the use of proton pump inhibitor drugs ("PPIs"). In Case Management Order ("CMO") No. 33, the Court created a process for bellwether selection, and in accordance with CMO No. 36, twenty plaintiffs were identified as those whose cases would be worked up as potential bellwethers.[1] In CMO No. 48, the Court selected six cases that were designated as the Bellwether Trial Cases and the parties have been preparing these cases for trial.[2] Trial in the first bellwether case, *Rieder*, is scheduled to begin on November 14, 2022, with trial in *Foster* scheduled on March 1, 2023, and trial in *Bales* scheduled on April 10, 2023.[3]

In CMO No. 50, amended by subsequent CMOs, including CMOs No. 75 and No. 76, the Court directed me to prepare Reports & Recommendations ("R&Rs") as to the parties' summary judgment motions, motions to exclude expert testimony under *Daubert v. Merrell Dow Pharmaceuticals, Inc.*,[4] and certain other motions in

[1] CMO No. 33, ECF No. 513; CMO No. 36, ECF No. 548.
[2] CMO No. 48, ECF No. 665. The six cases selected as the Bellwether Trial Cases are *Freddy Bales*, No. 2:17-cv-06124; *David Foster*, No. 2:17-cv-02475; *Steve Kersch*, No. 2:18-cv-03159; *Kimberly Lee*, No. 2:17-cv-00212; *Diane Nelson*, No. 2:17-cv-13727; and *James Rieder*, No. 2:19-cv-00850.
[3] CMO No. 76, ECF No. 801.
[4] 509 U.S. 579 (1993).

the six Bellwether Trial Cases.[5] To facilitate the preparation of my R&Rs, I requested oral argument from the parties as to certain motions. On April 4 and 5, 2022, I held those oral arguments; the transcript of the April 4 oral arguments on the *Daubert* motions is attached hereto as Exhibit No. 1.[6]

The Plaintiffs' Steering Committee ("PSC") filed briefs and presented arguments on behalf of the individual plaintiffs. AstraZeneca Pharmaceuticals LP and AstraZeneca LP (collectively "AstraZeneca") are defendants in all six of the Bellwether Trial Cases, and Merck Sharp & Dohme Corporation is named as a defendant in the *Rieder* and *Kersch* cases.[7] Takeda Pharmaceuticals Company Limited, Takeda Pharmaceuticals America, Inc., Takeda Development Center Americas, Inc. f/k/a Takeda Global Research & Development Center, Inc., and Takeda Pharmaceuticals U.S.A., Inc. (collectively "Takeda") are defendants in *Bales* only.

The PSC moved to exclude testimony by certain AstraZeneca and Takeda experts:[8]

1. Dr. Robert Gibbons on behalf of AstraZeneca in all six Bellwether Trial Cases;

[5] *See* CMO No. 50, ECF No. 685; CMO No. 75, ECF No. 784; CMO No. 76.
[6] Oral Args., Apr. 4, 2022, attached as Ex. 1.
[7] For purposes of this R&R, "AstraZeneca" also includes Merck Sharp & Dohme Corporation for those two cases.
[8] Pls.' Omnibus *Daubert* Mot. to Exclude Defense Experts, ECF No. 702.

2. Dr. Jennifer A. Pinto-Martin on behalf of AstraZeneca in all six Bellwether Trial Cases;

3. Dr. Janice Lansita on behalf of AstraZeneca in all six Bellwether Trial Cases;

4. Dr. Marianne Mann on behalf of AstraZeneca in all six Bellwether Trial Cases;

5. Dr. Rajat Deo on behalf of AstraZeneca in the *Rieder* and *Bales* cases;

6. Dr. Jonathan Opraseuth on behalf of AstraZeneca in the *Lee* case;

7. Dr. Caren S. Palese on behalf of AstraZeneca in the *Rieder* case;

8. Dr. Leonard-Segal on behalf of Takeda in the *Bales* case;

9. Dr. Jerry Hardisty on behalf of Takeda in the *Bales* case; and

10. Dr. Richard Hansen on behalf of Takeda in the *Bales* case.

AstraZeneca moved to exclude testimony by certain plaintiffs' experts:

1. Dr. David Ross on behalf of the plaintiffs in all six Bellwether Trial Cases;[9]

2. Dr. Gilbert Moeckel on behalf of the plaintiffs in all six Bellwether Trial Cases;[10]

[9] AstraZeneca's Mot. to Exclude Op. Test. from Dr. David Ross Under Federal Rule of Evid. 702, *as filed in Bales*, *Foster*, *Kersch*, *Lee*, *Nelson*, *& Rieder*, No. 2:19-cv-00850, ECF No. 33 [hereinafter AstraZeneca's Mot. to Exclude Ross]. For ease of reference, this R&R will only cite to one of the parallel motions filed on the individual dockets of multiple Bellwether Trial Cases.

[10] AstraZeneca's Mot. to Exclude Op. Test. from Dr. Gilbert Moeckel Under Federal Rule of Evid. 702, *as filed in Bales*, *Foster*, *Kersch*, *Lee*, *Nelson*, *& Rieder*, No. 2:19-cv-00850, ECF No. 38 [hereinafter AstraZeneca's Mot. to Exclude Moeckel].

3. Dr. Burt Gerstman on behalf of the plaintiffs in all six Bellwether Trial Cases;[11]

4. Dr. Wajahat Mehal on behalf of the plaintiffs in the *Bales*, *Foster*, *Lee*, *Nelson*, and *Rieder* cases;[12]

5. Dr. Martin Wells on behalf of the plaintiffs in all six Bellwether Trial Cases;[13]

6. Dr. David Charytan on behalf of the plaintiff in the *Rieder* case;[14]

7. Dr. Derek Fine's case specific causation testimony on behalf of the plaintiff in the *Rieder* case;[15]

8. Dr. Jeffrey Silberzweig on behalf of the plaintiffs in the *Foster* and *Kersch* cases;[16]

9. Dr. David Powers on behalf of the plaintiffs in the *Bales* and *Lee* cases;[17] and

---

[11] AstraZeneca's Mot. to Exclude Op. Test. from Pls.' General Causation Experts Under Federal Rule of Evid. 702, *as filed in Bales*, *Foster*, *Kersch*, *Lee*, *Nelson*, *& Rieder*, No. 2:19-cv-00850, ECF No. 37 [hereinafter AstraZeneca's Mot. to Exclude Pls.' General Causation Experts].

[12] AstraZeneca's Mot. to Exclude General Causation Experts.

[13] AstraZeneca's Mot. to Exclude Op. Test. from Dr. Martin Wells Under Federal Rule of Evid. 702, *as filed in Foster*, *Kersch*, *Lee*, *Nelson*, *& Rieder*, No. 2:19-cv-00850, ECF No. 34 [hereinafter AstraZeneca's Mot. to Exclude Wells].

[14] AstraZeneca's Mot. to Exclude Pls.' General Causation Experts.

[15] AstraZeneca's Mot. to Exclude Op. Test. From Pls.' Specific Causation Experts Under Federal Rule of Evid. 702, *as filed in Bales*, *Foster*, *Kersch*, *Lee*, *Nelson*, *& Rieder*, No. 2:19-cv-00850, ECF No. 35 [hereinafter AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts].

[16] AstraZeneca's Mot. to Exclude Pls.' General Causation Experts; AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts.

[17] AstraZeneca's Mot. to Exclude Pls.' General Causation Experts; AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts.

10. Dr. Richard Lafayette on behalf of the plaintiff in the *Nelson* case.[18]

AstraZeneca also moved to disqualify Dr. Gilbert Moeckel from testifying in the six Bellwether Trial Cases.[19]

Takeda moved to exclude the testimony by Dr. David Ross[20] and Dr. Gilbert Moeckel[21] in the *Bales* case. AstraZeneca and Takeda jointly moved to exclude the testimony of Dr. Martin Wells in the *Bales* case.[22]

On March 25, 2022, counsel for AstraZeneca, Takeda, and the PSC submitted a joint report withdrawing certain motions and narrowing the issues or waiving oral argument as to certain motions.[23] The PSC withdrew its motion to exclude the testimony of Dr. Pinto-Martin, and AstraZeneca withdrew its motion to exclude the testimony of Dr. Gerstman.[24] This R&R addresses certain of the parties' *Daubert* motions, where applicable as amended by the March 25, 2022 report. This R&R does not address experts Dr. Opraseuth, Dr. Hansen, Dr.

[18] AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts.
[19] AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, *as filed in Bales, Foster, Kersch, Lee, Nelson, & Rieder*, No. 2:19-cv-00850, ECF No. 36.
[20] Takeda's Mot. to Exclude Test. of Dr. David Ross, No. 2:17-cv-06124, ECF No. 77.
[21] Takeda's Mot. to Exclude Expert Test. of Dr. Gilbert Moeckel, No. 2:17-cv-06124, ECF No. 80.
[22] Defs' Mot. to Exclude Op. Test. from Dr. Martin Wells Under Federal Rule of Evid. 702, No. 2:17-cv-06124, ECF No. 76.
[23] Joint Report to the Special Master Re *Daubert* Mot. Oral Args., attached as Ex. 2.
[24] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 1.

Hardisty, Dr. Powers, Dr. Silberzweig, Dr. Lafayette, and Dr. Leonard-Segal, all of whom are designated in cases other than *Rieder*.[25]

This R&R first reviews the legal standard set forth in Federal Rule of Evidence 702 and *Daubert* and the Third Circuit's application thereof. It then contains recommendations regarding *Daubert* motions made by the PSC, followed by recommendations regarding *Daubert* motions made by AstraZeneca and Takeda, as well as a recommendation regarding AstraZeneca's motion to disqualify Dr. Moeckel.

II. OVERVIEW OF RELEVANT LEGAL STANDARD

Federal Rule of Evidence 702 provides that:

> 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.

[25] I will address the *Daubert* motions to exclude the testimony of Dr. Opraseuth, Dr. Dr. Hansen, Dr. Hardisty, Dr. Powers, Dr. Silberzweig, and Dr. Lafayette in separate Report & Recommendations. With respect to Dr. Leonard-Segal, I submitted a Report & Recommendation on June 17, 2022, recommending that the PSC's *Daubert* motion be held in abeyance pending resolution of the PSC's motion to disqualify her. No. 2:17-cv-06124, ECF No. 114.

A district court serves a "gatekeeping" function under Rule 702 concerning expert testimony and must ensure that any expert testimony is both relevant and reliable before allowing its admission.[26] The ultimate goal of this analysis is to ensure that the trier of fact is presented only with reliable testimony that will help it understand the evidence or determine the relevant facts.[27] The burden of proof that the expert's testimony will be both reliable and relevant rests on the party offering the expert testimony.[28]

The Third Circuit applies Rule 702 and *Daubert* through a "trilogy of restrictions" on admission of expert testimony, examining the qualifications of the expert, the reliability of the expert's opinion, and the fit of the expert's opinion to the issues presented in the particular case.[29] First, the expert may be qualified through "a broad range of knowledge, skills, and training[.]"[30] Second, the expert's testimony must be reliable and based on the "methods and procedures of science" rather than on "subjective belief or unsupported speculation."[31] Third, the testimony must fit the particular case "as a precondition to admissibility,"

[26] *Daubert*, 509 U.S. at 589.
[27] *In re: Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 858 F.3d 787, 800 (3d Cir. 2017).
[28] *In re Johnson & Johnson Talcum Powder Prods. Mktg., Sales Practices & Prods Litig.*, 509 F. Supp. 3d 116, 147-48 (D.N.J. 2020) (citing *Crowley v. Chait*, 322 F. Supp. 2d 530, 537 (D.N.J. 2004)).
[29] *Schneider ex rel. Estate of Schneider v. Fried*, 320 F.3d 396, 404 (3d Cir. 2003).
[30] *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 741 (3d Cir. 1994).
[31] *Daubert*, 509 U.S. at 590.

demonstrated by a "valid scientific connection" between the testimony and the issues presented in a particular case.[32]

The Third Circuit has recognized that, in performing its critical gatekeeping function under *Daubert* with respect to expert testimony, a trial court must bear in mind "the preference for admissibility of the Federal Rules of Evidence" and avoid excluding expert evidence solely because the court does not think it is ultimately the most persuasive evidence.[33] This preference for admissibility offsets the risk that a trial judge may interpret the "amorphous" reliability standard too strictly.[34]

A. Qualifications

The Third Circuit reads the qualification requirement broadly and interprets it liberally.[35] To satisfy the qualification requirement, an expert must possess specialized knowledge in the area of testimony.[36] An expert may be qualified by a "broad range of knowledge, skills, and training[,]" including both academic credentials and practical experience.[37] This policy does not require that an expert possess the best formal or substantive qualifications, and more generalized qualifications are satisfactory.[38]

---

[32] *See id.* at 591-92; *Paoli*, 35 F.3d at 742-43.
[33] *See Paoli*, 35 F.3d at 750.
[34] *Id.*
[35] *Pineda v. Ford Motor Co.*, 520 F.3d 237, 244 (3d Cir. 2008).
[36] *Waldorf v. Shuta*, 142 F.3d 601, 625 (3d Cir. 1998).
[37] *Pineda*, 520 F.3d at 244 (quoting *Paoli*, 35 F.3d at 741).
[38] *See Pineda* at 244; *Paoli*, 35 F.3d at 741.

Courts have applied these standards to specific disciplines. Physicians, for example, do not need to be highly specialized in the area on which they are to testify or treat patients with the medical condition or symptom in question for their expert testimony to be admissible; the quality and depth of their qualifications goes to the credibility and weight to be accorded their testimony.[39] Physicians who are serving as experts, however, must demonstrate some minimal relevant knowledge and experience.[40] Similarly, biostatisticians are not required to be specialists in the subject matter to which they apply their statistical methodologies.[41] With respect to Food and Drug Administration ("FDA") experts, courts have ruled that their regulatory training and experience while at the agency, coupled with their other professional credentials, are sufficient to qualify them to testify on regulatory topics.[42]

---

[39] *See Paoli*, 35 F.3d at 753 ("We hold that Dr. Sherman, while arguably a relatively poor clinician and less than fully credible witness, qualifies as an expert.").

[40] *See Diaz v. Johnson Matthey, Inc.*, 893 F. Supp. 358, 372-73 (D.N.J. 1995) (excluding testimony of a pulmonologist who had never treated a patient with the particular respiratory condition at issue, was unfamiliar with the literature on the condition, and lacked any additional qualifications that would render the pulmonologist's testimony helpful in other ways).

[41] *See Hospira, Inc. v. Amneal Pharms., LLC*, 285 F. Supp. 3d 776, 811 (D. Del. 2018) (allowing a biostatistician to offer a statistical analysis of drug formulation because it fell "squarely within his realm of expertise[,]" even though he was not an expert on drug development).

[42] *Wolfe v. McNeil-PPC, Inc. (Wolfe I)*, 881 F. Supp. 2d 650, 658 (E.D. Pa. 2012); *Terry v. McNeil-PPC, Inc. (In re Tylenol (Acetaminophen) Mktg., Sales Practices, & Prods. Liab. Litig.) (Terry I)*, No. 2:12-cv-07263, 2016 U.S. Dist. LEXIS 99177, at *17 (E.D. Pa. July 28, 2016).

B. Reliability

The reliability inquiry looks at the scientific validity of the methodology underlying the expert's opinion.[43] An expert's opinion is reliable if it is "based on the 'methods and procedures of science' rather than on 'subjective belief or unsupported speculation'; the expert must have 'good grounds' for his or her belief."[44] The expert's testimony "must be derived by the scientific method" and "supported by appropriate validation -- *i.e.*, 'good grounds,' based on what is known."[45]

Both the methodology and its application must be reliable for the testimony to be admissible.[46] To determine the reliability of expert testimony, the court must make a "preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid and of whether that reasoning or methodology properly can be applied to the facts in issue."[47] Pursuant to *Daubert* and its Third Circuit progeny, the trial court should consider eight key factors when making this determination:

> "(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

[43] *See Paoli*, 35 F.3d at 742; *Schneider*, 320 F.3d at 404.
[44] *Paoli*, 35 F.3d at 742.
[45] *Daubert*, 509 U.S. at 590.
[46] *In re: Zoloft*, 858 F.3d at 792.
[47] *Daubert*, 509 U.S. at 592.

> testifying based on the methodology; and (8) the non-judicial uses to which the method has been put."[48]

This list of factors is non-exhaustive and may not be applicable in every case.[49]

An expert must, at a minimum, identify the methodology or procedures used or explain how the conclusions were reached by that expert.[50] The reliability standard requires some showing of methodological soundness and consistency. Additionally, the data and materials considered by the expert must be available.[51] Both the methodology and its application must be reliable for the testimony to be admissible.[52] If any step in the expert's methodology or analysis is unreliable, the whole testimony based on that analysis is inadmissible.[53] Further, if the expert chooses to employ a non-standard methodology or applies the chosen methodology unevenly, the expert must thoroughly explain the decision to do so.[54]

---

[48] *Elcock v. Kmart Corp.*, 233 F.3d 734, 745-46 (3d Cir. 2000) (citing *Paoli*, 35 F.3d at 742 n.8).

[49] *See Kannankeril v. Terminix Int'l*, 128 F.3d 802, 806-07 (3d Cir. 1997); *see also Paoli*, 35 F.3d at 742 ("*Daubert* . . . indicates that the inquiry as to whether a particular scientific technique or method is reliable is a flexible one.").

[50] *See Sikkelee v. Precision Airmotive Corp.*, 522 F. Supp. 3d 120, 158 (M.D. Pa. 2021) ("[R]elying on an expert's *ipse dixit* alone does not ensure that reliable principles and methods were used. Because [the expert] provides nothing else, the Court cannot allow the jury to hear this testimony."); *Buzzerd v. Flagship Carwash of Port St. Lucie Inc.*, 669 F. Supp. 2d 514 (M.D. Pa. 2009) (a mechanic's failure to articulate any methodology by which to assess carbon monoxide accumulation rendered the method untestable).

[51] *In re Johnson & Johnson Talcum Powder*, 509 F. Supp. 3d at 155.

[52] *In re: Zoloft*, 858 F.3d at 795-96.

[53] *Id.* at 800.

[54] *In re: Zoloft*, 858 F.3d at 797-99.

The reliability prong is satisfied so long as the expert's opinion "reliably flow[s] from th[e] methodology and the facts at issue[.]"[55] The party seeking to admit expert testimony must prove only that the testimony is reliable, not prove to the court by a preponderance of the evidence that the expert's conclusion is correct.[56] The opinion does not need to have the strongest evidentiary foundation or be "supported by the best methodology or unassailable research" to survive a *Daubert* motion.[57] Nor must it rely on published, peer-reviewed studies, although such reliance is one indicium of reliability.[58] Surface-level flaws relating to methodology may be reserved for cross-examination, though "'there will be occasions when the proffered [expert evidence] is so flawed' that it is 'completely unhelpful to the trier of fact' and 'its probative value is substantially outweighed by its prejudicial effect.'"[59] In short, "the reliability requirement must not be used as a tool by which the court excludes all questionably reliable evidence."[60]

---

[55] *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 152 (3d Cir. 1999).
[56] *In re TMI Litig.*, 193 F.3d 613, 665 (3d Cir. 1999).
[57] *Id.*
[58] *See Heller*, 167 F.3d at 154; *In re TMI Litig.*, 193 F.3d at 663-64.
[59] *Bruno v. Buzzuto's, Inc.*, No. 3:09-cv-874, 2015 U.S. Dist. LEXIS 156339, at *140 (M.D. Pa. Nov. 19, 2015) (quoting *Malletier v. Dooney & Bourke, Inc.*, 525 F. Supp. 2d 558, 563 (S.D.N.Y. 2007)).
[60] *Paoli*, 35 F.3d at 744 (quoting *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829 (3d Cir. 1990).

Exclusion is appropriate only if the flaw in the methodology is "large enough that the expert lacks 'good grounds' for his or her conclusions."[61] Even if the judge believes "there are better grounds for some alternative conclusion," and there are some flaws in the scientist's methods, if there are "good grounds" for the expert's conclusion, it should be admitted.[62] The testimony may 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."[63]

With respect to medical experts, a physician's highly specialized academic and professional qualifications in the area on which that expert is to testify favor a finding of reliability.[64] Where a medical expert opines with respect to causation of a plaintiff's illness, the "medical expert's causation conclusion should not be

---

[61] *See Paoli*, 35 F.3d at 746; *Hoffeditz v. AM General*, No. 09-0257, 2017 U.S. Dist. LEXIS 123493, at *13-14 (D.N.J. Aug. 4, 2017) (noting that studies relied upon by challenged expert were subject to legitimate criticism from opposing party's experts but finding that such contradictions were appropriately addressed through cross-examination, not exclusion).

[62] *See Paoli*, 35 F.3d at 746; *Heller*, 167 F.3d at 153.

[63] *United States v. Mitchell*, 365 F.3d 215, 244 (3d Cir. 2004) (citing *Ruiz-Troche v. Pepsi Cola Bottling Co.*, 161 F.3d 77, 85 (1st Cir. 1998)); *Daubert*, 509 U.S. at 596 ("Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence."); *see also Heller*, 167 F.3d at 152.

[64] *See Schneider*, 320 F.3d at 407; *see also Keller v. Feasterville Fam. Health Care Ctr.*, 557 F. Supp. 2d 671, 677 (E.D. Pa. 2008) (admitting expert testimony about Alzheimer's Disease when the testifying physician was a well-respected expert in the field of neurodegenerative diseases).

excluded because he or she has failed to rule out every possible alternative cause of a plaintiff's illness."[65]

Courts have similarly found FDA regulatory expert testimony reliable when FDA experts rely on and apply the same methods used in their work at FDA with regard to regulation of drug approval and labeling.[66] Indeed, with regard to FDA experts testifying on regulatory issues, courts have found their experience at the agency to be particularly valuable, especially when coupled with additional industry or academic experience.[67] Questions regarding an FDA regulatory expert's methodology as to opinions on regulatory issues go to weight, not admissibility.[68]

---

[65] *See Heller*, 167 F.3d at 156; *see also Paoli*, 35 F.3d at 758-60 (applying flexible reliability standard and reversing district court's exclusion of physician testimony on differential diagnosis based solely on review of patient's medical records).

[66] In *Terry v. McNeil-PPC, Inc. (In re Tylenol (Acetaminophen) Mktg., Sales Practices, & Prods. Liab. Litig.) (Terry II)*, No. 2:12-cv-07263, 2016 U.S. Dist. LEXIS 117594, at *20 (E.D. Pa. Aug. 31, 2016), for example, the court found that any questions regarding the FDA expert's methodology went to weight, not admissibility. ("By all accounts, Dr. Jones' actual methods—reviewing and deciphering the information contained in documents provided her based on her professional experience—are reliable ways of reaching opinions about industry standards and the use of AERs."); *see also Johns v. CR Bard (In re Davol, Inc./C.R. Bard, Inc., Polypropylene Hernia Mesh Prods. Liab. Litig.)*, No. 2:18-cv-01509, 2021 U.S. Dist. LEXIS 143187, at *436 (S.D. Ohio Aug. 1, 2021) (stating that an expert's opinions were sufficiently reliable where her methodology was the one she was trained to use at the FDA); *Lemmon v. Wyeth. LLC*, No. 4:04-cv-01302, 2012 U.S. Dist. LEXIS 95924, at *27 (E.D. Mo. July 11, 2012) (admitting expert testimony regarding the drug approval process and analysis of the adequacy of the labeling because it was based upon specialized knowledge of the regulatory procedures, pharmaceutical labeling, and FDA standards and practice).

[67] *See Wolfe I*, 881 F. Supp. 2d at 650; *Terry I*, 2016 U.S. Dist. LEXIS 99177, at *4.

[68] *See, e.g., Terry II*, 2016 U.S. Dist. LEXIS 117594, at *20.

C. Fit

Expert testimony must fit the particular case and help the trier of fact understand the evidence or determine a fact in issue. This fit requirement speaks to the relevance of the expert opinion. "[A] valid scientific connection to the pertinent inquiry [is] a precondition to admissibility."[69] The standard is "not that high" but is "higher than bare relevance."[70] Even if the opinion is reliable, "scientific validity for one purpose is not necessarily scientific validity for other, unrelated purposes."[71] Expert testimony may fit even though it does not directly relate to the main legal issue. Scientific or medical expert testimony is not inherently unhelpful or confusing for the trier of fact simply because it is complex.[72]

III. PLAINTIFFS' MOTIONS

A. Dr. Marianne Mann[73]

AstraZeneca seeks to offer expert testimony by Dr. Marianne Mann on the adequacy of the warnings provided by AstraZeneca for Nexium with regard to renal

---

[69] *Daubert*, 509 U.S. at 592.
[70] *Paoli*, 35 F.3d at 745.
[71] *Daubert*, 509 U.S. at 591.
[72] *Keller*, 557 F. Supp. 2d at 679.
[73] As I disclosed during oral arguments, I worked with Dr. Mann years ago when I was a partner at Arnold & Porter and was representing American Home Products Inc. and Wyeth Pharmaceuticals in connection with the Diet Drug Litigation. Oral Args. 8:11-17, Apr. 4, 2022 ("One thing . . . I wanted to raise just in the way of full disclosures upfront . . . I don't know any of these experts personally except one who I did meet years ago, somewhere between 15 and 20 years ago, and that's [Marianne] Mann, and I think I had one meeting with her in connection with a case I was working on at the time.").

impairment and the appropriateness of FDA's decisions regarding the Nexium labeling. The PSC's motion to exclude Dr. Mann's opinion testimony rests upon two of the three criteria applied in the Third Circuit: qualifications and reliability. Specifically, the PSC argues that Dr. Mann is "unqualified to render an opinion on the causal association between PPIs and kidney injury" and that her testimony is unreliable because she lacks basic knowledge of FDA regulations and has not independently reviewed source data, instead relying on summaries prepared by FDA and the New Drug Application ("NDA") sponsor.[74] For the reasons discussed below, I recommend that this motion be denied.

1. Qualifications

Dr. Mann received an M.D. from the Medical College of Pennsylvania, completed her residency in internal medicine at Albert Einstein Medical Center and the University of Connecticut Health Center, and completed a fellowship in pulmonary and critical care medicine at the University of Connecticut Health Center.[75] She is currently board-certified in internal medicine and was previously board-certified in pulmonary care medicine and critical care medicine.[76]

[74] PSC's Mem. in Supp. of Pls.' Omnibus *Daubert* Mot. to Exclude Defense Experts 10-13, ECF No. 703 [hereinafter PSC's Omnibus Mem.].
[75] PSC's Omnibus Mem., Ex. 1 [hereinafter Mann Expert Report] at 1, ECF No. 703-1.
[76] Mann Expert Report, App. A.

Prior to joining FDA in 1994, Dr. Mann was a practicing physician with a specialty in pulmonary care from 1992-1994 and was a volunteer staff pulmonologist at National Naval Medical Center from 1994-2004. From 1994-2003, she held three positions at FDA: Medical Officer in the Division of Antiviral Drug Products/Division of Special Pathogens and Immunologic Drug Products, Deputy Director of the Division of Reproductive and Urologic Drug Products, and Deputy Director of the Division of Pulmonary and Allergy Drug Products.[77]

Dr. Mann's work at FDA included: reviewing clinical data and making approval recommendations for Investigational New Drug Applications ("INDs") and NDAs; participating in decisions on whether to put a study on hold; leading labeling discussions both with NDA sponsors and within the agency and addressing labeling changes; and managing safety issues that arose with products in both the pre-approval phase and during post-marketing experience. Dr. Mann summarizes her experience as follows: "[i]n total, I have had nine years of FDA experience in three different review divisions, including experience making final regulatory decisions, many of which concerned safety, about a wide variety of medications."[78] Dr. Mann received awards in recognition of her work at FDA, including: DHHS Secretary's Award for Distinguished Service, FDA Award of Merit, two FDA

[77] Mann Expert Report, App. A.
[78] Mann Expert Report 2.

Commendable Service Awards, and the Center for Drug Evaluation and Research's ("CDER") Excellence in Communication Award.[79]

From 2003-2004, Dr. Mann served as Branch Chief in the Respiratory Disease Branch Division of Microbiology and Infectious Disease at the National Institute of Health ("NIH") and since then has been a private consultant working on clinical and regulatory drug development.[80]

The PSC does not challenge Dr. Mann's qualifications generally. Instead, the PSC argues that Dr. Mann is not qualified to offer opinions on medical causation – whether and to what extent PPIs cause renal impairment. This argument is contrary to both the facts and the law.

First, AstraZeneca has made clear that it is not offering Dr. Mann as a medical causation expert. This appears consistent with her report, which focuses on regulatory history, regulatory decision-making, and the use of clinical and post-marketing surveillance data to inform labeling decisions. To support her opinions on these topics, Dr. Mann necessarily needed to review, analyze, and interpret data pertinent to whether and to what extent there is an association between PPI use and renal impairments. For example, she considers whether there were data sufficient, in her opinion as a former FDA officer, to constitute a signal of an association and/or to warrant a labeling change.

[79] Mann Expert Report, App. A.
[80] Mann Expert Report 2.

Dr. Mann is trained in internal medicine and, while at FDA, reviewed and analyzed pre-clinical and clinical trial data, adverse event data, and product labeling.[81] The fact that she is not holding herself out as an expert in nephrology does not mean that she is incapable of providing expert opinions about the data related to the association, if any, between PPI use and renal impairment and what, if anything, those data mean for labeling decisions. Review of data to assess risk and potential association is what senior FDA pharmaceutical regulators such as Dr. Mann do. Even if Dr. Mann had been offered to give testimony as to general medical causation in this case, she would be sufficiently qualified to do so under the liberal Third Circuit standard.

The PSC takes a few statements made at Dr. Mann's deposition out of context to attack her qualifications. First, she testified that she did not know specifically how long chronic kidney disease ("CKD") takes to develop, but knew it was a long process.[82] The PSC argues that this statement alone renders her "unqualified to give an expert medical opinion on whether a drug is associated with chronic kidney disease."[83] Perhaps if she were being offered to testify as to specific causation, her lack of specific knowledge would be a cause for concern, although even that is doubtful under the liberal Third Circuit standard.[84] It is certainly not an obstacle to her testimony here,

[81] Mann Expert Report 1.
[82] PSC's Omnibus Mem., Ex. 2 at 123:3-14 [hereinafter Mann Dep.], ECF No. 703-2.
[83] PSC's Omnibus Mem. 11.
[84] *See Wolfe v. McNeil-PPC, Inc. (Wolfe II)*, No. 07-348, 2011 U.S. Dist. LEXIS 47710, at *13 (E.D. Pa. May 3, 2011).

where she is being proffered to testify about data analysis concerning the potential association of PPIs with renal impairment from a regulatory perspective.[85]

Similarly, the PSC's citation of a statement in Dr. Mann's deposition that it is not her area of expertise to make individual case specific assessments of causation has no bearing on her qualification to testify as a regulatory expert. She is not being offered by AstraZeneca as a case specific causation expert.

2. Reliability

The PSC further argues that Dr. Mann's testimony is not reliable. First, the PSC argues that Dr. Mann "lacks basic knowledge of the regulations on which she claims to be an expert."[86] For this proposition, the PSC cites one response to a question in Dr. Mann's deposition in which she says that she has not reviewed enough adverse reaction sections of product labeling to say whether a company is permitted to add more detail to them. This one sentence, taken out of context, ignores her nine years of experience at FDA working on labeling and safety issues for multiple products. In context, the sentence appears to reflect a "thinking out loud" approach to a very specific question. She later went on to say that "[she doesn't] think being . . . in the adverse reactions section precludes adding slight

[85] *Lemmon*, 2012 U.S. Dist. LEXIS 95924, at *27 (finding that expert testimony regarding the drug approval process and analysis of the adequacy of product labeling was admissible because it was based upon specialized knowledge of the regulatory procedures, pharmaceutical labeling, and FDA standards and practices).
[86] PSC's Omnibus Mem. 12.

additional detail at times."[87] If the PSC believes that this point is relevant to any issue at trial, she can be cross-examined about it, but it hardly forms a basis to exclude her testimony.

Second, the PSC argues that because some of the materials Dr. Mann reviewed were summaries prepared by AstraZeneca or regulatory agencies, her methodology is unreliable. In support of this argument, the PSC points to several data points that it claims were excluded by AstraZeneca from its submission to the European Medicines Agency's Pharmacovigilance Risk Assessment Committee ("PRAC"), which Dr. Mann reviewed and about which she offered opinions.[88] More generally, the PSC criticizes her reliance on internal FDA reports – a type of document with which, as a former FDA officer, she has significant familiarity – because she could not say what information had been omitted from them. If the PSC's position is that no expert can ever rely on an agency report, a summary of data, or even a published article without going back and looking at all the source data, that is an extreme position that does not reflect the state of the law in the Third Circuit. To the extent the PSC wants to highlight any limits on the scope of data that Dr. Mann reviewed, the PSC may do so through cross-examination.

[87] Mann Dep. 112:13-16.
[88] PSC's Omnibus Mem. 13-15.

Finally, the PSC asserts that Dr. Mann's finding that AstraZeneca's conduct and certain labeling decisions were reasonable should be excluded because she "offers no yardstick by which her opinions . . . can be verified, tested and measured."[89] Again, that is not the law as to reliability of expert regulatory opinions. To the contrary, courts have found testimony of FDA regulatory experts to be reliable when the expert applies the same methodology used in the expert's work at FDA.[90]

3. Fit

The PSC does not challenge the fit of Dr. Mann's testimony, and there is no basis in the record to question the fit of her testimony.

B. Dr. Janice Lansita

AstraZeneca seeks to offer the testimony of toxicologist Dr. Janice Lansita, who opines that the "esomeprazole bridging studies met the criteria and requirements outlined in FDA guidance on new stereoisomers (1992) as referenced by FDA in the esomeprazole Pre-IND meeting minutes (1997)."[91] Dr. Lansita also stated in her report that the scientific principles for the bridging studies and toxicology study designs have not materially changed, and thus omeprazole and esomeprazole would

[89] PSC's Omnibus Mem. 18.
[90] *See, e.g.*, *Terry II*, 2016 U.S. Dist. LEXIS 117594, at *20; *Johns*, 2021 U.S. Dist. LEXIS 143187, at *436; *Lemmon*, 2012 U.S. Dist. LEXIS 95924, at *27.
[91] PSC's Omnibus Mem., Ex. 13 [hereinafter Lansita Expert Report] at 1, ECF No. 703-13.

likely be approved by FDA today.[92] Her report also included a sentence regarding the cost of developing a drug from discovery to marketing.[93] The PSC moved to exclude Dr. Lansita's testimony and asserts that Dr. Lansita is not qualified to opine on chronic progressive nephropathy ("CPN") and whether CPN is relevant to humans; Dr. Lansita is not qualified to opine on the cost of developing esomeprazole and/or the cost of drug development generally; and Dr. Lansita cannot provide a reliable opinion on whether the FDA would likely approve Prilosec or Nexium today.[94]

AstraZeneca subsequently stipulated that it does not oppose the PSC's motion "[t]o the extent Plaintiffs seek to prevent Dr. Lansita from offering an opinion on the pathological criterion or significance of [CPN] to humans"[95] and that it does not oppose the PSC's motion "[t]o the extent Plaintiffs seek to prevent Dr. Lansita from offering an opinion on the historical cost of bringing Prilosec or Nexium to market[.]"[96]

For the reasons set forth below, I recommend that the Court grant the PSC's motion in part and deny it in part. I recommend that:

- the PSC's motion be granted to the extent it seeks to prevent Dr. Lansita from offering an opinion on the pathological criterion or significance of CPN to humans, per the stipulation by AstraZeneca, and that it be

[92] Lansita Expert Report 14.
[93] Lansita Expert Report 1.
[94] PSC's Omnibus Mem. 43.
[95] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 6.
[96] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 7.

denied to the extent it otherwise seeks to prevent Dr. Lansita from offering her opinion on the nonclinical studies she reviewed;

- the PSC's motion be granted to the extent it seeks to prevent Dr. Lansita from offering on opinion on the historical cost of bringing Nexium or Prilosec to market, per the stipulation by AstraZeneca;
- the PSC's motion be granted to the extent it seeks to prevent Dr. Lansita from offering an opinion on the cost of bringing a drug to market generally;
- the PSC's motion be granted to the extent that it seeks to prevent Dr. Lansita from offering an opinion on whether PPIs would be approved by FDA today, but that it be denied to the extent it seeks to bar Dr. Lansita from opining on the sufficiency of the nonclinical studies to support FDA approval; and
- the PSC's motion be otherwise denied.

1. Qualifications

Dr. Lansita is a board-certified regulatory toxicologist with a B.A. in Biochemistry from Barnard College of Columbia University and a Ph.D. in Toxicology from the Massachusetts Institute of Technology ("MIT"). She worked as a regulatory toxicologist at Biogen, where she "learned to evaluate the toxicology of

novel drugs for first-in-human clinical trials."[97] From 2009-2014, Dr. Lansita worked as a Pharmacologist/Toxicologist for FDA in the CDER Division of Special Pathogen and Transplant Products where she "reviewed numerous … drug applications to determine if the nonclinical data were adequate to support drug safety in patients."[98] From 2012-2014, she served as Co-Chair of the CDER Pharmacology/Toxicology Coordinating Committee Nonclinical Biologics Subcommittee, where she was responsible for "leading discussions relevant to the nonclinical review of biologics for a group of ~35 pharmacology/toxicology reviewers across Divisions in CDER[.]"[99] Dr. Lansita estimates that she reviewed over one hundred drug applications to determine whether the nonclinical data, including laboratory and animal studies, were adequate to support drug safety in patients, and if not, what additional nonclinical studies should be performed.[100] Since she left FDA in 2014, Dr. Lansita has "worked with numerous start-up, pharmaceutical, and biotechnology companies (>60) to provide advice on toxicology studies, design toxicology studies, oversee the conduct of toxicology studies at contract research organizations (CRO), analyze and interpret the data from these studies, and use these data to evaluate the nonclinical safety of new drugs for clinical development."[101]

[97] Lansita Expert Report 1.
[98] Lansita Expert Report 1.
[99] Lansita Expert Report, App. C, 3.
[100] Lansita Expert Report 1.
[101] Lansita Expert Report 1.

As noted above, AstraZeneca has conceded that it does not oppose the PSC's motion to exclude Dr. Lansita from offering an opinion on the pathological criterion or significance of CPN to humans, and that it does not oppose the PSC's motion to exclude Dr. Lansita from offering an opinion on the historical cost of bringing Nexium or Prilosec to market.[102] The PSC challenges Dr. Lansita's qualifications on other grounds.

First, the PSC argues that Dr. Lansita is not qualified to testify about her evaluation of the nonclinical studies she reviewed and her interpretation of the results of those studies, including their discussion of CPN, because she is not an expert on kidney disease and relies upon the testimony of another defense expert regarding the pathology of CPN.[103] I believe that Dr. Lansita's work at FDA and in the private sector as a toxicology expert are sufficient for her to be qualified to opine on the results of the nonclinical studies she reviewed.[104] To the extent the PSC seeks to argue that Dr. Lansita's opinion should be given less weight because she is not a kidney disease expert, the PSC can do so through cross-examination at trial.

---

[102] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶¶ 6, 7.
[103] PSC's Omnibus Mem. 44.
[104] I note that the PSC's position is somewhat inconsistent with the position of the PSC's counsel at oral argument, who noted that plaintiffs' expert Dr. Ross was qualified to opine on case reports, adverse event reports, and other evidence relevant to the review of a warning in a drug label, as that is often done at FDA by internal medicine doctors, not specialists such as cardiologists or nephrologists. Oral Args. 91:21-92:15, Apr. 4, 2022 ("they are not specifically limited to the fields that they may have been trained in and specialized in.").

Second, the PSC challenges Dr. Lansita's qualification to opine on the cost of bringing a drug to market generally, as well as with respect to Nexium and Prilosec specifically. Dr. Lansita acknowledged that she is not able to speak to how much it cost to bring Nexium or Prilosec to market.[105] AstraZeneca does not oppose the PSC's motion to exclude Dr. Lansita from testifying regarding the historical cost of bringing Nexium or Prilosec to market,[106] leaving only the question of whether she is qualified to offer an opinion as to the cost of bringing a drug to market generally. AstraZeneca argues that Dr. Lansita is qualified to opine on the cost of bringing a drug to market generally based on her work at FDA, as well as her work in private practice before and after her time at FDA, and her reliance on a report from PhRMA, a pharmaceutical industry trade association.[107] The record, however, reflects that Dr. Lansita's experience at FDA was, and in private practice was and is, focused on nonclinical data and studies. There is nothing in the record to suggest, and AstraZeneca does not argue, that Dr. Lansita has experience or training in the costs

[105] PSC's Omnibus Mem., Ex. 14 [hereinafter Lansita Dep.] at 84:13-21, ECF No. 703-14.

[106] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 7.

[107] AstraZeneca's Mem. of Law in Opp'n to Pls.' Omnibus *Daubert* Mot. to Exclude Defense Experts 34-35 [hereinafter AstraZeneca's Opp'n to PSC's Omnibus Mem.] ECF No. 734. "PhRMA represents the nation's leading biopharmaceutical research companies" and "strive[s] to conduct effective advocacy for public policies that encourage the discovery of important, new medicines for patients by biopharmaceutical research companies." *See* https://phrma.org/About (accessed June 24, 2022). AstraZeneca and Takeda are members of PhRMA. *Id.*

associated with bringing a drug to market in the United States to the extent those costs are not associated with the costs of the nonclinical studies and data with which she is familiar by experience. Accordingly, I recommend that Dr. Lansita be excluded from offering any testimony as to the cost of bringing a drug to market generally.

2. Reliability

The PSC asserts that Dr. Lansita should be prevented from opining on whether Nexium or Prilosec would be approved by FDA today because such an opinion would be unreliable and speculative.[108] While she offered that opinion in her expert report, at her deposition Dr. Lansita acknowledged that she had "not reviewed any of the clinical data and can't offer an opinion" that the clinical data were sufficient.[109] Accordingly, I recommend that the motion be granted to the extent it would preclude Dr. Lansita from offering any opinion that clinical data were sufficient to justify FDA approval of Nexium or Prilosec.

This leaves the issue of whether Dr. Lansita may offer the narrower opinion she adopted at her deposition – that the nonclinical data she reviewed would be sufficient to support FDA approval today, as she "did not identify any gaps in the data package that would preclude approval."[110] Dr. Lansita's narrowed opinion is based on her review of the nonclinical materials she identified and her experience,

[108] PSC's Omnibus Mem. 48.
[109] Lansita Dep. 144:20-22.
[110] Lansita Dep. 143:1-3.

including her time at FDA reviewing nonclinical studies and in the private sector.[111] As noted above, courts have found FDA regulatory expert testimony reliable when FDA experts rely on and apply the same methods used in their work at FDA with regard to regulation of drug approval and labeling.[112] Here, the PSC has not asserted that Dr. Lansita employed a different methodology than when she worked at FDA, or even in her experience in the private sector before or after her time at FDA. I recommend that the PSC's motion be denied to the extent it seeks to preclude Dr. Lansita from opining that, based on her experience at FDA, the nonclinical data she reviewed would be sufficient to support FDA approval today.

3. Fit

The PSC does not challenge the fit of Dr. Lansita's testimony, and there is no basis in the record to question the fit of her testimony.

C. Dr. Robert Gibbons

AstraZeneca proposes to present Dr. Robert Gibbons as a general causation expert to testify on "[t]he strengths and limitations of the scientific literature concerning proton pump inhibitors (PPIs) and chronic kidney disease (CKD)" and "[w]hether the available evidence supports a causal relationship between PPIs and

[111] Lansita Expert Report 1.
[112] *See, e.g.*, *Terry II*, 2016 U.S. Dist. LEXIS 117594, at *20; *Johns*, 2021 U.S. Dist. LEXIS 143187, at *436; *Lemmon*, 2012 U.S. Dist. LEXIS 95924, at *27.

CKD."[113] The PSC seeks to exclude Dr. Gibbons's testimony on two grounds: first, that Dr. Gibbons is not qualified to provide such testimony because he is a biostatistician, not an epidemiologist, and lacks specialized nephrology training;[114] and second, that Dr. Gibbons's methodology is unscientific and unreliable because it unreasonably excludes certain data and contains erroneous calculations.[115] For the reasons set forth below, I recommend that the PSC's motion be denied.

1. Qualifications

Dr. Gibbons is a professor of biostatistics at the University of Chicago with extensive experience developing statistical methods to analyze drug safety data.[116] He has authored a book on statistics in drug safety and pharmacoepidemiology and hundreds of peer-reviewed papers.[117] He is an elected member of the National Academy of Medicine ("NAM") and the National Academy of Sciences ("NAS"), and he served for six years on the NAM Board on Health Sciences Policy.[118]

Although his principal focus in recent years has been on statistical analysis and pharmacoepidemiologic analysis with respect to psychoactive drugs, Dr.

[113] PSC's Omnibus Mem., Ex. 20 [hereinafter Amended Gibbons Expert Report] at 6, ECF No. 703-20.
[114] PSC's Omnibus Mem. 50.
[115] PSC's Omnibus Mem. 51-54.
[116] Amended Gibbons Expert Report 4-5.
[117] Amended Gibbons Expert Report 4, App. 2.
[118] Amended Gibbons Expert Report 4.

Gibbons has experience with kidney-related research.[119] He works with the NAM's Committee on Organ Transplantation on issues "focuse[d] heavily on kidney transplantation and chronic kidney disease" and performed other work involving kidney disease.[120] He also "reviewed a wide range of articles that describe the underlying background of chronic kidney disease."[121]

The PSC contends that, notwithstanding Dr. Gibbons's academic credentials and history of consulting work related to kidney disease, he lacks sufficient expertise to present his proposed statistical opinions regarding causation.[122] In particular, the PSC notes that he is a biostatistician, not an epidemiologist, and, more importantly, that he has no specialized training in nephrology or gastroenterology.[123] The PSC argues that, as a result of his lack of training in nephrology, he does not have a sufficient understanding of the meaning of the data considered to reach accurate conclusions. For example, the PSC states that Dr. Gibbons did not know that acute interstitial nephritis ("AIN") is an acute kidney injury ("AKI") and that, therefore, his treatment of AIN and AKI as independent variables skews his analysis.[124]

---

[119] AstraZeneca's Opp'n to PSC's Omnibus Mem., Ex. T [hereinafter Gibbons Dep.] at 47:17-21, 49:9-11, 51:15-22, ECF No. 734-21.
[120] Gibbons Dep. 47:6-21.
[121] Gibbons Dep. 206:10-12.
[122] PSC's Omnibus Mem. 50-51.
[123] PSC's Omnibus Mem. 50.
[124] PSC's Omnibus Mem. 50.

The PSC's criticism that Dr. Gibbons is not a formally trained nephrologist or gastroenterologist should be rejected for two reasons. First, Dr. Gibbons's practical experience with the NAM and extensive academic training and credentials in biostatistics qualify him to offer an expert opinion on questions of statistics. Biostatisticians have expertise in statistics, data analysis, and data interpretation and do not need to be experts regarding the disease pathology or treatment being analyzed.[125] Such a requirement would set an unreasonably high bar for expert epidemiological and biostatistical testimony that has no support in Third Circuit precedent.[126]

Second, the PSC's criticism is misplaced because it does not address the thrust of Dr. Gibbons's proposed testimony. His opinion evaluates the studies' methodologies and evidence of alleged causation from a statistical perspective. He considers the variables as defined in the studies, the methodological rigor of the studies, the potential role of confounding factors, and the quality of the statistical analysis of the studies. It is a statistical review and critique regarding the strength, or lack thereof, of suggested correlations as reflected in data, not an analysis of disease mechanisms and pathology. Such testimony is within his area of expertise.

---

[125] *See Hospira, Inc.*, 285 F. Supp. 3d at 811.

[126] *See, e.g.*, *Waldorf*, 142 F.3d at 626 ("[O]rdinarily an otherwise qualified witness is not disqualified merely because of a lack of academic training."); *Paoli*, 35 F.3d at 753.

To the extent that the PSC believes that Dr. Gibbons's alleged lack of knowledge regarding kidney function and disease may affect the reliability of his opinions, counsel can engage in cross-examination to challenge his credibility and address what weight the jury should give his opinions.[127]

2. Reliability

The PSC does not dispute that Dr. Gibbons used well-recognized, peer-reviewed statistical methods in developing his opinion. Rather, the PSC challenges Dr. Gibbons's application of these methods, arguing that he erroneously analyzed the Bradford Hill criteria in assessing the causal link between PPIs and adverse renal events by misapplying "temporality" criteria and purportedly "cherry-picking" data from some of the studies.[128] The PSC also argues that Dr. Gibbons erroneously grouped data in his analysis.[129] Thus, it argues, these flaws in applying his methodology render his opinion unreliable.[130]

a. Dr. Gibbons's Reliability as to His Evaluations of Other Studies

A careful review of the criticisms in the PSC's brief, Dr. Gibbons's Amended Report, and the relevant deposition testimony does not support the conclusion that Dr.

---

[127] *See U.S. v. Mitchell*, 365 F.3d at 244-45.
[128] PSC's Omnibus Mem. 51-55.
[129] PSC's Omnibus Mem. 56.
[130] *See* PSC's Omnibus Mem. 56*; In re: Zoloft*, 858 F.3d at 795 (noting that both the expert's methodology and its application must be reliable for the testimony to be admissible).

Gibbons's application of the Bradford Hill criteria is unreliable. Dr. Gibbons's analysis takes into account the potential confounding factors present in the non-randomized trial literature upon which the PSC relies, and he evaluates those studies to determine whether such confounding factors affect the reliability of those studies.[131] Dr. Gibbons's discussion of body mass index ("BMI") as a risk factor for CKD comes in the context of an in-depth review of 132 pieces of literature, not just the Lazarus, Xie, Peng, and Cho articles. Dr. Gibbons thoroughly explains his reasoning where he disagrees with the conclusions expressed by some of the authors based on their use of the data or discounts the reliability of some of the data.[132] His disagreement with the conclusions of the authors of some of the literature that he reviewed and the conclusions of the experts relied upon by the PSC does not render his analysis unreliable.

The specific examples cited by the PSC (*e,g.*, their criticism of Dr. Gibbons's discussion of the Xie study's application of the "temporality" criterion and their criticism of Dr. Gibbons' discussion of BMI as a risk factor for CKD) do not refute this conclusion.[133] As to both of these, he explains his rationale for and the methodology he used in arriving at his opinions.[134]

---

[131] *See* Amended Gibbons Expert Report 17, 30-33, 37.
[132] *See* Amended Gibbons Expert Report 18-51; AstraZeneca's Opp'n to PSC's Omnibus Mem. 39-44.
[133] PSC's Omnibus Mem. 51-52.
[134] *See* Amended Gibbons Expert Report 27-28 (Dr. Gibbons noted that FDA criticized the Xie publication on grounds similar to his); Gibbons Dep. 270:10-271:6, 282:7-287:13.

Disagreements as to the appropriate statistical evaluation of the relevant literature and the data therein are proper subjects for cross-examination at trial.[135] However, they are not sufficient to warrant exclusion under the "flexible" reliability requirement, which "is not to be used as a tool by which the court excludes all questionably reliable evidence."[136]

b. Reliability of Grouping of Data in AstraZeneca Studies

The PSC also challenges Dr. Gibbons's work as unreliable because he concededly initially improperly grouped certain AstraZeneca clinical trial data within his meta-analysis and then, after re-running his statistical models, purportedly failed adequately to modify his Report.[137]

Dr. Gibbons's initial error is not a basis for exclusion because the PSC does not dispute that it was corrected in Dr. Gibbons's Amended Report. Thus, regardless of whether the initial meta-analysis properly grouped data, the Amended Report resolves this issue. Moreover, the Amended Report was provided to the PSC prior to Dr. Gibbons's deposition, so the PSC had the opportunity to cross-examine him on the issue.[138] The PSC can cross-examine Dr. Gibbons on the issue at trial and

[135] *See Daubert*, 509 U.S. at 596.
[136] *Paoli*, 35 F.3d at 744.
[137] *See* PSC's Omnibus Mem. 56-58.
[138] *See* PSC's Omnibus Mem. 56.

can argue that the jury should consider the initial error in determining what if any weight and credibility it affords Dr. Gibbons's testimony.

More importantly, the PSC's argument that Dr. Gibbons's initial error materially affected his analysis and Amended Report does not withstand scrutiny. A comparison of the relevant charts and amended text shows that the impact was limited and that Dr. Gibbons modified his expert report to address it. The Amended Report contains a revised chart and modifies the text to state that treatment by duration interactions *were* statistically significant, as opposed to not significant in the initial draft.[139] However, it still shows (as did the initial chart) that "the estimated [glomerular filtration rate] changes from baseline are identical at 65 weeks and in fact PPI use was associated with *better* kidney function than comparators from 65 to 104 weeks."[140] Thus, while the charts look different, on their face they appear to support the same conclusion reached by Dr. Gibbons. To the extent the PSC believes that the modifications have some other significance, they can be addressed on cross-examination.

3. Fit

The PSC does not challenge the fit of Dr. Gibbons's testimony, and there is no basis in the record to question the fit of his testimony.

---

[139] *Compare* Amended Gibbons Expert Report 20-21, *with* PSC's Omnibus Mem., Ex. 15 [hereinafter Gibbons Expert Report] at 20, ECF No. 703-15.
[140] *Compare* Amended Gibbons Expert Report 20, *with* Gibbons Expert Report 20.

D. Dr. Rajat Deo

AstraZeneca seeks to offer expert testimony by Dr. Rajat Deo on the issue of specific causation – namely, that hypertension, in conjunction with other comorbidities, was a substantial contributing factor to Plaintiff Rieder's and Plaintiff Bales's CKD.[141] Specifically as to *Rieder*, AstraZeneca seeks to offer Dr. Deo's opinion that "Mr. Rieder's long-standing hypertension caused and substantially contributed to the development and progression of Mr. Rieder's CKD."[142] Similarly in *Bales*, AstraZeneca seeks to offer Dr. Deo's opinion that Plaintiff Bales's "long-standing history of hypertension, including his exaggerated stress response, and chronic [non-steroidal anti-inflammatory drug ("NSAID")] use contributed to his kidney disease[.]"[143] Additionally, in both cases, Dr. Deo's testimony is intended to rebut the testimony of Plaintiff Rieder's and Bales's specific causation expert, Dr. Morton R. Rinder, who "purports to rule out cardiovascular disease as contributing to Plaintiffs' CKD."[144]

---

[141] *See* AstraZeneca's Opp'n to PSC's Omnibus Mem. 11-13, 15-16; PSC's Omnibus Mem., Ex. 4 [hereinafter Deo Expert Report in *Bales*], ECF No. 703-4; PSC's Omnibus Mem., Ex. 5 [hereinafter Deo Expert Report in *Rieder*], ECF No. 703-5.
[142] Deo Expert Report in *Rieder* 1.
[143] Deo Expert Report in *Bales* 3.
[144] AstraZeneca's Opp'n to PSC's Omnibus Mem. 15. *See also* AstraZeneca's Opp'n to PSC's Omnibus Mem., Ex. J [hereinafter Rinder Expert Report in *Bales*] at 3, ECF No. 734-11 ("I conclude that neither hypertension nor renovascular disease were contributory factors in his development of CKD."); AstraZeneca's Opp'n to PSC's Omnibus Mem., Ex. K [hereinafter Rinder Expert Report in *Rieder*] at 3, ECF No. 734-12 ("I conclude that the etiology of Mr. Rieder's chronic kidney disease

The PSC has moved to exclude Dr. Deo's opinion testimony on two grounds: (1) that Dr. Deo is not qualified to provide a specific causation opinion as to whether Plaintiffs' PPI use caused their CKD because he is a cardiologist without specialized training in renal physiology, pharmacology, or pathology; and (2) that Dr. Deo's opinion is not reliable because he did not consider the Plaintiffs' PPI use as a potential cause of their CKD.[145] For the reasons set forth below, I recommend that the motion to exclude Dr. Deo's expert testimony be denied. However, I also recommend that, to avoid the risk of jury confusion, the Court consider giving instructions to the jury that Dr. Deo was not asked to and did not consider or form any opinion with respect to whether Plaintiff Rieder's or Plaintiff Bales's PPI use was a cause of either of their CKD.

1. Qualifications

Dr. Deo, a graduate of MIT and the University of Michigan Medical School, is trained in internal medicine and is a board-certified cardiologist and cardiac electrophysiologist. He is a clinical researcher at the University of Pennsylvania Perelman School of Medicine and his clinical practice focuses on the management of cardiac arrhythmias, especially in patients with advanced kidney disease.[146] He

---

cannot be attributed to an underlying cardiovascular disease."); Deo Dep 225:10-16; 434:22-435:5.

[145] PSC's Omnibus Mem. 23.

[146] Deo Expert Report in *Rieder* Ex. A; Deo Expert Report in *Bales* Ex. A.

also has an NIH-funded research program that focuses on understanding the link between cardiovascular disease and CKD.[147]

The PSC argues that Dr. Deo is not qualified to give a specific causation opinion regarding the causation between PPI use and Plaintiffs' CKD: (i) because although Dr. Deo's clinical practice and academic research involve the intersection of cardiovascular disease and kidney disease, Dr. Deo is a cardiologist, not a nephrologist, and lacks specialized training in renal physiology, pharmacology, or pathology; and (ii) because Dr. Deo's focus is on cardiac disease incidental to kidney disease, he does not treat patients for CKD and, if he observes CKD in his patients, he refers those patients to nephrologists for treatment of their CKD.[148] However, Dr. Deo is not, for either plaintiff, offering an opinion that PPI use did not cause their CKD.[149] Rather, as set forth more fully below, he is opining that their hypertension and other comorbidities and conditions were substantial contributing factors to both Plaintiffs' development of CKD.

[147] Deo Expert Report in *Rieder* Ex. A; Deo Expert Report in *Bales* Ex. A.
[148] PSC's Omnibus Mem. 25-27.
[149] AstraZeneca's Opp'n to PSC's Omnibus Mem., Ex. G [hereinafter Deo Dep.] at 354:4-6, Sep. 9, 2021, ECF No. 734-8 ("I'm not commenting one way or another on the role PPI either did or did not contribute to Mr. Rieder's CKD."); Deo Dep. 175: 11-15, Sep. 9, 2021 ("I was asked to review the Bales case especially with regards to cardiovascular disease, cardiovascular risk factors and their effect on his chronic kidney disease.").

Dr. Deo is sufficiently qualified under Third Circuit *Daubert* law. Dr. Deo is trained in internal medicine and, with board certifications in internal medicine, cardiovascular diseases and clinical cardiac electrophysiology, participates in research related to CKD, specifically the management of cardiac disease in patients with CKD.[150] Once an expert meets the baseline threshold of sufficient qualifications to proffer an expert opinion, the extent of the expert's qualifications goes to the credibility and weight to be accorded his testimony.[151] Given Dr. Deo's background, education, experience and clinical research specifically related to the intersection of cardiovascular disease and CKD,[152] he is sufficiently qualified to opine about Plaintiffs' cardiovascular issues and how they relate to Plaintiffs' CKD. Moreover, as discussed below, if Plaintiffs are permitted to present a cardiologist to opine that cardiovascular issues are not the cause of Plaintiffs' CKD, as a matter of fairness Defendants must be permitted to present a cardiologist to rebut such testimony.

2. Reliability

The PSC also asserts that Dr. Deo's testimony regarding causation fails to satisfy the reliability prong because Dr. Deo concededly did not evaluate the key causation issue in the case – whether Plaintiffs' PPI use was a cause of their CKD.[153]

---

[150] Deo Expert Report in *Rieder* Ex. A; Deo Expert Report in *Bales* Ex. A.
[151] *Id.*
[152] Deo Expert Report in *Rieder* Ex. A; Deo Expert Report in *Bales* Ex. A.
[153] *See* PSC's Omnibus Mem. 23.

This lack of reliability is exacerbated, in the PSC's view, because Dr. Deo considered other potential causes of their CKD and attributed their CKD in part to those other conditions. Specifically, as to Plaintiff Rieder, Dr. Deo states in his report that:

> [C]onsistent with [Plaintiff Rieder's] medical history, as well as assessment of his own treating providers, it is my opinion, to a reasonable degree of medical and scientific certainty, that Mr. Rieder's CKD and renal decline is attributable to hypertension and NSAID and COX-2 inhibitor use. There are also multiple other factors throughout his records that caused or contributed to his CKD including metabolic syndrome, obesity, diabetes, and years of smoking.[154]

Similarly, with regard to Plaintiff Bales, Dr. Deo states in his report that:

> [I]t is my opinion to a reasonable degree of scientific and medical certainty that . . . hypertension and exaggerated blood pressure response with stress testing, concomitant use of NSAIDs, extensive smoking history, advanced COPD – all in combination were the substantial contributing factors to [Plaintiff Bales's] CKD. These conditions preceded development of his minor CKD, which is of far less significance to his overall prognosis than his other comorbidities such as reduced lung function/ventilatory capacity.[155]

In the PSC's view, Dr. Deo's consideration of a host of potential causative factors except Plaintiffs' PPI use renders Dr. Deo's opinion testimony unreliable and potentially misleading to the jury.[156]

The PSC's argument regarding the reliability of Dr. Deo's testimony raises an issue of the potential for jury confusion. As the Third Circuit observed in *Paoli*, "the

[154] Deo Expert Report in *Rieder* 5.
[155] Deo Expert Report in *Bales* 4.
[156] PSC's Omnibus Mem. 23-25.

core of differential diagnosis is a requirement that experts at least consider alternative causes . . . ."[157] Given that Dr. Deo addressed a variety of potential causes of Plaintiffs' CKD, Dr. Deo's omission of any discussion of Plaintiffs' PPI use, the cause alleged by plaintiffs in these cases, while not rendering his opinion completely unreliable, does bear on the credibility of his testimony.

Importantly, as previously noted, AstraZeneca has represented that it intends to call Dr. Deo specifically to rebut Dr. Rinder's opinion that cardiovascular issues were not a cause of both Plaintiffs' CKD.[158] In his expert reports, Dr. Rinder opines that Plaintiffs' CKD cannot be attributable to cardiovascular disease.[159] Like Dr. Deo, Plaintiffs' expert, Dr. Rinder, also a cardiologist, offers no opinion as to whether PPI use contributed to Plaintiffs' CKD. Dr. Deo also understood that he was being asked to consider and respond directly to Dr. Rinder's opinions[160] and he specifically did so in his reports.[161] In that context, Dr. Deo's disavowal of any

---

[157] *Paoli*, 35 F.3d at 759.
[158] *See* AstraZeneca's Opp'n to PSC's Omnibus Mem. 15-16.
[159] Rinder Expert Report in *Bales* at 3 ("I conclude that neither hypertension nor renovascular disease were contributory factors in [Plaintiff Bales's] development of CKD."); Rinder Expert Report in *Rieder* at 3 ("I conclude that the etiology of [Plaintiff] Rieder's chronic kidney disease cannot be attributed to an underlying cardiovascular disease.").
[160] Deo Depo 225:10-16; 434:22-435:5.
[161] Deo Expert Report in *Rieder* 6 ("[Dr. Rinder] improperly omits any discussion of hypertension as a cause of Mr. Rieder's CKD."); Deo Expert Report in *Bales* 4 ("I have reviewed Dr. Rinder's report…. Dr. Rinder minimizes the effects that the patient's other comorbidities such as COPD and advanced ventilatory dysfunction can have on CKD and CKD progression.").

evaluation or opinion on the impact (if any) of these Plaintiffs' PPI use on their kidney function is understandable. Given that Plaintiffs Rieder and Bales are offering their expert cardiologist, Dr. Rinder, to opine that cardiovascular disease can be ruled out as a cause of their CKD, AstraZeneca should be allowed to offer its own expert cardiologist, Dr. Deo, to opine that Dr. Rinder is incorrect and that cardiovascular disease cannot be ruled out as a cause of Plaintiffs' CKD.

3. Fit

The PSC does not challenge the fit of Dr. Deo's testimony in either *Rieder* or *Bales*, and there is no basis in the record to question the fit of his testimony in those cases.

E. Dr. Caren Palese

AstraZeneca seeks to offer Dr. Caren Palese, a gastroenterologist, as a specific causation expert to testify that Plaintiff Rieder's CKD predated his Nexium use. The PSC moved to exclude Dr. Palese's specific causation opinions as to the cause of Plaintiff Rieder's CKD. Her primary basis for this conclusion is her calculation of Plaintiff Rieder's estimated glomerular filtration rate ("eGFR")[162] in January 2002, prior to his Nexium use; she asserts that it shows abnormal kidney function at that time. The PSC challenges Dr. Palese's qualifications to give such testimony and the reliability of her testimony, given her inability to identify adequately the

[162] eGFR is calculated with a formula that accounts for blood creatinine levels and some combination of other characteristics, including age.

methodology she used to perform her calculation to arrive at her conclusion, and several misstatements made in her deposition testimony about Plaintiff Rieder's age in January 2002 (age being a data point required to calculate eGFR).[163]

For the reasons set forth below, I recommend that Dr. Palese's testimony be excluded because her conclusion that Plaintiff Rieder's CKD predated his Nexium use is not based on a defined, replicable, and reliable methodology. Admitting such testimony therefore would not "help the trier of fact to understand the evidence or to determine a fact in issue;" instead, it would create a substantial risk that the jury would be confused or misled.[164]

1. Qualifications

Dr. Palese is a board-certified gastroenterologist.[165] She completed her residency in internal medicine and was – but is not presently – board-certified in internal medicine.[166] She testified that she was "very comfortable taking care of patients with kidney disease."[167] However, she also testified that when treating patients with CKD,

[163] PSC's Omnibus Mem. 28-35.
[164] Fed. R. Evid. 702(a).
[165] PSC's Omnibus Mem., Ex. 9 [hereinafter Palese Expert Report] at 1, ECF No. 703-9.
[166] Palese Expert Report 1.
[167] PSC's Omnibus Mem., Ex. 10 [hereinafter Palese Dep.] at 145:3-4, ECF No. 703-10.

she worked on a team with nephrologists because "[u]sually you'd like to have a kidney doctor involved if the patient had chronic kidney disease."[168]

Expert testimony by physicians is very rarely excluded in the Third Circuit for lack of qualifications, and Dr. Palese satisfies the liberal Third Circuit standard for qualifications. Dr. Palese is a well-credentialed gastroenterologist with ample experience treating patients with CKD for their gastrointestinal conditions, including with PPIs.[169] She works alongside nephrologists as a member of multidisciplinary teams for her patients with CKD.[170] She reviewed over 250 documents, including peer-reviewed studies, FDA materials, and professional association guidance documents.[171] Under the Third Circuit's liberal standard, she is sufficiently qualified to provide expert testimony on the purported causal relationship between Plaintiff Rieder's PPI use and his CKD.

2. Reliability

To determine reliability, a court must look at the scientific validity of the methodology upon which the expert bases an opinion.[172] As set forth above, an

[168] Palese Dep. 143:21-23.
[169] Palese Dep. 71:3-72:5, 75:14-76:2.
[170] *See, e.g.*, Palese Dep. 143:2-23.
[171] Palese Expert Report Ex. B. Dr. Palese's qualifications considerably exceed those of the doctor who was excluded as unqualified in *Diaz v. Johnson Matthey, Inc.*, 893 F. Supp. 358, 372 (D.N.J. 1995), because he had never treated a patient with the particular respiratory condition at issue, was unfamiliar with the literature on the condition, and lacked any other qualifications beyond his general training and credentials.
[172] *Paoli*, 35 F.3d at 742.

expert must identify the methodology or procedures used to explain how the expert's conclusions were reached, and the data and materials considered by the expert must be available.

The relevant facts do not appear to be in dispute. Dr. Palese does not routinely calculate eGFR for her patients in her practice as a gastroenterologist.[173] To support her opinion that Plaintiff Rieder suffered from CKD in January 2002, prior to his Nexium use, Dr. Palese went on the internet and found a formula that she says that she used to calculate Plaintiff Rieder's eGFR using his creatinine levels, age, and gender.[174] Dr. Palese did not keep any record of that calculation or of the inputs she used and could not identify with certainty at her deposition the formula she used.[175] She erroneously stated throughout her deposition that Plaintiff Rieder was in his thirties in January 2002, when he was actually forty-four at that time.[176] Though she corrected this error in later deposition testimony after being shown a document that

[173] Palese Dep. 187:12-19.
[174] Palese Dep. 187:20-188:4; Oral Args. 178:10-15, Apr. 4, 2022.
[175] Palese Dep. 189:3-21. Defense counsel at oral argument agreed that Dr. Palese could not identify the formula she had used: "And Ms. Martines is right, [Dr. Palese] cannot remember the website … to which she inputted, but what she says is that … combining her experience and with the calculations that she did, it results in an eGFR of 60." Oral Args. 178:10-15, Apr. 4, 2022. In other words, Dr. Palese could not recall where she got the formula that she used, but nonetheless concluded that 60 was the correct number – even though at her deposition she misstated one of the key inputs (age) multiple times and admitted that she did not make this calculation routinely in her practice.
[176] *See, e.g.*, Palese Dep. 158:17-22, 161:16-22, 162:5-24.

contained his date of birth, there is no record in her report of the age she used in her eGFR calculation.[177] The only potential evidence that she used the correct age is her *ipse dixit* assertion at deposition that she did use the correct age, after being corrected about repeatedly misstating Plaintiff Rieder's age in her deposition testimony.[178]

AstraZeneca asserts that calculating eGFR is just like converting Fahrenheit to Celsius, so it does not matter that Dr. Palese cannot show her work. My review of the available internet eGFR calculators reveals that they are not all identical, so it is possible that the specific calculator used would affect the result.[179] Because Dr. Palese kept no records of her calculation and does not know where she got the

[177] Palese Dep. 162:15-163:16.
[178] Palese Dep. 172:13-21.
[179] A review of eGFR calculators available on the internet shows that there is variability as to inputs. The National Kidney Foundation one uses: serum creatinine (mg/dL); serum cystatin C (mg/L); age (years); gender (m/f); standard assays (y/n/not sure); adjust for body surface (y/n/not sure). Nat'l Kidney Foundation, *eGFR Calculator*, https://www.kidney.org/professionals/kdoqi/gfr_calculator (last visited June 24, 2022). A "Medline Plus" calculator from the National Library of Medicine uses creatinine, age, weight, height, gender, and race. MedlinePlus, *Glomerular Filtration Rate (GFR) Test*, https://medlineplus.gov/lab-tests/glomerular-filtration-rate-gfr-test/ (last visited June 24, 2022). A calculator from DaVita Kidney Care uses serum creatinine, age, and gender. DaVita Kidney Care, *GFR Calculator*, https://www.davita.com/tools/gfr-calculator (last visited June 24, 2022). One available on "Calculator.net" uses serum creatinine (mg/dL), age, gender, race (black/not black). Calculator.net, *GFR Calculator*, https://www.calculator.net/gfr-calculator.html (last visited June 24, 2022).

calculator on the internet, she has not identified a methodology that can be evaluated by the Court or that can be repeated by Dr. Palese or others.[180]

Courts in this Circuit presented with similar circumstances have rejected expert opinions as unreliable. In *In re Johnson & Johnson Talcum Powder Prods. Mktg., Sales Practices & Prods. Litig.*, the court noted that where the data the expert used in his analysis were permanently unavailable and the analysis could not possibly be repeated, the methodology was unreliable.[181] Similarly, in *Buzzerd*, an expert's testimony was ruled inadmissible when he failed to articulate any methodology used to develop his opinion and relied solely on his observations and *ipse dixit* conclusions.[182]

The same is true here. Dr. Palese's methodology consists of searching online for an eGFR formula, choosing one, and using it to calculate Plaintiff Rieder's eGFR without recording which formula she chose, the source of the formula, the data she inputted, or consideration of the availability of alternative methodologies. Dr. Palese's calculation of Plaintiff Rieder's eGFR cannot be reproduced because it is

[180] The PSC's counsel noted in oral argument that she had attempted to replicate Dr. Palese's analysis and result using a calculator that Dr. Palese had indicated was one that she might have used but was unable to replicate Dr. Palese's calculated result. Oral Args. 174:15-19, Apr. 4, 2022.

[181] *In re Johnson & Johnson Talcum Powder*, 509 F. Supp. 3d at 155.

[182] *See Buzzerd*, 669 F. Supp. 2d at 523; *U.S. v. Mitchell*, 365 F.3d at 235 (noting other factors that may be relevant include "whether a method consists of a testable hypothesis" (quoting *Paoli*, 35 F.3d at 742 n.8)).

unknown what calculator she used or what inputs she put into it, and she cannot demonstrate how this calculation generated the result she claims to have gotten.

3. Fit

The PSC does not challenge the fit of Dr. Palese's testimony, and there is no basis in the record to question the fit of her testimony.

IV. DEFENDANTS' MOTIONS

A. Dr. David Ross

The PSC seeks to offer expert testimony by Dr. David Ross on FDA's process for approving drug labeling, requiring and evaluating post-marketing safety and efficacy data, considering label modifications, and the adequacy of the warnings provided by AstraZeneca for Nexium and Takeda for Prevacid (in *Bales*) regarding a possible causal association between these drugs and renal impairment. AstraZeneca seeks to exclude Dr. Ross's opinion testimony for lack of qualifications, reliability, and fit.[183] Additionally, AstraZeneca seeks to exclude his potential testimony relating to the FDA's level of understanding of the difference between acute tubulointerstitial nephritis ("ATIN") and chronic tubulointerstitial nephritis ("CTIN") and the adequacy of FDA staffing and resources.[184] Takeda

[183] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Ross 1-2 [hereinafter AstraZeneca's Mem. in Supp. of Mot. to Exclude Ross], No. 2:19-cv-00850, ECF No. 33-1; *Daubert*, 509 U.S. at 589-92.
[184] AstraZeneca's Mem. in Supp. of Mot. to Exclude Ross 1-2.

moves to exclude Dr. Ross's opinion on the grounds of reliability and fit, as well as additional arguments that Dr. Ross may not, as a matter of law, opine that the warnings were inadequate at the time of Prevacid approval and that his opinions about Takeda's pharmacovigilance improperly constitute a "fraud on the FDA" claim.[185] For the reasons discussed below, I recommend that these motions be denied in substantial part. With regard to two narrow arguments made by AstraZeneca, as discussed in more detail below, I recommend that the motion be granted.

1. Qualifications

Dr. Ross has multiple degrees and post-doctoral training relevant to the issues in these cases. He received both an M.D. and a Ph.D. in Biochemistry from New York University and a master's degree in Biometrics from Oregon Health Sciences University.[186] He completed a residency in internal medicine at New York University ("NYU") and a fellowship in infectious disease at Yale University School of Medicine.[187]

Prior to joining FDA in 1996, Dr. Ross was a practicing physician focusing on HIV/AIDS patients from 1991-1996. From 1996-2006, Dr. Ross held multiple

[185] Mem. in Supp. of Takeda's Mot. to Exclude Test. of Dr. David Ross 14 [hereinafter Takeda's Mem. in Supp. of Mot. to Exclude Ross], No. 2:17-cv-06124, ECF No. 77-1.
[186] AstraZeneca's Mot. to Exclude Ross, Ex. A [hereinafter Ross Expert Report] at Ex. A, 1, No. 19-cv-00850, ECF No. 33-3.
[187] Ross Expert Report Ex. A, 1.

positions at FDA: Medical Officer at the Division of Anti-Infective Drug Products, Senior Medical Reviewer at the Division of Anti-Infective Drug Products, Medical Team Leader at the Division of Anti-Infective Drug Products, Deputy Director at the Office of Drug Evaluation VI, and Associate Director for Regulatory Science at the Office of Oncology Drug Products.[188] His work at FDA involved reviewing and making approval recommendations for INDs and NDAs, reviewing labeling changes (including Changes Being Effected ("CBEs")), providing guidance on post-marketing surveillance of adverse events, reviewing reports submitted to FDA by NDA sponsors, and ultimately supervising and directing more junior medical reviewers at FDA.

Dr. Ross was repeatedly recognized for professional excellence at FDA: for example, he received the CDER Excellence in Communication Award (ODE IV/PhRMA Working Group), the CDER Team Excellence Award (Maxipime® Review Team), the CDER Group Recognition Award (Inter-Divisional Working Group on Antibiotic Resistance), the FDA Commendable Service Award (Linezolid Review Team), the FDA Award of Merit (CDER Counter-Terrorism Response Team), and the CDER Team Excellence Award (CDER TOPOFF 2 Exercise Team).[189]

Since 2006, Dr. Ross has been the Director of HIV, Hepatitis, and Related Conditions Programs in the Office of Specialty Care Services at the Veteran's Health

[188] Ross Expert Report 2-3.
[189] Ross Expert Report Ex. A, 3-4.

Administration and has also served as a staff physician at the VA Medical Center in Washington, DC. He is board-certified in internal medicine and infectious diseases and has an extensive list of publications and presentations, most relating to infectious disease issues and some relating to drug development and study design.[190]

AstraZeneca does not challenge Dr. Ross's qualifications generally, but only as to the following: (1) his opinions regarding whether PRAC properly analyzed data submitted by AstraZeneca; and (2) his opinions regarding pharmacology, toxicology, and nephrology, particularly as applied to preclinical and clinical trials.

Dr. Ross is trained in internal medicine and has over a decade of experience at FDA reviewing preclinical and clinical trial data, adverse event data, and product labeling relating to a variety of medical specialties. The fact that he is not holding himself out as an expert in nephrology, for example, does not mean that he is incapable of providing expert opinions about the adequacy and interpretation of preclinical or clinical trial data or subsequent analyses of those data simply because he is not an expert in that particular substantive field.[191] FDA reviewers have expertise in reviewing, interpreting, and analyzing data and that is what he is proposing to do here. Likewise, the fact that he did not ever work for PRAC does

[190] Ross Expert Report 3-17.

[191] Indeed, AstraZeneca has argued that Dr. Lansita, an expert in toxicology, is qualified to offer an expert opinion on the regulatory significance of animal studies she reviewed despite the fact that she is not an expert in nephrology.

not preclude him from opining about the adequacy of PRAC's data analysis.[192] Here, Dr. Ross is being proffered to testify about data analysis from a regulatory perspective. Dr. Ross is highly qualified under applicable Third Circuit law to testify about this subject matter given his decade-long experience doing just that at FDA.[193]

2. Reliability

AstraZeneca and Takeda both argue that Dr. Ross's testimony fails to satisfy *Daubert*'s reliability prong because Dr. Ross fails to provide adequate explanations for how he reached his conclusions about an association between Nexium use and ATIN and CTIN.[194]

Dr. Ross provided a 275-page report in which he described the voluminous materials that he reviewed as well as the approach that he took in reviewing these materials and reaching his conclusions.[195] He explained the regulatory process

---

[192] As the PSC's brief notes, Dr. Ross's criticisms focus largely on analyses of the data that he believes that AstraZeneca, not PRAC, should have performed. PSC's Mem. in Supp. of its Opp'n to AstraZeneca's Mot. to Exclude Dr. David Ross 37-38, ECF No. 737 [hereinafter PSC's Opp'n Mem. to AstraZeneca's Mot. to Exclude Ross].

[193] *See Terry I*, 2016 U.S. Dist. LEXIS 99177, at *14-15 (finding that an expert with eighteen years of experience who contributed to the labeling and promotional materials of more than one hundred different products was qualified to conduct research in the same way FDA would); *Wolfe I*, 881 F. Supp. 2d at 658 (finding FDA experts to be qualified to testify regarding a drug's regulatory compliance even when their work done at FDA did not include review of draft labeling and they only received general "regulatory science" training).

[194] *See* AstraZeneca's Mem. in Supp. of Mot. to Exclude Ross 7-10; Takeda's Mem. in Supp. of Mot. to Exclude Ross 7-12.

[195] Ross Expert Report 14-16, Ex. C.

governing pharmaceuticals, including the process for obtaining initial approval, how and when a manufacturer may seek to modify label warnings and the applicable regulations, and FDA's historical practice in considering such applications.[196] He described his methodology based on his education, training, and experience at FDA applying the applicable FDA regulations.[197] While Defendants may disagree with his analysis, it cannot fairly be said that his methodology is not systematic and explained.

An expert's methodology is reliable 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.[198] As noted above, courts have found the experience at FDA to be particularly valuable for FDA experts testifying on regulatory issues, especially when coupled with additional industry or academic experience.

The cases relied upon by Defendants are distinguishable and reflect extreme situations not presented here. In *In re Trasylol Prods. Liab. Litig.*, Dr. Suzanne Parisian's report suffered from several fatal flaws not present in this case.[199] First, unlike in this case, there was a substantial question whether Dr. Parisian, whose FDA experience related to medical devices, was qualified to testify regarding FDA

[196] Ross Expert Report 19-73.
[197] *See* Ross Expert Report 15-16.
[198] *See* Fed. R. Evid. 702; *Paoli*, 35 F.3d at 741.
[199] *In re Trasylol Prods. Liab. Litig.*, 709 F. Supp. 2d 1323 (S.D. Fla. 2010).

regulatory processes involving pharmaceuticals, which are subject to different regulations and handled by a separate division.[200] Second, in *Trasylol*, Dr. Parisian's conclusion required a causal opinion that she could not give.[201] Third, Dr. Parisian "conducted only a cursory and conclusory look at Trasylol from the perspective of the plaintiffs in this case" and included problematic opinions based exclusively on speculation concerning FDA's and Bayer's intent, including statements that Bayer continued to expand the Trasylol sales force when they were aware that FDA changed its risk-benefit profile and assumptions about FDA's concerns regarding the warnings.[202] Fourth, as Defendants correctly noted, the court in *Trasylol* found that Dr. Parisian generally took a collection of facts, speculated to impute motive, and drew unsupported conclusions unrelated to her regulatory expertise.[203] Dr. Ross's report is far different from Dr. Parisian's report. Rather, Dr. Ross's report is an in-depth review and analysis of voluminous records, data, peer-reviewed literature and data analysis of the type he regularly reviewed at FDA and from which he draws supported conclusions related to his regulatory expertise that he adequately explains. Finally, unlike in this case, *Trasylol* involved a witness whom the court

[200] *Id.* at 1331.
[201] *Id.*
[202] *Id.* at 1338.
[203] *See id.* at 1348; AstraZeneca's Mem. in Supp. of Mot. to Exclude Ross 9.

found to be evasive and not credible when questioned and who had been repeatedly rejected as an expert or criticized by other courts.[204]

*In re TMI Litiga*tion is similarly distinguishable in that the expert Dr. Vladimir Shevchenko's methodology was open to attack due to his admission that he relied on "his own ipse dixit, rather than on something more verifiable" and that his methodology changed in response to challenges.[205]

It is clear that Dr. Ross, with a decade of experience reviewing INDs, NDAs, labeling proposals, and adverse drug event data and recommending

---

[204] *See, e.g.*, *Trasylol*, 709 F. Supp. 2d at 1345 n.29 ("In the past, courts have had trouble limiting Dr. Parisian's testimony, despite her and the plaintiffs[']assurance, that she would not exceed its proper scope. . . . Dr. Parisian also demonstrated at the *Daubert* hearing that she was unable or unwilling to connect her opinions to any valuable regulatory expert analysis and opined on matters that were far beyond her expertise." (citation omitted)); *see also Rowland v. Novartis Pharms. Corp.*, 9 F. Supp. 3d 553 (W.D. Pa. 2014) (excluding Dr. Parisian's causation testimony); *Bartoli v. Novartis Pharms. Corp.*, No. 3:13-0724, 2014 U.S. Dist. LEXIS 52956 (M.D. Pa. Apr. 17, 2014) (limiting Dr. Parisian's regulatory testimony and excluding all her other proposed testimony); *In re Human Tissue Prods. Liab. Litig.*, 582 F. Supp. 2d 644 (D.N.J. 2008) (finding Dr. Parisian's reliability particularly troubling and granting the motion to exclude); *In re Prempro Prods. Liab. Litig.*, 554 F. Supp. 2d 871, 879-87 (E.D Ark. 2008) (noting that Dr. Parisian's testimony should not have been permitted); *Lopez v. I-Flow Inc.*, No. CV 08-1063, 2011 WL 1897548 at *11 (D. Ariz, Jan. 26, 2011) (finding that Dr. Parisian's testimony lacked reliability and helpfulness to the jury); *Hines v. Wyeth*, No. 2:04-0690, 2011 WL 2680842 at *5 (S.D. W.Va, July 8, 2011) (finding that Dr. Parisian's testimony was "neither relevant nor reliable under *Daubert* and Rule 702"); *In re Fosamax Prods. Liab. Litig.*, 645 F. Supp. 2d 164, 192 (S.D. N.Y. 2009) (limited Dr. Parisian's commentary to explaining the regulatory context in which they were created and stating that she was not permitted to read, quote from, or regurgitate her reports).

[205] *In re TMI Litig.*, 193 F.3d at 687-88.

regulatory action based on his review, is employing a reliable methodology to do the same in these cases.

3. Fit

Defendants argue that Dr. Ross's testimony concerning the potential association between PPIs and ATIN and CTIN should be excluded because it is not a fit with the issues presented in these six Bellwether Trial Cases. Their argument is that because all six plaintiffs claim to have developed CKD, there is no fit between (1) Dr. Ross's proposed testimony regarding the information available to AstraZeneca and Takeda about the association between PPI use and development of ATIN and CTIN and his conclusion that the labeling at various points in time was inadequate and (2) the injuries claimed by the plaintiffs in the six Bellwether Trial Cases.

In making this argument, Defendants ignore the scientific/medical relationship between ATIN/CTIN and CKD, oversimplify and misstate the failure to warn claims made by these plaintiffs, and take isolated testimony given by Dr. Ross about CKD entirely out of context.

The crux of Defendants' lack of fit argument is that the PSC is alleging that AstraZeneca and Takeda failed to warn specifically of an association between PPI use and CKD and that Dr. Ross's testimony pertains to whether and when AstraZeneca and Takeda had sufficient information about an association between

PPI use and development of ATIN or CTIN. This argument misses the point. The PSC argues that AstraZeneca and Takeda were on notice as early as 1995 of an association between ATIN and PPI use, and by 2003 of an association between CTIN and PPI use, and that they should have provided adequate warnings of these associations because, among other things, these conditions can lead to CKD.[206]

Dr. Ross's report likewise makes it clear that ATIN or CTIN are relevant to this litigation because if these conditions develop and are undetected and/or left untreated, they can lead to CKD.[207] Dr. Ross's report contains a lengthy and detailed review of scientific publications, clinical trial data, and post-marketing adverse event data linking PPI use with ATIN and CTIN.[208] Based upon these data, he concluded, "The connection between acute and chronic injury in the tubulointerstitium is grounded in the understanding that interstitial nephritis constitutes "a final common pathway to all forms of end-stage renal disease.'"[209]

He further concludes that the risk that PPI use could have an adverse effect on the kidneys was known to AstraZeneca and Takeda by the late 1990's and that "the

---

[206] PSC's Mem. in Supp. of its Opp'n to Takeda's Mot. to Exclude Test. of Dr. David Ross 5-6, ECF No. 745 ("PPI use is known to cause a kidney injury known as interstitial nephritis ("IN"), now called tubulointerstitial nephritis ("TIN"). It has been recognized for decades that TIN can manifest as acute tubulointerstitial nephritis ("ATIN") or chronic tubulointerstitial nephritis ("CTIN") and that both of these entities separately can lead to [CKD] and End Stage Renal Disease ("ESRD").")

[207] Ross Expert Report 94-98.

[208] Ross Expert Report 98-248.

[209] Ross Expert Report 270.

threshold of reasonable evidence of a causal association between PPI use and chronic, progressive renal toxicity was crossed by early 2003."[210] Failure to warn of this risk, in Dr. Ross's view, resulted in the lack of monitoring and treatment of PPI users so that the renal injury would go undetected until it had progressed to CKD.[211]

With this context, Defendants' reliance on two quotes from Dr. Ross do not support Defendants' argument of lack of fit. AstraZeneca asserts that "Dr. Ross testified unequivocally during his deposition that the conditions with which he was concerned, ATIN and CTIN, are different ailments from CKD."[212] Of course Dr. Ross made this distinction, because ATIN and CTIN are in fact different from CKD. However, this argument ignores Dr. Ross's views that are discussed above about the relevance of ATIN and CTIN to this litigation – that left untreated, they can and do lead to CKD. Similarly, Defendants cite the statement in Dr. Ross's report that "[i]n 2016, Lazarus *et al*, was the first group of scientists to report on the association between PPI and CKD" for the proposition that there could be no failure to warn claim prior to 2016.[213] Again, that is not an accurate characterization of Dr. Ross's opinions, which link ATIN and CTIN to potential development of CKD.

[210] Ross Expert Report 271-272.
[211] Ross Expert Report 272-274.
[212] AstraZeneca's Mem. in Supp. of Mot. to Exclude Ross 5.
[213] Ross Expert Report 133.

Defendants will of course present experts who disagree with Dr. Ross's conclusions and will cross-examine him vigorously, and the jury will need to decide who is right on this critical issue. However, there is no question that Dr. Ross's proposed testimony bears directly on key issues in this litigation.

4. Additional Arguments

a. AstraZeneca

AstraZeneca makes two additional arguments for excluding portions of Dr. Ross's testimony. First, it argues that any testimony relating to FDA's understanding of the difference between ATIN and CTIN should be excluded. In Dr. Ross's deposition, AstraZeneca's counsel asked him whether he thought FDA understood the difference and he responded that he did not.[214] I do not understand that the PSC intends to offer affirmative testimony by Dr. Ross regarding FDA's understanding of the difference between ATIN and CTIN. Further, it is not entirely clear to me why AstraZeneca chose to elicit this testimony at his deposition. In any event, it would be speculative and should not be offered at trial, and to that extent, I recommend granting AstraZeneca's motion.[215] However, if on cross-examination at trial AstraZeneca

[214] AstraZeneca's Mem. in Supp. of Mot. to Exclude Ross, Ex. B [hereinafter Ross Dep.] at 318:19-319:1, No. 2:17-cv-06124, ECF No. 33-3 ("Q. You think FDA understands the difference between acute ATIN and chronic TIN for purposes of labeling? . . . The Witness: All I can say is they do not. They say acute or chronic so . . . .").

[215] *Paoli*, 35 F.3d at 742.

seeks to use Dr. Ross's deposition testimony, or again to elicit testimony from Dr. Ross that he believes FDA did not understand the difference between ATIN and CTIN, for purposes of impeachment or otherwise, then AstraZeneca will have opened the door to such testimony and it should be permitted.[216]

Second, AstraZeneca seeks to exclude any testimony about FDA's staffing and resources. To the extent Dr. Ross is relying both upon his personal experience at FDA and upon objective evidence of such issues, including FDA staffing and enforcement data, at or around the period when he contends newly acquired information warranted additional PPI label warnings (*e.g.*, the 2007 Institute of Medicine report),[217] he should be permitted to testify as to that evidence.[218] However, I recommend that AstraZeneca's motion be granted to exclude any speculative testimony about FDA's resources in 2020 and their impact on the agency's ability to negotiate labeling changes at that time.[219] Dr. Ross's tenure at FDA ended in 2006 so that his personal experience is not likely to be relevant to the staffing and resources of the agency fourteen years later.

---

[216] *Healy v. Haverford Twp.*, 462 Fed. Appx. 224 (3d Cir. 2012) **(**"The doctrine of 'opening the door,' sometimes referred to as 'curative admissibility,' provides that when one party introduces inadmissible evidence, the opposing party thereafter may introduce inadmissible evidence to rebut or explain the prior evidence." (citing *Gov't of V.I. v. Archibald*, 987 F.2d 180, 187 (3d Cir. 1993)).

[217] Ross Expert Report 48 n.36.

[218] *See, e.g.*, Ross Expert Report 12-14.

[219] *See* Fed. R. Evid. 611.

b. Takeda

Takeda likewise makes two additional arguments for excluding portions of Dr. Ross's testimony, both of which should be rejected. First, it argues that Dr. Ross's testimony concerning the language that he believes should have been in the labeling "by 1995" is an impermissible attack on the initial FDA-approved Prevacid labeling and thus, by law, must be excluded. In support of this argument, it cites one First Circuit case, *Celexa*, which found that a plaintiff's claim about the inadequacy of the initial labeling was preempted.[220] Takeda then cites cases excluding testimony that was found to be contrary to established law.[221] The *Celexa* holding, however, is far from established law. For example, *Gaetano v. Gilead Scis., Inc.*, a decision from the District of New Jersey that found that there was no law preventing Gilead from implementing stronger warning language prior to approval so there was no preemption, was not even cited by Takeda.[222] Further, one of the cases cited by Takeda, *Stube v. Pfizer*,[223] directly contradicts the *Celexa* holding, finding that defendants could have submitted stronger warning language prior to the approval of the drug, and thus there

[220] Takeda's Mem. in Supp. of Mot. to Exclude Ross 13 (citing *In re Celexa and Lexapro Marketing and Sales Prac. Litig.*, 779 F.3d 34 (1st Cir. 2015)).
[221] Takeda's Mem. in Supp. of Mot. to Exclude Ross 13-14 (citing *Terry II*, 2016 U.S. Dist. LEXIS 117594; *In re Gadolinium-based Contrast Agents Prods. Liab. Litig.*, No. 1:08-GD-50000, 2010 U.S. Dist. LEXIS 43444 (N.D. Ohio May 4, 2010)).
[222] *Gaetano v. Gilead Scis., Inc.*, 529 F. Supp. 3d 333, 345 (D.N.J. 2021).
[223] 446 F. Supp. 3d 424, 435-36 (W.D. Ark. 2020).

was no preemption.[224] That appears to be exactly Dr. Ross's opinion here, and there is no legal basis to argue that such testimony should be excluded.

Second, Takeda also makes a cursory argument that Dr. Ross's testimony about Takeda's conduct regarding their regulatory obligations somehow constitutes a fraud on the FDA claim. They provide no legal support for this proposition, and, as the PSC points out, there is case law finding that former FDA officials relying on their training and experience at FDA may testify as to the appropriateness of a company's regulatory conduct.[225]

B. Dr. Martin Wells

The PSC has proffered the testimony of Dr. Martin Wells, a biostatistician at the University of Chicago, to analyze Defendants' 2016 submissions to PRAC regarding the safety of their PPI products.[226] Dr. Wells performed meta-analyses of data submitted by AstraZeneca and Takeda to PRAC in 2016 and opines that his analyses show a statistically significant decrease in renal function, as measured by eGFR, in PPI

[224] *See* Takeda's Mot. to Exclude Ross 13-14 (citing *Stube v. Pfizer, Inc.*, 446 F. Supp. 3d 424, 435-36 (W.D. Ark. 2020)).
[225] PSC's Mem. in Supp. of its Opp'n to Takeda's Mot. to Exclude Test. of Dr. David Ross 43 (citing *In re Mirena IUD Prods. Liab. Litig.*, 169 F. Supp. 3d 396, 480 (S.D.N.Y. 2016); *Kruszka v. Novartis Pharms. Corp.*, 28 F. Supp. 3d 920, 931 (D. Minn. 2014)).
[226] PSC's Mem. in Opp'n to Defs.' Mot. to Exclude Op. Test. from Dr. Martin T. Wells 5, ECF No. 739 [hereinafter PSC's Opp'n Mem. to Wells].

users as compared to non-users.[227] AstraZeneca and Takeda challenge Dr. Wells's opinions as unreliable claiming that he (1) first performed an analysis of AstraZeneca's data including their four-week studies and then, because he was unhappy with the result, excluded those four-week studies from his analysis so as to get his desired result, and (2) lacked a valid basis for including data from the eight-week AstraZeneca study in his analyses of AstraZeneca's data.[228] Defendants also argue that his opinion does not fit the issues in these cases.[229] The PSC subsequently stipulated that it does not oppose the Defendants' motions to the extent they seek to prevent Dr. Wells from offering an opinion on general causation that PPIs cause CKD or an opinion that Dr. Wells's analyses establish that PPIs are harmful to the kidneys.[230]

For the reasons set forth below, I recommend that the Court grant the Defendants' motions to the extent that they prohibit Dr. Wells from offering an opinion that PPIs cause CKD or an opinion that his analyses establish that PPIs are harmful to the kidneys, per the PSC's stipulation, but recommend denying the

---

[227] Mem. in Supp. of AstraZeneca's Mot. to Exclude Expert Test. of Dr. Martin Wells, Ex. D at 9-10 [hereinafter Wells Expert Report] No. 2:17-cv-00850, ECF No. 34-5.
[228] *See* AstraZeneca's Mem. of Law in Supp. of Defs.' Mot. to Exclude Expert Test. of Dr. Martin Wells 9-11, No. 2:17-cv-00850, ECF No. 34-1 [hereinafter Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells]; AstraZeneca and Takeda's Joint Mem. in Supp. of Defs.' Mot. to Exclude Expert Test. of Dr. Martin Wells 9-11, No. 2:17-cv-06124, ECF No. 76-1 [hereinafter Defs.' Joint Mem. to Exclude Wells].
[229] *See* Mem. in Supp. of Defs.' Mot. to Exclude Wells 4; Defs.' Joint Mem. to Exclude Wells 4.
[230] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 11.

Defendants' motions to exclude Dr. Wells' testimony to the extent that evidence regarding PRAC or its conclusions is offered into evidence at trial in any of the six Bellwether Trial Cases.[231]

1. Qualifications

Defendants do not challenge Dr. Wells's qualifications, and there is no basis in the record to question his qualifications to offer his stated opinions.

2. Reliability

AstraZeneca and Takeda assert that Dr. Wells's opinions are unreliable because he found a statistically significant decrease in eGFR in PPI users only after allegedly "cherry-picking" the data by excluding the results of studies involving only four weeks of use.[232]

---

[231] At oral argument, in response to my question whether AstraZeneca would be offering PRAC data at trial, AstraZeneca's counsel stated that "AstraZeneca intends to move to exclude foreign regulatory [submissions]" and one should "not assume that [AstraZeneca] will be relying on PRAC at trial." Oral Args. 15:15-20, Apr. 4, 2022. In the *Rieder* case, while AstraZeneca moved to exclude evidence of PPI labels approved by foreign regulatory agencies, neither party moved to exclude all evidence of data submitted to PRAC. AstraZeneca's Mot. *In Limine* to Exclude Evid. of Foreign PPI Labels, No. 2:19-cv-00850, No. ECF 60.

[232] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells 12; Mem. in Supp. of Defs.' Mot. to Exclude Wells 12. Defendants also criticize Dr. Wells for not including an analysis of all 22 AstraZeneca trials in his expert report. However, AstraZeneca's counsel received the data files from plaintiffs' counsel and questioned Dr. Wells about the files at his deposition. *See* AstraZeneca's Mot. to Exclude Wells, Ex. B [hereinafter Wells Dep.] at 46:10-48:4, No. 2:19-cv-00850, ECF No. 34-4; *see also Reed v. Binder*, 165 F.R.D. 424, 429 (D.N.J. Mar. 27, 1996) ("The test of a[n expert] report is whether it was sufficiently complete, detailed and in compliance with the [Federal Rules of Civil Procedure] so that surprise is eliminated, unnecessary

Dr. Wells's testimony is unclear as to precisely when he decided to exclude AstraZeneca's four-week studies from his analysis of AstraZeneca's data. Dr. Wells testified that his decision to exclude the four-week studies was not made after he completed an initial analysis of the AstraZeneca data; rather, he did so "early on" when he read a comment by a PRAC member that highlighted the potential issues with studies shorter than twelve weeks and when he became aware that Takeda, in contrast to AstraZeneca, had submitted only those studies to PRAC that were longer than three months, consistent with the PRAC member's comment.[233] Dr. Wells testified that that he "wanted to follow the same rules across . . . the two analyses. And so that's when [he] made the decision" to exclude the data from the four-week studies from his analysis of AstraZeneca data.[234] Other parts of Dr. Wells's testimony are a bit murkier as to

---

depositions are avoided, and costs are reduced."). As set forth in more detail herein, Defendants, however, have not demonstrated that Dr. Wells decided to exclude the four-week studies after performing an initial analysis of AstraZeneca's data.

[233] Wells Dep. 83:1-21. European Meds. Ass'n, Signal Assessment Report 11 ("The limitation in duration [of renal function adverse events in clinical trials ≥ 12 weeks duration] is based on the Kidney Disease Outcomes Quality Initiative (KDOQI) definition of CKD."). At the time of Takeda's submissions to PRAC, KDOQI defined CKD as the presence of kidney damage and/or decreased GFR for three or more months. *Compare* Nat'l Kidney Foundation, Kidney Disease Outcomes Quality Initiative, Clinical Practice Guidelines For Chronic Kidney Disease: Evaluation, Classification and Stratification 44-59 (2002), https://www.kidney.org/sites/default/files/docs/ckd_evaluation_classification_stratification.pdf (EMA definition), *with* Kidney Disease Improving Global Outcomes, KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease 5 (2012), https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf.

[234] Wells Dep. 83:13-21.

exactly when he made the decision to exclude the four-week studies.[235] However, Defendants have not identified any testimony that he actually performed any statistical analysis of the AstraZeneca data before he decided to exclude the four-week studies.

Dr. Wells has provided other explanations for his decision to exclude four-week studies: the comment by the PRAC member;[236] his discussions with Dr. Lafayette and Dr. Powers, whom Dr. Wells understood to say that they would not expect to see elevated eGFR in four weeks;[237] his review of literature;[238] and the results of his heterogeneity analysis of the data of the four-week studies.[239] Thus, even if he decided to exclude the four-week studies after he performed an initial analysis of all 22 studies from AstraZeneca's PRAC data, Dr. Wells has adequately explained his reasons for doing so.

---

[235] Dr. Wells testified that one of the reasons he did not need to do a subgroup analysis before excluding the four-week studies from the AstraZeneca data from his analysis was because had spoken to two nephrologists retained by plaintiffs' counsel in this litigation, Dr. Richard Lafayette and Dr. David Powers, and they told Dr. Wells that the four-week studies would not show an effect. Wells Dep. 142:9-143:3. At another point, Dr. Wells testified that he could not remember whether he had performed any statistical analysis prior to speaking to them in around February or March 2021. Wells Dep. 145:14-24. At another point, Dr. Wells testified that it was his intent to exclude the four-week studies from his analysis of AstraZeneca's data before he performed any of his statistical analyses because he "wanted to have a balance between what Takeda did and what AstraZeneca did." Wells Dep. 83:22-84:10.

[236] Wells Dep. 83:13-21.

[237] Wells Dep. 170:24-172:12.

[238] Wells Dep. 145:19-146:3, 147:4-7.

[239] AstraZeneca's Mot. to Exclude Wells, Ex. C [hereinafter Wells Expert Report] at 6-7, App. A at Figures 1-2, No. 2:19-cv-00850, ECF No. 34-5.

Defendants also argue that Dr. Wells's analyses are internally inconsistent – and thus unreliable – because he included an eight-week study in his analysis of the AstraZeneca data but only used twelve-week studies in his analysis of the Takeda data. They point to the decisions in the *Byetta* litigation for the proposition that such disparate treatment is arbitrary and undercuts the reliability of his opinion.[240] However, this is not the apples-to-apples comparison the Defendants suggest – there were no Takeda studies under twelve-weeks submitted to PRAC. Viewing Dr. Wells's decision as to include all studies greater than four-weeks in his analyses, he has treated the AstraZeneca and Takeda data the same. It is simply because there are no Takeda studies under twelve weeks that were submitted to PRAC that there are none included in his analyses of Takeda's data.

To the extent Defendants are arguing that Dr. Wells's inclusion of the eight-week AstraZeneca study data undercuts reliability because it is inconsistent with one of his grounds for exclusion of the AstraZeneca four-week study data, the argument is unpersuasive.[241] As explained above, while Dr. Wells did note that one of his grounds for excluding four-week study data was that Takeda had not submitted data

[240] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells 8; Mem. in Supp. of Defs.' Mot. to Exclude Wells 8; *In re Incretin-Based Therapies Prods. Liab. Litig.*, 524 F. Supp. 3d 1007, 1038 (S.D. Cal. 2021); *In re Byetta Cases*, No. JCCP4574, 2021 WL 2462800, at *5-6 (Cal. Super. Ct. Apr. 6, 2021.

[241] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells 10-11; Mem. in Supp. of Defs.' Mot. to Exclude Wells 10-11.

from studies less than twelve weeks' duration, his testimony also reflected other grounds for excluding studies of four weeks' duration. To the extent Defendants seek to challenge Dr. Wells on his decisions, it is a matter for cross-examination as to the explanations he has provided, not a basis for exclusion.[242]

AstraZeneca and Takeda cite out-of-circuit federal and state court decisions in litigation involving the drug Byetta, in which Dr. Wells's testimony was excluded as unreliable.[243] The facts in those cases are distinguishable. In those cases, unlike here, Dr. Wells could not explain why it made sense to exclude data from one randomized clinical trial ("RCT") but not another, and it was the plaintiffs' counsel who decided which data to exclude from his analysis.[244] Unlike in this case, in *Byetta*, Dr. Wells erroneously excluded a study from his meta-analysis based on a misunderstanding of the facts about that study and did not correct that error when he learned of the correct facts.[245]

---

[242] *Daubert*, 509 U.S. at 596; *see also Heller*, 167 F.3d at 152.
[243] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells 8 (citing *In re Incretin-Based Therapies Prods. Liab. Litig.*, 524 F. Supp. 3d at 1037-40; *In re Byetta Cases*, 2021 WL 2462800, at *5-6); Mem. in Supp. of Defs.' Mot. to Exclude Wells 8 (citing same).
[244] *See In re Incretin-Based Therapies Prods. Liab. Litig.*, 524 F. Supp. 3 at 1038; *In re Byetta Cases*, 2021 WL 2462800, at *5-6.
[245] *See In re Byetta Cases*, 2021 WL 2462800, at *6; *In re Incretin-Based Therapies Prods. Liab. Litig.*, 524 F. Supp. at 1038.

Defendants' final challenge to the reliability of Dr. Wells's testimony is that he used summary statistics instead of patient-level data.[246] While Defendants argue that patient-level data of all of the AstraZeneca studies would change his results, they do not argue that patient-level data of the same studies Dr. Wells actually used, excluding the four-week studies, would change the results of the analyses that Dr. Wells performed. Further, Defendants do not dispute that the summary-level data that Dr. Wells analyzed were data that they themselves provided to PRAC and fail to explain why relying on those summary-level data, even if they were not the best data, should result in exclusion of his testimony. Rather, these points are ones that Defendants can make on cross-examination.

3. Fit

AstraZeneca and Takeda also challenge Dr. Wells's testimony on the grounds that it does not fit the case because it pertains only to their PRAC submissions, which they may choose not to introduce at trial.[247] While AstraZeneca's counsel indicated at oral argument that one cannot assume AstraZeneca will introduce PRAC data at trial, neither Plaintiff Rieder nor AstraZeneca sought to exclude or limit evidence of PRAC in their motions *in*

[246] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells 11; Mem. in Supp. of Defs.' Mot. to Exclude Wells 11.
[247] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells 4-7; Defs.' Joint Mem. to Exclude Wells 4-7.

limine. Takeda's counsel indicated at oral argument that Takeda does not plan to introduce PRAC data at trial.[248]

At this time, it is unclear whether evidence of data provided to PRAC or PRAC's analysis or conclusions will be introduced into evidence at trial in any of the six Bellwether Trial Cases. To the extent such evidence is admissible, Dr. Wells's analysis satisfies the fit prong.

C. Dr. David Charytan

The PSC seeks to offer an opinion on general causation from Dr. David Charytan that the use of PPIs increases the risk of adverse renal outcomes, including development of CKD. AstraZeneca has moved to exclude Dr. Charytan, claiming that his testimony is unreliable because he purportedly used a conclusion-oriented methodology for evaluating medical literature and studies and he was purportedly inconsistent and biased in the weight that he gave to the study findings that support his opinion.[249] For the reasons set forth below, I recommend that AstraZeneca's motion to exclude Dr. Charytan's general causation testimony be denied.

1. Qualifications

AstraZeneca does not challenge Dr. Charytan's qualifications, and there is no basis in the record to question his qualifications to offer his stated opinions.

---

[248] Oral Args. 16:3-7, Apr. 4, 2022.

[249] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 17-23, No. 2:19-cv-00850, ECF No. 37-1.

2. Reliability

a. Use of Bradford Hill Criteria

Dr. Charytan's testimony is based upon a significant body of medical literature that he opines supports a causal relationship between PPIs and CKD. He reviewed observational studies, including Lazarus *et al.* (2016) and Xie *et al.* (2016), and meta-analyses of observational studies, as well as individual case reports and case series.[250] He concluded that "the observational studies, in the aggregate" demonstrate a causal relationship between PPI use and kidney disease.[251] In forming his opinion, Dr. Charytan relied on the Bradford Hill criteria, nine metrics commonly used by epidemiologists to distinguish a causal connection from a mere association.[252]

AstraZeneca does not dispute that the Bradford Hill criteria are a well-recognized methodology for assessing causation that can satisfy the *Daubert* reliability standard.[253] However, AstraZeneca relies on the Third Circuit's statement

---

[250] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts, Ex. BB [hereinafter Charytan Expert Report] at 19-22, No. 2:19-cv-00850, ECF No. 37-30.

[251] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts, Ex. C at 201:3-13 [hereinafter Charytan Dep.] No. 2:19-cv-00850, ECF No. 37-5.

[252] *See* Charytan Expert Report 34-37; *see, e.g.*, *In re: Zoloft*, 858 F.3d at 795 (citing and explaining Bradford Hill criteria).

[253] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 15-16; *In re: Zoloft*, 858 F.3d at 796; *Glynn v. Merck Sharp & Dohme Corp. (In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.)*, No. 11-5304, 2013 U.S. Dist. LEXIS 51552, at *10 (D.N.J. Apr. 10, 2013).

that "[t]o ensure that the Bradford Hill/weight of the evidence criteria 'is truly a methodology, rather than a mere conclusion-oriented selection process . . . there must be a scientific method of weighting that is used and explained.'"[254] AstraZeneca argues that Dr. Charytan's assessment of study findings using the Bradford Hill criteria was "arbitrary" and that the methodology he applied to evaluate and weigh these study findings was a "conclusion-oriented selection process" as opposed to "scientific method."[255]

The Third Circuit has held that if an expert applies a recognized methodology unevenly "without explanation, this raises an inference of unreliable application of methodology."[256] Accordingly, in assessing reliability, it is necessary to address the Dr. Charytan's application of the Bradford Hill criteria and his explanations for any apparent inconsistencies.

b. Application of Bradford Hill Criteria

Dr. Charytan explained at considerable length his application of the Bradford Hill criteria and his underlying reasoning in affording varying degrees of weight to the numerous studies he reviewed.[257] His expert report and deposition testimony

---

[254] *In re: Zoloft*, 858 F.3d at 796 (citing *Magistrini v. One Hour Martinizing Dry Cleaning*, 180 F. Supp. 2d 584, 607 (D.N.J. 2002)).
[255] *See In re: Zoloft*, 858 F.3d at 796.
[256] *Id.* at 797.
[257] Three pages of his expert report and a significant portion of his deposition testimony discuss each of the nine Bradford Hill criteria in relation to the medical literature he reviewed. *See* Charytan Expert Report 34-37; Charytan Dep. 187:11-215:23.

discuss the numerous randomized controlled trials ("RCTs"), observational studies, reports, and case series that he reviewed before offering his opinion that there is an increased risk of CKD when using PPIs.[258] Dr. Charytan's report and testimony also reflect that he identified and discussed the comparative strengths and weaknesses of different types of studies (*e.g.*, RCTs vs. observational studies),[259] as well as design and other limitations that affect the reliability of those studies in detecting potential causal relationships.[260]

Thus, to the extent Dr. Charytan does not give all of the literature equal weight, that decision is not "without explanation" and therefore does not, on its face, undermine the reliability of his application of the Bradford Hill criteria.[261] As a general matter, criticisms of an expert's explanations for reliance on, or rejection of, particular studies, are appropriately addressed through cross-examination, not through wholesale exclusion of the expert testimony.[262] That is the appropriate course here.

---

[258] Charytan Expert Report 16-24.
[259] Charytan Dep. 190:5-191:25, 260:7-266:17, 272:4-8, 302:1-304:1.
[260] *See* Charytan Expert Report 19-24; Charytan Dep. 192:9-194:19, 303:22-318:6.
[261] *See In re: Zolo*ft, 858 F.3d at 797.
[262] *See Hoffeditz*, 2017 U.S. Dist. LEXIS 123493, at *13-14. In its reply brief, AstraZeneca cites *Loeffel Steel Prods., Inc. v. Delta Brands, Inc.*, 387 F. Supp. 2d 794, 800 (N.D. Ill. 2005), but that out-of-circuit case is factually distinguishable. *See* Reply Mem. in Further Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 3, No. 2:19-cv-00850, ECF No. 55. There, unlike here, the court excluded the testimony as unreliable because the expert used a unique, idiosyncratic definition of an economic term that was not peer-reviewed or generally accepted in the profession and relied on defendant-provided information the validity of which he was "incapable of assessing." *Loeffel Steel Prods., Inc.*, 387 F. Supp. 2d at 803-07.

AstraZeneca's other specific criticisms do not demonstrate that Dr. Charytan's methodology was so arbitrary and unreliable as to require exclusion under Rule 702 and *Daubert*.

First, AstraZeneca criticizes Dr. Charytan for not applying a specific evaluation tool when assessing "the potential for bias in each of the observational studies on which he relies."[263] In particular, AstraZeneca argues that Dr. Charytan's disagreement with a conclusion in an FDA Department of Epidemiology review that the Lazarus *et al.* (2016) and Xie *et al.* (2016) studies suffered from design flaws which precluded finding a causation link between the use of PPIs and developing CKD is unreliable because he did not use "any formal tool to assess it."[264] However, AstraZeneca cites no law requiring the use of a "formal tool." Dr. Charytan explained his reasoning: he testified that he believed FDA's findings were too conservative and failed to look at some evidence and science that he would have considered.[265] The issue implicated here – "evaluation of possible biases or confounding factors found in the studies" – is properly addressed through cross-examination, rather than exclusion.[266]

---

[263] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 22.
[264] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 23.
[265] Charytan Dep. 292:2-294:12.
[266] *See* PSC's Mem. in Opp'n to AstraZeneca's Mot. to Exclude Pls.' General Causation 9, ECF No. 743; *Fosamax* 2013 U.S. Dist. LEXIS 51552, at *10-11 (allowing a general

Second, AstraZeneca asserts that Dr. Charytan's criticism of the reliability of the Moayyedi *et al.* 2019 study because of, among other things, its reliance on telephone interviews, while simultaneously relying on the Lazarus study, which also used telephone interviews, is inconsistent and arbitrary.[267] Dr. Charytan testified, however, that it is not the telephone interview technique itself that can result in bias, but the purpose and execution of the telephone interviews,[268] which he evaluated when determining how to assess the risk of bias.[269] He explained that the Moayyedi study failed to explain sufficiently how investigators obtained information during their phone calls.[270] Dr. Charytan also noted additional grounds for questioning the reliability of the Moayyedi study.[271] Dr. Charytan has provided an explanation for

---

causation expert to testify when the expert's methodology was sufficiently reliable and explicitly noting that any issues could be addressed on cross-examination).

[267] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 19.

[268] Charytan Dep. 306:8-13, 307:7-9. Dr. Charytan admitted the bias introduced by the use of the telephone to obtain information would be present in RCT and observational studies and explains, "you have to get into the weeds and figure out exactly what questions they asked, when they were asking it, how, what information they were seeking, but…it's not specific to the telephone interview per se, or the use of telephone…I think it depends on the questions asked…and the information being looked for."

[269] Charytan Dep. 305:8-308:2.

[270] *See* Charytan Dep.306:8-308:13; Charytan Expert Report 23.

[271] These additional grounds included that the PPI portion of the study was designed to detect gastrointestinal bleeding prevention as opposed to CKD; creatinine levels, which are a common indicator of kidney function, were only tested during initial screening instead of with routine checks; and over 22% of the participants already had CKD at the start of the study. Charytan Expert Report 22-23.

the purported inconsistencies that AstraZeneca can probe and challenge on cross-examination.

Third, AstraZeneca criticizes Dr. Charytan's conclusion that the three-year follow up period in Moayyedi "may have been too short to detect most cases of CKD."[272] Dr. Charytan identified several reasons why a longer reporting period may be preferential, including under-reporting or delayed reporting of symptoms when interviewed during studies or questioned by doctors in less-obvious cases.[273] Again, AstraZeneca can challenge Dr. Charytan's explanation on cross-examination.

Finally, AstraZeneca argues that Dr. Charytan should have given more weight than he did to the Attwood article, which did not identify CKD as a serious adverse event associated with PPI use.[274] The Attwood article summarizes certain safety data obtained from two AstraZeneca trials, titled SOPRAN and LOTUS, where researchers studied the effects of PPIs omeprazole and esomeprazole, respectively.[275] Dr. Charytan provided several reasons why he does not believe the

---

[272] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 19; Charytan Dep. 306:14-307:9, 308:3-8.
[273] *See* Charytan Dep. 169:7-172:10.
[274] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 20.
[275] Stephen E. Attwood *et al.*, *Long-term safety of proton pump inhibitor therapy assessed under controlled, randomized clinical trial conditions: data from the SOPRAN and LOTUS studies*, 41 Alimentary Pharmacology & Therapeutics 1162, 1162 (2015).

findings of the two trials disprove his opinion that PPI use can cause CKD.[276] The trials were designed to evaluate the effectiveness of PPIs, rather than renal safety. There was no detailed description of the data on kidney function reported. The mean age of participants was young, and the trials excluded people with "significant comorbidities, suggesting that they enrolled populations at low risk of kidney disease."[277] The sample sizes for the two trials were small, 154 and 266 participants, respectively.[278] In short, Dr. Charytan provided an explanation for why the fact that CKD was not identified as a serious adverse event associated with PPI use during either the SOPRAN or LOTUS trials did not necessarily mean that PPI use is not a risk factor for development of renal disease.[279] Again, AstraZeneca can cross-examine him as to whatever flaws it sees in that explanation.[280]

3. Fit

AstraZeneca does not challenge the fit of Dr. Charytan's testimony, and there is no basis in the record to question the fit of his testimony.

---

[276] Charytan Expert Report 23.
[277] Charytan Expert Report 23.
[278] Charytan Expert Report 23.
[279] Charytan Expert Report 23.
[280] Dr. Charytan explained that CKD "would rarely be reported as a [serious adverse event ("SAE")] because it's generally not going to be considered as an SAE unless you're specifically looking for it in the trial and defining it as such" and that "this would be an issue where trying to assess the occurrence of CKD in a clinical trial on the basis of SAE reports would likely lead to marked under-counting of the events." Charytan Dep. 313:6-9, 314:13-16.

D. Dr. Wajahat Mehal

The PSC proffered Dr. Wajahat Mehal, a gastroenterologist and professor at the Yale School of Medicine, to testify regarding general causation, the adequacy of Nexium labeling, and issues regarding marketing and purported overprescribing of PPIs. AstraZeneca moved to exclude all of Dr. Mehal's testimony, arguing that he is not qualified to testify regarding marketing and the adequacy of labeling, his testimony regarding general causation is unreliable, and his testimony regarding an objective test for diagnosing gastroesophageal reflux disease ("GERD") is irrelevant and does not fit the case.[281] The PSC subsequently agreed that it does not oppose AstraZeneca's motion to the extent it seeks to prevent Dr. Mehal from testifying "on the adequacy of the label in a regulatory context."[282]

For the reasons set forth below, I recommend that the motion to exclude Dr. Mehal be granted to the extent it seeks to prevent Dr. Mehal from testifying about the adequacy of the labeling in the regulatory context, per the stipulation from the PSC, medical marketing generally, and the impact of medical marketing on sales, but otherwise denied. However, this would not prevent Dr. Mehal from testifying about the "Montreal definition" in cases where specific testing for GERD did not occur.

---

[281] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 33-35.

[282] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 10.

1. Qualifications

AstraZeneca argues that Dr. Mehal is not qualified to offer an expert opinion on the adequacy of labeling or on the role of medical marketing and its impact on the prescribing of PPI products.[283]

Dr. Mehal earned his medical degree from the University of Oxford in England in 1989 and subsequently completed his residency in internal medicine and fellowship in gastroenterology at the Yale School of Medicine.[284] He has been on the faculty at Yale since 2001.[285] He has been board-certified in internal medicine since 1997 and obtained a sub-certification in gastroenterology in 2001.[286] He is currently a tenured Professor of Medicine, a practicing clinician specializing in digestive diseases and gastroenterology, and a researcher in the areas of gastrointestinal disease and tissue injury and repair.[287]

At his deposition, Dr. Mehal testified that he is not a regulatory expert "so [he] won't be speaking about regulatory issues such as label warnings

[283] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 39-40.
[284] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts, Ex. A [hereinafter Mehal Expert Report] at 4-5, No. 2:19-cv-00850, ECF No. 37-3.
[285] Mehal Expert Report 5.
[286] Mehal Expert Report 5.
[287] Mehal Expert Report 5.

specifically."[288] Dr. Mehal and the PSC also stipulated at his deposition that Dr. Mehal will not be offering an opinion about the adequacy of the 2020 labeling.[289] Subsequently, the PSC stipulated that it does not oppose AstraZeneca's motion to the extent it seeks to prevent Dr. Mehal from testifying "on the adequacy of the label in a regulatory context."[290] Thus, there is no dispute that Dr. Mehal cannot testify about the adequacy of the labeling.

Dr. Mehal proposes to opine regarding medical marketing of PPIs and its impact. In his report he cites articles noting the increase in spending on medical marketing across all medications, including PPIs, from 1997 to 2016.[291] He also opines on some concerns regarding medical marketing by citing to articles regarding the economic impact of coupons and rebates and selective information, and notes that marketing strategies include disease awareness campaigns prior to launching a product. He states that changes in medical marketing over the past 20 years have had "direct bearing on the high use of PPIs" and that the large numbers of patients exposed to PPIs worldwide are "attributable in great part to medical marketing efforts of the defendant manufacturers."[292]

---

[288] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts, Ex. B [hereinafter Mehal Dep.] at 360:12-14, No. 2:19-cv-00850, ECF No. 37-4.
[289] Mehal Dep. 357:2-22.
[290] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 10.
[291] Mehal Expert Report 48-49.
[292] Mehal Expert Report 48, 50.

The PSC asserts that Dr. Mehal's opinions regarding medical marketing are based on the marketing he has seen and his clinical judgment as a gastroenterologist and prescriber of PPIs and is supported by peer-reviewed medical literature.[293] However, Dr. Mehal does not identify any marketing he has seen as a clinician or in preparing his testimony, and his citations to information about medical marketing spending overall and general criticisms about medical marketing generally do not provide a basis to link unidentified marketing of unidentified drugs to an increase in PPI use. The PSC does not suggest that Dr. Mehal has any formal training on medical marketing or its impact on sales of PPIs or any particular product. I credit Dr. Mehal's own testimony on the matter when he testified that he is *not* an expert on regulatory labeling or medical marketing issues.[294]

2. Reliability

As with Dr. Charytan, AstraZeneca does not dispute that Dr. Mehal's general causation opinion is based on a review and lengthy discussion of the abundant literature on PPIs, including RCTs, observational studies, reports, case series, and meta-analyses and consideration of the Bradford-Hill factors.[295] And, as with Dr. Charytan, AstraZeneca argues that Dr. Mehal's opinion is not reliable because it

[293] PSC's Mem. in Opp'n to AstraZeneca's Mot. to Exclude Pls.' General Causation 102-04.
[294] Mehal Dep. 80:10-81:21.
[295] *See* Mehal Expert Report 23-47, 52-63; Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 17-24, 33-35.

disagrees with his conclusions regarding the methodological strength and reliability of the various studies and his conclusion that the RCTs are not conclusive on the issue of causation.[296] AstraZeneca argues that Dr. Mehal's analysis was result-driven and he "failed to base his opinion on 'sufficient facts and data' or reliably apply 'principles and methods to the facts of the case' to satisfy Rule 702 standards of admissibility.[297]

In particular, AstraZeneca does not agree with Dr. Mehal's analysis in which he does not deem as dispositive the results of two RCTs, the Moayyedi and Attwood studies, which he determined to be flawed.[298] Dr. Mehal explained that he did not give the Moayyedi and Attwood studies conclusive weight because they "were not specifically designed to investigate whether PPIs cause CKD."[299] His explanation and other discussion in his report are sufficient to satisfy the Third Circuit's *Daubert* reliability standards.[300]

AstraZeneca also asserts that Dr. Mehal "cherry-picked" and did not use a consistent methodology because he did not reject observational studies on which he relied that, like the RCTs, "were not specifically designed" to investigate whether

---

[296] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 33-35.
[297] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 33-35.
[298] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 33-35; Mehal Expert Report 30-32.
[299] Mehal Expert Report 31-32.
[300] *See Heller*, 167 F.3d at 152; *In re TMI Litig.*, 193 F.3d at 665; *Paoli*, 35 F.3d at 744-46; *Hoffeditz*, 2017 U.S. Dist. LEXIS 123493, at *13-14.

PPIs cause CKD.[301] AstraZeneca maintains that this disparate treatment indicates that he did not reliably weigh all the evidence, but instead gave more weight to studies that support his desired conclusion.[302] However, this ignores the extensive explanation in Dr. Mehal's report and deposition of the multiple factors that informed his determination regarding what weight he assigned to a study's findings, including the scale, design, power, and manner of collecting data.[303]

The reliability requirement does not mandate a particular type of study, and AstraZeneca does not cite to any authority that would prohibit an expert from looking beyond RCTs to other types of studies to assess general causation.[304] Here, Dr. Mehal has explained his reasoning for not giving conclusive weight to the RCTs and giving greater weight to other studies. AstraZeneca can cross-examine Dr.

---

[301] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 34.

[302] Reply Mem. in Further Supp. of AstraZeneca's Mot. to Exclude General Causation Experts 33, No. 2:19-cv-00850, ECF No. 55.

[303] *See* Mehal Expert Report 23-47, 52-63; *see also* Mehal Expert Report 25 ("[E]ach of the described lines of evidence have both strengths and weaknesses, but they complement each other. Thus, if the findings are consistent across multiple studies of varying types, even if not perfectly correlated, they provide a very high level of conviction that a cause-and-effect relationship has been established. In addition to examining the types of studies which are providing evidence, it is important to examine the tempo of the findings. Were there a few early studies based on incomplete data, which could not be reproduced, or has the evidence been building up year after year as more data is collected? In my opinion, the latter is true regarding PPI-induced nephrotoxicity of PPIs."); Mehal Dep. 244:7-24, 417:24-418:7.

[304] *See*, *e.g.*, *Heller*, 167 F.3d at 154-55 (declining to require a physician to rely on definitive published studies to make a diagnosis because the physician reliably used a different generally accepted methodology).

Mehal to challenge his reasoning, but I believe that the proposed testimony satisfies the Third Circuit's reliability requirement.

AstraZeneca relies on *Hollander v. Sandoz Pharms. Corp.*[305] to argue that Dr. Mehal's opinion is unreliable because it relies on observational studies which it claims cannot, standing alone, establish causation.[306] But that out-of-circuit case is distinguishable. Unlike in this case, where Dr. Mehal relies on numerous epidemiological studies and meta-analyses, the experts in *Hollander* did not rely on epidemiological studies.[307] And, unlike in *Hollander*, Dr. Mehal is not relying on evidence that the court has determined is unreliable.[308]

AstraZeneca also seeks to exclude Dr. Mehal's proposed testimony that the majority of patients who stop using PPIs resume taking them due to exacerbation of their symptoms because Dr. Mehal based his opinion on studies in healthy patients, not patients with GERD.[309] However, the record reflects that Dr. Mehal based his opinion on studies, multiple peer-reviewed publications, and meta-analyses,[310] as well as his own experience as a practicing gastroenterologist who prescribes PPIs

---

[305] 289 F.3d 1193 (10th Cir. 2002).
[306] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 34.
[307] *Hollander*, 289 F.3d at 1211.
[308] *Id.* at 1208.
[309] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 38.
[310] Mehal Expert Report 15.

for GERD.[311] He testified that in order to determine "whether PPIs can result in rebound, you need to do it in healthy patients, because these are people who don't have GERD. If you do this study in GERD patients…and they get symptoms, it's difficult to know if it's rebound to PPIs or if it's just recurrence of their prior disease."[312] Given Dr. Mehal's experience and the literature upon which he relies, I do not find AstraZeneca's argument persuasive. AstraZeneca can challenge Dr. Mehal on cross-examination on these issues at trial.

3. Fit

Plaintiffs' claims include that "[d]efendants made statements, affirmations and representations of fact concerning their PPI products through their advertisements, educational campaigns and multi-platform marketing and promotional initiatives directed at consumers, patients and healthcare providers promoting unnecessary and dangerous use and overuse of their PPI products."[313] Dr. Mehal opines that the broadened, functional definition of GERD developed at a meeting in Montreal in 2006 (the "Montreal definition") and included in a publication funded by AstraZeneca led to an increase in GERD diagnoses and subsequent "overuse" of PPIs. AstraZeneca argues that Dr. Mehal's testimony on this issue should be excluded because it does not fit the issues in this case.

---

[311] Mehal Dep. 40:4-19.
[312] Mehal Dep. 169:6-13.
[313] Pls.' Master Long Form Compl. and Jury Demand ¶ 381, ECF No. 118.

It is undisputed that PPIs are used to treat GERD. It is also undisputed that plaintiffs' claims include the assertion that multiple defendants overpromoted PPIs through various methods, including educational campaigns. However, not every case involves the allegation that a particular plaintiff was put on PPIs as a result of the Montreal definition. If in any case there is evidence that the individual plaintiff was placed on PPIs as a result of the application of the Montreal definition of GERD, rather than testing specifically confirming GERD, Dr. Mehal's testimony on the issue, as applied to that individual plaintiff, would satisfy the fit standard. Otherwise, I recommend that his proposed testimony on this issue should be excluded.

E. Dr. Derek Fine

The PSC has proffered Dr. Derek Fine, a nephrologist at Johns Hopkins Hospital, as a specific causation expert to testify that Plaintiff Rieder's use of Nexium was a cause of his CKD, as well as the progression of his kidney disease.[314] Dr. Fine has also offered opinions on general causation in a separate report from his opinions on Plaintiff Rieder,[315] but AstraZeneca has not moved to exclude Dr. Fine's

[314] AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts, Ex. X [hereinafter Fine Specific Causation Expert Report] at 8-12, No. 2:19-cv-00850, ECF No. 35-26.

[315] PSC's Br. Opposing Defs.' Mots. for Summ. J. on Failure to Warn Preemption, Ex. 329 [hereinafter Fine General Causation Expert Report], ECF No. 731-83.

general causation opinions.[316] AstraZeneca asserts that Dr. Fine's specific causation testimony as to Plaintiff Rieder should be excluded as unreliable because Dr. Fine purportedly fails to explain why hypertension and obesity are not the only causes of Plaintiff Rieder's CKD and because there is not a sufficient evidentiary basis for Dr. Fine's conclusion that Nexium substantially contributed to Plaintiff Rieder's CKD.[317] For the reasons set forth below, I recommend that AstraZeneca's motion to exclude Dr. Fine's specific causation testimony as to Plaintiff Rieder be denied**.**

1. Qualifications

AstraZeneca does not challenge Dr. Fine's qualifications, and there is no basis in the record to question his qualifications to offer his stated opinions.

2. Reliability

AstraZeneca, relying on *Heller*, argues that Dr. Fine does not reliably explain why hypertension and obesity are not the only causes of Plaintiff Rieder's CKD.[318] In *Heller*, the Third Circuit, citing *Paoli*, stated that "where a defendant points to a plausible alternative cause and the doctor offers *no* explanation for

[316] At oral argument, AstraZeneca's counsel acknowledged that AstraZeneca is not challenging Dr. Fine's testimony on general causation. Oral Args. 118:2-3, Apr. 4, 2022 ("[W]e are not challenging Dr. Fine's general causation report here[.]").
[317] Mem. Of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts 26-27, No. 2:19-cv-00850, ECF No. 35-1 [hereinafter AstraZeneca's Specific Causation Mem.].
[318] AstraZeneca's Specific Causation Mem. 28.

why he or she has concluded that was not the sole cause, that doctor's methodology is unreliable."[319]

Dr. Fine does not dispute that hypertension, when poorly controlled, can cause CKD, but disagrees that hypertension was the sole cause of Plaintiff Rieder's CKD.[320] Dr. Fine testified that Plaintiff Rieder's hypertension was generally well controlled with medication so that his blood pressure was not severely elevated in most of the available readings, with the exception of one time in 2003.[321] As further evidence that hypertension was not the sole cause of Plaintiff Rieder's CKD, Dr. Fine pointed to times when Plaintiff Rieder's GFR was declining even when his blood pressure was well controlled.[322] Dr. Fine explained "there were times when [Plaintiff Rieder's blood pressure] was beautifully controlled, and GFR was still overall declining. So I don't think there is enough evidence to say that hypertension was a substantial contributor."[323]

AstraZeneca challenges Dr. Fine's explanation by noting that the goal for CKD patients is to keep systolic blood pressure at less than 130 mmHg and that Plaintiff Rieder's systolic blood pressure was at or above 130 mmHg on forty-six of the ninety

---

[319] *Heller*, 167 F.3d at 156.
[320] AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts, Ex. Y [hereinafter Fine Dep.] at 71:16-72:3, 160:1-8, No. 2:19-cv-00850, ECF No. 35-27.
[321] Fine Dep. 322:6-10.
[322] Fine Dep. 303:11-305:17.
[323] Fine Dep. 322:11-15.

dates.[324] But AstraZeneca did not question Dr. Fine at his deposition as to the significance, if any, of Plaintiff Rieder's occasionally but not consistently high systolic blood pressure readings or how elevated his systolic blood pressures would need to have been, how consistently, and for how long, in order for Dr. Fine to have considered hypertension to have caused Plaintiff Rieder's CKD. Overall, the record does not support a claim that Dr. Fine has provided no reasoned, scientifically based explanation for his exclusion of hypertension as a sole cause of Plaintiff Rieder's CKD. AstraZeneca can cross-examine Dr. Fine on these points at trial, but it has not shown that his testimony on this issue is so unreliable as warrant exclusion under *Daubert*.

The same is true as to obesity. Dr. Fine acknowledges that obesity has been associated with the development of CKD, although he observes that the actual role of obesity in the etiology of CKD is controversial.[325] Dr. Fine observed that Plaintiff Rieder was only mildly, not extremely, obese.[326] Dr. Fine further opined that the changes in Plaintiff Rieder's creatinine levels (which can indicate kidney disease) over time were inconsistent with kidney disease in a person with his actual level of

[324] Reply Mem. in Further Supp. of AstraZeneca's Mot. to Exclude Specific Causation Experts 31-32, No. 2:19-cv-00850, ECF No. 54.
[325] Fine Specific Causation Expert Report 11 (opining that "[i]t is more likely that obesity instead associates with diabetes and hypertension such that any association of obesity with renal injury is driven by obesity's impact on these two health conditions." (internal citation omitted)).
[326] Fine Dep. 275:2-6.

obesity.[327] AstraZeneca disputes Dr. Fine's conclusions as to the role of obesity in his CKD, arguing that Plaintiff Rieder's BMI was over twenty-five for an extended period of time and that his proteinuria levels decreased when he lost weight.[328] These points are appropriately the subject of cross-examination, but do not support exclusion of Dr. Fine's testimony.

3. Fit

AstraZeneca does not challenge the fit of Dr. Fine's testimony, and there is no basis in the record to question the fit of his testimony.

F. Dr. Gilbert Moeckel

The PSC has proffered the testimony of Dr. Gilbert Moeckel on the animal studies performed by PPI manufacturers, including AstraZeneca and Takeda, as part of the drug approval process. AstraZeneca has moved both to disqualify Dr. Gilbert Moeckel from testifying[329] and to exclude his testimony, contesting his qualifications to opine on animal pathology and the reliability and fit of his testimony.[330] Takeda has also moved to exclude Dr. Moeckel from testifying on the

[327] Fine Dep. 303:19-305:17.
[328] Reply Mem. in Supp. of AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts 32-33, No. 2:19-cv-00850, ECF No. 54.
[329] Mem. of Law in Supp. of AstraZeneca's Mot. to Disqualify Dr. Moeckel, No. 2:19-cv-00850, ECF No. 36-1 [hereinafter AstraZeneca's Mem. to Disqualify Moeckel].
[330] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Dr. Moeckel 1, No. 2:19-cv-00850, ECF No. 35-1 [hereinafter AstraZeneca's Mem. to Exclude Moeckel].

same grounds of qualification, reliability, and fit.[331] The PSC stipulated that it does not oppose the Defendants' motions to the extent that they seek to prevent Dr. Moeckel from offering an opinion that PPIs cause acute or chronic kidney disease in humans or from using animal evidence to prove general causation.[332]

For the reasons set forth below, I recommend that AstraZeneca's motion to disqualify Dr. Moeckel be denied. I recommend that the Defendants' motions to preclude Dr. Moeckel from offering an opinion that PPIs cause acute and chronic kidney disease in humans or from using animal evidence to prove general causation be granted, per the PSC's stipulation, but they be denied as to the rest of Dr. Moeckel's opinions. To the extent that Defendants have raised issues about whether Dr. Moeckel's testimony and opinions are credible and well-supported by the data that he reviewed, they can address such issues through cross-examination of Dr. Moeckel at trial.

1. Motion to Disqualify Dr. Moeckel

AstraZeneca contends that Dr. Moeckel "surreptitiously switched sides" by becoming an expert for plaintiffs after meeting once with counsel for AstraZeneca, leading AstraZeneca to "operate[] under a reasonable assumption that the parties entered a confidential consulting relationship for nearly four years."[333] In

[331] Mem. of Law in Supp. of Takeda's Mot. to Exclude Dr. Moeckel 1-2, No. 2:17-cv-06124, ECF No. 80 [hereinafter Takeda's Mem. to Exclude Moeckel].
[332] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 12.
[333] Mem. of Law in Supp. of AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel 1, No. 2:19-cv-00850, ECF No. 36-1.

opposition, the PSC argues that while Dr. Moeckel met with AstraZeneca's counsel once and subsequently received notebooks with medical literature from them, he was never retained by them nor did he receive any payment from them or learn any confidential information from them.[334] For the reasons set forth below, I recommend that AstraZeneca's Motion to Disqualify Dr. Moeckel be denied.

The record reflects the following facts relevant to AstraZeneca's motion to disqualify: On November 14, 2016, counsel for AstraZeneca from the law firm Ice Miller LLP telephoned Dr. Moeckel and then sent a confirmatory e-mail stating "[t]hank you for your time today to speak with Katherine regarding consulting with us in the Nexium/kidney litigation. At your convenience, would you please forward us your retainer agreement via return e-mail."[335] Two days later, counsel at Ice Miller sent another e-mail reiterating their interest in working with Dr. Moeckel and requesting a CV.[336] In response, Dr. Moeckel provided a fee schedule and a one-page document titled "CONSULTING AGREEMENT BETWEEN DR. GILBERT MOECKEL AND ICEMILLER LEGAL COUNSEL" that was signed by Dr.

[334] *See* AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, Ex. E, [hereinafter Declaration of Katherine Althoff] No. 2:19-cv-00850, ECF No. 36-7; Oral Args. 43:1-44:1, Apr. 4, 2022.
[335] AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, Ex. A [Hawkins E-mail, Nov. 14 & 16, 2016] No. 2:19-cv-00850, ECF No. 36-3.
[336] Hawkins E-mail, Nov. 14 & 16, 2016.

Moeckel.[337] This so-called "Consulting Agreement" contained Dr. Moeckel's fee terms but did not contain any provisions regarding the scope of work or confidentiality. Ice Miller never signed that "Consulting Agreement," nor did it ever provide Dr. Moeckel with any retainer agreement of its own.[338]

Dr. Moeckel met with AstraZeneca's counsel on January 16, 2017, for two hours. AstraZeneca asserts that it shared confidential information with Dr. Moeckel at that meeting and would not have done so if it did not believe that a confidential consulting relationship had existed with him.[339] However, at no time did counsel for AstraZeneca provide Dr. Moeckel with any form of nondisclosure or confidentiality agreement.[340] The PSC argues that no confidential information was disclosed at that meeting; rather, the PSC asserts, based on the declaration of AstraZeneca counsel, that Dr. Moeckel and AstraZeneca counsel discussed the following topics: Dr. Moeckel's professional background and research, medical literature, AstraZeneca's

[337] AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, Ex. C [Legal Fee Schedule] No. 2:19-cv-00850, ECF No. 36-5; AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, Ex. D [hereinafter Consulting Agreement Between Dr. Gilbert Moeckel & IceMiller] No. 2:19-cv-00850, ECF No. 36-6.
[338] Oral Args. 31:3-24, 48:10-49:4, Apr. 4, 2022.
[339] Mem. of Law in Supp. of AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel 5-6. Declaration of Katherine Althoff 2.
[340] Oral Args. 42:11-14, Apr. 4, 2022.

scientific and medical theories, Dr. Moeckel's initial professional opinions, and other potential consulting experts.[341]

On January 30, 2017, AstraZeneca counsel sent Dr. Moeckel two binders containing medical literature about PPIs.[342] Dr. Moeckel testified that he never reviewed them.[343] Counsel for AstraZeneca asserts that 28 of the 30 articles contained in these binders were referenced in his expert report.[344]

AstraZeneca's counsel and Dr. Moeckel had no contact from January 2017 until November 2020. During this period, Dr. Moeckel did not submit any invoices, nor did he receive any payment from AstraZeneca's counsel.[345] When AstraZeneca's counsel contacted Dr. Moeckel in November 2020, he stated, "[u]nfortunately I am not available for legal consultation in the foreseeable future."[346]

Dr. Moeckel began working with Plaintiffs' counsel in late 2018, and his expert report was provided to Defendants in April 2021.[347] He was deposed in July

---

[341] PSC's Resp. to Mot. to Disqualify Moeckel 14-15 (citing Declaration of Katherine Althoff).
[342] Declaration of Katherine Althoff 3.
[343] AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, Ex. B at 209:20-22 [hereinafter Moeckel Dep., July 7, 2021] No. 2:19-cv-00850, ECF No. 38-4.
[344] AstraZeneca's Br. in Resp. to Pls.' Opp'n to Defs.' Mot. to Disqualify Gilbert Moeckel 11 n.8, No. 2:19-cv-00850, ECF No. 49.
[345] *See* Moeckel Dep. 201:9-11, July 7, 2021; Oral Args. 33:22-24, Apr. 4, 2022.
[346] AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, Ex. H [Moeckel E-mail, Nov. 24, 2020] No. 2:19-cv-00850, ECF No. 36-16.
[347] *See* Moeckel Dep. 59:6-8, July 7, 2021; Oral Args. 39:19-20, Apr. 4, 2022 (Mr. Pennock: So it was in November of 2018 that we first started having contact with him.); Declaration of Katherine Althoff 3.

2021, at which time AstraZeneca's counsel first raised the issue of their earlier communications with him.

In the Third Circuit, in determining whether disqualification is appropriate, the court must make two determinations: (1) whether it was "objectively reasonable for the party seeking disqualification to have concluded that a confidential relationship existed with the expert[,]" and (2) whether the party seeking disqualification "disclose[d] any confidential information to the expert[.]"[348]

AstraZeneca argues that it had an objectively reasonable belief that it had retained Dr. Moeckel and shared confidential information with him at the January 2017 meeting and in its selection of materials it sent him thereafter. The PSC and Dr. Moeckel dispute these conclusions. Dr. Moeckel testified at his deposition that he did not believe he had been retained and that he never looked at the notebooks.[349]

In considering whether there was an objectively reasonable belief of retention, courts in the Third Circuit have considered: (1) the length of the relationship and the frequency of contact; (2) whether the moving party funded or directed the formation of the opinion to be offered at trial; (3) whether the parties entered into a formal confidentiality agreement; (4) whether the expert was retained to assist in the

[348] *See Fed. Trade Comm'n v. Innovative Designs, Inc.*, No. 16-1669, 2018 U.S. Dist. LEXIS 42510, at *16-17 (W.D. Pa. Mar 15, 2018); *see also In re Diet Drugs Prods. Liab. Litig.*, No. 07–20144, 2009 WL 1886131, at *3 (D.N.J. June 26, 2009).
[349] Moeckel Dep. 202:6-12, 209:20-22, July 7, 2021.

litigation; (5) whether the expert was paid a fee; and (6) whether the expert was asked to agree not to discuss with opposing parties or counsel.[350] The burden of proof rests on the party moving for disqualification.[351]

While there was undoubtedly sloppiness in documentation and communication by everyone involved, I conclude that, collectively, the facts here do not support an objectively reasonable belief that Dr. Moeckel was retained by AstraZeneca's counsel. First, there is no retention agreement signed by both parties. Dr. Moeckel sent AstraZeneca's counsel a fee schedule and a document that he signed that purported to be a "Consulting Agreement" in November 2016; however, AstraZeneca's counsel never signed it. Nor did AstraZeneca's counsel ever send Dr. Moeckel a standard retainer agreement, as is typical when counsel retain experts for litigation. Such retainer agreements typically contain confidentiality provisions, which Dr. Moeckel's one-page document did not, as well as terms relating to scope of work, payment amount and timing, and billing requirements. Dr. Moeckel's "consulting agreement" looks nothing like a typical expert retainer agreement. It does not appear to be different from his fee schedule other than the document's title.

---

[350] *Innovative Designs, Inc.*, 2018 U.S. Dist. LEXIS 42510, at *17-18 (quoting *Syngenta Seeds, Inc. v. Monsanto Co.*, No. 02-1331, 2004 U.S. Dist. LEXIS 19817, at *2 (D.N.J. Sept. 27, 2004)).

[351] *See, e.g.*, *Syngenta Seeds, Inc.*, No. 02-1331, 2004 U.S. Dist. LEXIS 19817, at *2 (D.N.J. Sept. 27, 2004) (declining to disqualify an expert witness when the moving party did not point to specific confidential information that it disclosed to the expert).

Second, Dr. Moeckel never submitted a bill nor received any compensation from AstraZeneca. Third, the nearly four-year period where there was absolutely no communication between Dr. Moeckel and AstraZeneca's counsel hardly supports a belief that they were working together. Finally, as noted above, there was no confidentiality agreement or other agreement spelling out with whom Dr. Moeckel could or could not communicate.

With regard to disclosure of confidential information, AstraZeneca states in its Motion that during the January 2017 meeting, "Ms. Althoff shared confidential case strategy with Dr. Moeckel and solicited his opinions on key defense arguments as well as on potential consulting experts."[352] However, as noted, AstraZeneca never provided a confidentiality or retention agreement to Dr. Moeckel at that meeting or any other time. It is somewhat incongruous now to assert an expectation that the discussion at that meeting was confidential when no effort at the time was made to memorialize that expectation in a legally binding document, as is commonplace when working with third parties in litigation. Moreover, Dr. Moeckel testified that the topics discussed at that meeting did not involve disclosure of confidential information.[353]

AstraZeneca also asserts that the selection of materials for the binders sent to Dr. Moeckel in January 2017 reflects attorney thought processes and thus are also

[352] AstraZeneca's Mem. to Disqualify Moeckel 12.
[353] Moeckel Dep. 204:7-209:22, July 7, 2021.

confidential information.[354] First, Dr. Moeckel testified that he never looked at these notebooks.[355] The fact that he submitted no bills to AstraZeneca for time spent reviewing them tends to support that testimony. Additionally, AstraZeneca has not presented any evidence that the materials included in the notebooks were not publicly available. The fact that 28 out of 30 of them were referenced in Dr. Moeckel's expert report, according to AstraZeneca, does not prove that he was using confidential information provided to him by AstraZeneca's counsel in his work for plaintiffs; it merely shows that what he was provided were materials relevant to the issues in this litigation.

The factual record does not support an "objectively reasonable" belief that Dr. Moeckel had been retained by AstraZeneca under the criteria utilized by courts in the Third Circuit. Accordingly, I recommend that AstraZeneca's motion to disqualify Dr. Moeckel be denied.

2. Motions to Exclude Dr. Moeckel

AstraZeneca and Takeda argue that Dr. Moeckel's testimony should be excluded under *Daubert* on the grounds that he is not qualified to give the proposed testimony, his methodology is not reliable, and his proposed testimony does not fit with the issues presented in these cases. For the reasons set forth below, I recommend that the motions to exclude Dr. Moeckel's expert testimony be denied.

---

[354] AstraZeneca's Mem. to Disqualify Moeckel 12.
[355] Moeckel Dep. 209:20-22, July 7, 2021.

a. Qualifications

Defendants' fundamental argument is that Dr. Moeckel is not qualified to give the proposed testimony because his primary expertise is in human, not animal, renal pathology.[356] While it is correct that his primary expertise is in human pathology, Dr. Moeckel has also conducted and reviewed animal pathology on multiple occasions throughout his lengthy career.

Dr. Moeckel's general qualifications are undoubtedly impressive. He is a Professor of Pathology at the Yale School of Medicine, where the University named a research laboratory after him.[357] He is board-certified in pathology and has over thirty years of medical experience. He has served as a peer reviewer for the National Science Foundation and the American Heart Association and is on the Editorial Board for several medical journals, including the Journal of the American Society of Nephrology, Nephrology Dialysis & Transplantation, and the Kidney International Scholarly Research Network.[358] He has authored over 100 reports and publications related to CKD.[359] Additionally, his deposition testimony makes clear

[356] AstraZeneca's Mem. to Exclude Moeckel 8; Takeda's Mem. to Exclude Moeckel 8.
[357] AstraZeneca's Mot. to Exclude Op. Test. from Dr. Moeckel, Ex. A, [hereinafter Moeckel Expert Report (AstraZeneca)] No. 2:19-cv-00850, ECF No. 35-3; Takeda's Mot. to Exclude Dr. Moeckel, Ex. B [hereinafter Moeckel Expert Report (Takeda)] No. 2:17-cv-06124, ECF No. 80-4.
[358] Moeckel Expert Report (AstraZeneca) 3; Moeckel Expert Report (Takeda) 4.
[359] Moeckel Expert Report (AstraZeneca) Ex. A 7, 9-10; Moeckel Expert Report (Takeda) Ex. A 7, 9-10.

that he has conducted and reviewed studies relating to renal toxicity in animals on multiple occasions throughout his career.[360] He has been a speaker on a number of topics involving renal toxicity in animals.[361]

The fact that Dr. Moeckel may not have precise expertise relating to beagle kidneys, as argued by AstraZeneca, does not render him unqualified to offer any opinions about preclinical animal studies conducted by the Defendants in the six Bellwether Trial Cases. Rather, the extent of his experience is an appropriate topic for cross-examination at trial. Likewise, Dr. Moeckel's opinions about the presence or absence of CPN in some of the rat studies differ from those of Defendants' experts. Because the Court's gatekeeping function extends only to the reliability of an expert's methodology, not the Court's opinion on the correctness of the expert's conclusions, the discrepancies between the opinions of Dr. Moeckel and Defendants' experts can be addressed through cross-examination at trial.

Third Circuit law makes clear that an expert need not be the best or most qualified to testify at trial.[362] It is quite possible that there are other experts who are

---

[360] *See* Moeckel Dep. 72:11-23, July 7, 2021 (testifying that he looked at hundreds upon hundreds of rat and mouse kidneys and is very familiar with their kidney pathologies).

[361] Moeckel Expert Report (AstraZeneca) Ex. A, at 7, 9-10 (Dr. Moeckel has given presentations on the protective effect of Citrate on renal phosphate crystal formations in rats, and the effect of dietary phosphate and dehydration of crystal formation in rats).

[362] *See Pineda*, 520 F.3d at 244 ("[I]t is an abuse of discretion to exclude testimony simply because the trial court does not deem the proposed expert to be the best

better able to address the animal studies and what they do or do not show. That, however, is not a basis for excluding entirely the testimony of an expert with robust credentials like Dr. Moeckel's.[363]

b. Reliability

Defendants challenge Dr. Moeckel's methodology of reviewing slides of animal kidneys, particularly that the slides were not blinded as to drug administration, he did not use a numerical grading system, he kept only "mental notes" and did not create a written record of his review process, and he only looked at certain studies, excluding ones that were "negative."[364] Essentially, they argue

---

qualified or because the proposed expert does not have the specialization that the court considers most appropriate." (citing *Holbrook v. Lykes Bros. S.S. Co.*, 80 F.3d 777, 782 (3d Cir. 1996)).

[363] It also seems rather incongruous for AstraZeneca to argue on the one hand that Dr. Moeckel should be disqualified because of AstraZeneca's prior communications with him and expressed desire to have him work with them and on the other hand that he is not qualified to testify. Counsel at oral argument attempted to explain this apparent incongruity by asserting that it was their intent to have him testify only as to human pathology. Oral Args. 53:14-16, Apr. 4, 2022. But, since there is no retention agreement spelling out what he was to do, this cannot be confirmed. Furthermore, the materials provided to Dr. Moeckel by AstraZeneca included at least one animal study. Moeckel Expert Report (AstraZeneca) Ex. B; Moeckel Expert Report (Takeda) Ex. B.

[364] AstraZeneca's Reply in Supp. of Defs.' Mot. to Exclude Expert Test. of Dr. Gilbert Moeckel 7, No. 2:19-cv-00850, ECF No. 48 [hereinafter AstraZeneca's Reply Br. on Moeckel] (noting that Dr. Moeckel "specifically stated that he did not take any notes, other than 'mental notes,' and only took screenshots of the slides that looked interesting to him, not all 1,100 available slides"); Takeda's Mem. to Exclude Moeckel 2 (stating that "Dr. Moeckel simply selected a handful of slides that he knew were not in the animal studies control group, made 'mental notes,' and used

that Dr. Moeckel "cherry-picked" data that supported his conclusions and had no discernable methodology.[365]

Defendants have raised legitimate concerns about the objectivity and replicability of Dr. Moeckel's methodology. The question is whether his methodology is so unreliable as to warrant exclusion. While this is a close call, I recommend that the testimony be allowed, recognizing that these methodological issues can be raised during cross-examination to challenge his conclusions.

Defendants rely on *In re Diet Drugs*, which excluded an expert's proposed testimony that utilized a scientifically unreliable methodology.[366] In that case, the expert, Dr. Colin Bloor, visually observed pathology slides from a particular study and recorded narrative descriptions of what he saw in each. He organized those descriptions into verbal categories and then collapsed and converted the categories into numerical scores. Each step was done without reexamining the slides. Because the slides were not prepared in a manner that would best reveal heart structures, Dr. Bloor could only comment to a reasonable degree of medical

---

them in his report, discarding the thousands of other slides that did not support his conclusion.").

[365] AstraZeneca's Reply Br. on Moeckel 2 (arguing that Dr. Moeckel's methodology lacks scientific basis, and his report is premised upon cherry-picked data and litigation-driven, preformulated opinions); Takeda's Mem. to Exclude Moeckel 2.

[366] *See* AstraZeneca's Mem. to Exclude Moeckel 13 (citing *In re Diet Drugs Prods. Liab. Litig.*, No. 99-cv-20593, 2001 U.S. Dist. LEXIS 1174 (E.D. Pa. Feb. 1, 2001); Takeda's Mem. to Exclude Moeckel 13 (citing same).

certainty as to the myocardium of each rat's heart, not the valves that were the heart structure at issue in that case.[367]

The court in *In re Diet Drugs* emphasized the fact that Dr. Bloor's semi-quantitative scoring methodology had not been demonstrated to have a known or potential rate of error, was not shown to be replicable (because Dr. Bloor scored his recategorizations of the narrative descriptions and never actually assigned a numerical score to any of the slides), and did not have any control standards in place for application of the scoring system.[368]

Dr. Moeckel's methodology is distinguishable from Dr. Bloor's in *In re Diet Drugs*. As noted above, Dr. Moeckel's thirty years of experience in reviewing pathology and review of relevant literature informed his analysis. He states that he reviewed thousands of histopathology slides and compared his findings between dosed groups and control groups, males and females, and adults and neonatal animals.[369] He did not create a subjective numerical valuation of data as Dr. Bloor did. His purpose was to evaluate lesions identified by Defendants' pathologists in

[367] *In re Diet Drugs Prods. Liab. Litig.*, No. 99-cv-20593, 2001 U.S. Dist. LEXIS 1174, at *31 (E.D. Pa. Feb. 1, 2001).
[368] *Id.* at *37.
[369] Moeckel Expert Report (AstraZeneca) 7-8; Moeckel Expert Report (Takeda) 6-7.

their review of Defendants' preclinical studies and determine whether he concurred in their characterization.[370]

Dr. Moeckel's methodology is also distinguishable from that described in *Carnegie Mellon Univ. v. Hoffmann-LaRoche, Inc.*, also relied upon by Defendants.[371] In that case, the expert, who had a significant financial interest in the outcome of the litigation, departed from standard practices by reinterpreting published data without considering the quality of the data, experimental controls that refuted his opinion, and more probable explanations for the published results.[372] Unlike that expert, Dr. Moeckel states that he reviewed every slide in the forty studies provided to him by AstraZeneca and Takeda, documented his own pathological findings, and compared his findings to a large body of scientific literature and related materials, ultimately selecting a handful of studies to discuss in his expert reports.[373] Thus, Dr. Moeckel's methodology is "ground[ed] in the methods and procedures of science" and can be appropriately addressed on cross-examination.[374]

---

[370] *See* Moeckel Expert Report (AstraZeneca) 6; Moeckel Expert Report (Takeda) 5-6.
[371] AstraZeneca's Reply Br. on Moeckel 8 (citing *Carnegie Mellon Univ. v. Hoffmann-LaRoche, Inc.*, 55 F. Supp. 2d 1024, 1034 (N.D. Cal 1999)). Takeda's Mem. to Exclude Moeckel 13.
[372] *Carnegie Mellon Univ. v. Hoffmann-LaRoche, Inc.*, 55 F. Supp. 2d 1024, 1034 (N.D. Cal 1999).
[373] *See* Moeckel Expert Report (AstraZeneca) 4-8; Moeckel Expert Report (Takeda) 5-6.
[374] Daubert, 509 U.S. at 590.

The Third Circuit in *Paoli* held that to determine reliability, a court must look at the scientific validity of the methodology upon which the expert bases an opinion.[375] The expert must, at a minimum, identify the methodology or procedures used or explain how they reached their conclusions.[376] While Dr. Moeckel's description of his methodology is not perfect, its flaws can be addressed and highlighted for the jury through cross-examination. On balance, I do not believe the flaws pointed out by Defendants as to Dr. Moeckel's methodology rise to the level of its probative value being substantially outweighed by its prejudicial effect.[377]

c. Fit

The crux of Defendants' argument regarding lack of fit is that Dr. Moeckel's opinions about the presence of CPN versus acute tubular injuries in rat kidneys would not be helpful to a trier of fact in trying to make determinations about the presence or absence of data supporting a link between PPIs and CKD in humans.

Defendants' position seems to be that there is a lack of fit because (1) Dr. Moeckel is opining only about what he sees occurring in the dosed animal group in the preclinical studies, not about the ultimate issue of whether PPIs can cause CKD in humans, and (2) Dr. Moeckel's conclusions about those preclinical studies are that

[375] *Paoli*, 35 F.3d at 742.
[376] *See Sikkelee*, 522 F. Supp. 3d at 158; *see also Buzzerd*, 669 F. Supp. 2d at 514.
[377] *See Bruno*, 2015 U.S. Dist. LEXIS 156339, at *140 (internal quotation omitted).

the animals experienced acute tubular lesions (rather than CPN as AstraZeneca concluded) and that findings of acute lesions are irrelevant to discussions of CKD.

I recommend that these arguments be rejected for two reasons: First, Dr. Moeckel reviewed pathology from animals in preclinical studies submitted to FDA in support of the manufacturers' NDAs for these PPIs. Defendants may not agree with Dr. Moeckel's conclusions and can challenge them on cross-examination, but there is no dispute that animal studies provide FDA, the scientific community, and juries with important information about a drug's safety and efficacy. That Dr. Moeckel is not being offered to testify as to whether PPIs can cause acute or chronic injuries in humans, per the stipulation by the PSC, does not render his observations about these preclinical studies and their proper interpretation irrelevant.

Second, a key issue in this litigation is the relationship between a finding of AKI and CKD. Dr. Moeckel opines that some dosed animals experienced acute lesions in the preclinical studies and that these lesions were incorrectly identified by Defendants as CPN.[378] Defendants will have an opportunity to cross-examine Dr. Moeckel on the significance, if any, of these opinions to the issues in these cases. The fact that they involve acute injuries does not mean they do not fit with the issues

[378] Moeckel Expert Report (AstraZeneca) 26-27; Moeckel Expert Report (Takeda) 21.

in this case, in particular given Dr. Ross's testimony regarding untreated AKIs.[379]

In *Paoli*, the court noted that the standard for valid scientific connection to the pertinent inquiry is higher than bare relevance and must help the trier of fact understand the evidence.[380] Dr. Moeckel's work may not help the jury in making determinations about the presence or absence of a link between PPIs and CKD, but it may be helpful in understanding the nonclinical studies relied upon by Defendants.

V. CONCLUSION

For the reasons set forth herein, I recommend that the *Daubert* and related motions discussed in this Report and Recommendation be decided as set forth above.[381]

A proposed order is attached.

Respectfully submitted,

ELLEN REISMAN
Special Master

[379] *Compare* Moeckel Expert Report (AstraZeneca) 25-27, and Moeckel Expert Report (Takeda) 21, *with* Ross Expert Report 94.

[380] *See Paoli*, 35 F.3d at 743, 745; *Daubert*, 509 U.S. at 591 ("Rule 702's 'helpfulness' standard requires a valid scientific connection to the pertinent inquiry as a precondition to admissibility.").

[381] To the extent the parties have raised in their briefing any arguments not expressly addressed in this R&R, I have considered them and recommend that they be rejected.

EXHIBIT 1

UNITED STATES DISTRICT COURT

DISTRICT OF NEW JERSEY

_____

IN RE: PROTON-PUMP INHIBITOR PRODUCTS LIABILITY LITIGATION

2:17-MD-2789(CCC)(MF)

(MDL 2789)

Judge Claire C. Cecchi

This Document Relates to:

All Actions

_____

- - -

REMOTE HEARING

BEFORE SPECIAL MASTER ELLEN REISMAN

Monday, April 4, 2022

- - -

This is the Remote Hearing In Re: Proton-Pump Inhibitor Products Liability Litigation, commencing at 10:00 a.m., Monday, April 4, 2022, before Juliana F. Zajicek, Registered Professional Reporter, Certified Shorthand Reporter and Certified Realtime Reporter.

– – –

A P P E A R A N C E S :
(All Parties Appeared Remotely)

ON BEHALF OF THE PLAINTIFFS:

LAMINACK, PIRTLE & MARTINES LLP
5020 Montrose Boulevard, 9th Floor
Houston, Texas 77006-6533
713-292-2750
BY: BUFFY MARTINES, ESQ.
buffym@lpm-triallaw.com

MORGAN & MORGAN
333 West Vine Street, Suite 1200
Lexington, Kentucky 40507
859-899-8785
BY: JOSH AUTRY, ESQ.
jautry@forthepeople.com

MORGAN & MORGAN
350 Fifth Avenue, Suite 6705
New York, New York 10118
212-738-6299
BY: PAUL PENNOCK, ESQ.
ppennock@forthepeople.com;
JONATHAN M. SEDGH, ESQ.
jsedgh@forthepeople.com

DOUGLAS & LONDON, P.C.
59 Maiden Lane, 6th Floor
New York, New York 10038
212-566-7500
BY: MICHAEL LONDON, ESQ.
mlondon@douglasandlondon.com;
STEPHANIE O'CONNOR, ESQ.
soconnor@douglasandlondon.com;
ANNE (BESS) E. DeVAUGHN, ESQ.
bdevaughn@douglasandlondon.com;
SARA CASTRONUOVA, ESQ.
scastronuova@douglasandlondon.com

A P P E A R A N C E S :
(All Parties Appeared Remotely)

ON BEHALF OF THE PLAINTIFFS (Continued):
ANAPOL WEISS
One Logan Square
130 North 18th Street, Suite 1600
Philadelphia, Pennsylvania 19103
215-735-0773
BY: TRACY A. FINKEN, ESQ.
tfinken@anapolweiss.com

ON BEHALF OF DEFENDANT ASTRAZENECA PHARMACEUTICALS LP AND ASTRAZENECA LP:
ARNOLD & PORTER KAYE SCHOLER LLP
250 West 55th Street
New York, New York 10019-9710
212-836-8572
BY: ARTHUR E. BROWN, ESQ.
arthur.brown@arnoldporter.com;
JULIE B. DU PONT, ESQ.
julie.dupont@arnoldporter.com;
JEFFREY H. HOROWITZ, ESQ.
jeffrey.horowitz@arnoldporter.com;
MICHAEL SCHISSEL, ESQ.
michael.schissel@arnoldporter.com;
THOMAS BIRD, ESQ.
thomas.bird@arnoldporter.com;
JAKE MILLER, ESQ.
jake.miller@arnoldporter.com;

WILLIAMS & CONNOLLY LLP
725 Twelfth Street, N.W.
Washington, D.C. 20005
202-434-5567
by: JESSICA BODGER RYDSTROM, ESQ.
jrydstrom@wc.com;
ANDREW RUDGE, ESQ.
arudge@wc.com;
J. LIAT ROME, ESQ.
lrome@wc.com

A P P E A R A N C E S :
(All Parties Appeared Remotely)

ON BEHALF OF DEFENDANT ASTRAZENECA PHARMACEUTICALS LP AND ASTRAZENECA LP (Continued):

ICE MILLER LLP
One American Square, Suite 2900
Indianapolis, Indiana 46282-0200
317-236-5924
BY: KATHERINE D. ALTHOFF, ESQ.
katherine.althoff@icemiller.com;
OLGA VOINAREVICH, ESQ.
olga.voinarevich@icemiller.com

ON BEHALF OF GLAXOSMITHKLINE:

REED SMITH LLP
Three Logan Square
1717 Arch Street, Suite 3100
Philadelphia, Pennsylvania 19103
215-851-8121
BY: STEPHEN J. McCONNELL, ESQ.
smcconnell@reedsmith.com

ON BEHALF OF PROCTOR & GAMBLE:

ULMER & BERNE LLP
312 Walnut Street, Suite 1400
Cincinnati, Ohio 45202-4029
513-698-5000
BY: GINA M. SAELINGER, ESQ.
gsaelinger@ulmer.com

ON BEHALF OF PFIZER:

DLA PIPER
51 John F. Kennedy Parkway, Suite 120
Short Hills, New Jersey 07078-2704
BY: STEPHEN C. MATTHEWS, ESQ.
stephen.matthews@dlapiper.com;
ANDREW ANDRZEJEWSKI, ESQ.
andrew.andrzejewski@dlapiper.com

A P P E A R A N C E S :
(All Parties Appeared Remotely)

ON BEHALF OF PFIZER (Continued):
DLA PIPER
33 Arch Street , 26th Floor
Boston, Massachusetts 02110-1447
617-406-6046
BY: KATIE INSOGNA, ESQ.
katie.insogna@dlapiper

DLA PIPER
1251 Avenue of the Ameircas
New York, New York 10020-1104
212-335-4846
BY: LOREN H. BROWN, ESQ.
loren.brown@dlapiper.com

ON BEHALF OF DEFENDANTS TAKEDA/ABBOTT:
TUCKER & ELLIS LLP
233 South Wacker Drive, Suite 6950
Chicago, Illinois 60606
312-624-6307
BY: JAMES W. MIZGALA, ESQ.
james.mizgala@tuckerellis.com

TUCKER ELLIS LLP
950 Main Avenue, Suite 1100
Cleveland, Ohio 44113
216-696-4456
BY: MICHAEL J. RUTTINGER, ESQ.
michael.ruttinger@tuckerellis.com

TUCKER ELLIS LLP
515 South Flower Street, Forty-Second Floor
Los Angeles, California 90071
720-897-4401
BY: K. MICHELE ANDERSON, ESQ.
michele.anderson@tuckerellis.com

A P P E A R A N C E S :
(All Parties Appeared Remotely)

ON BEHALF OF DEFENDANTS TAKEDA/ABBOTT (Continued):

VENABLE LLP
750 East Pratt Street, Suite 900
Baltimore, Maryland 21202
410-244-7400
BY: JASON C. ROSE, ESQ.
jcrose@venable.com
CRAIG A. THOMPSON, ESQ.
cathompson@venable.com

ALSO PRESENT:

ETHAN GREENE, ESQ.
ANDY KARRON, ESQ.
JULIAN MOSS, Law Clerk;
Reisman Karron Greene LLP
DANIEL HEALEY
MEG THOMPSON
Morgan & Morgan

DARCELLE ADLER, ESQ.
Senior Counsel at AbbVie
LEO RAKITIN, ESQ.
Senior Counsel at AstraZeneca

EMILY SY, ESQ.
Litigation Counsel at Takeda;
MARGARET IVES, ESQ.
U.S. Litigation & Investigations, Takeda

THE SPECIAL MASTER: All right. So let's go on the record. And so what we are doing today is oral argument on the various Daubert motions and on our defense motions for summary judgment. And a couple of things I just wanted to say upfront.

I looked at the outline that we did, the procedures outline, and I think we left out the Mann -- Mann's name on -- on the oral argument on plaintiffs' omnibus motion to exclude experts. I think it should have been on there.

I also noted that it looks to me like we are having argument on four plaintiff experts and five defense experts and I -- you know, the timeframes are a little bit longer as to the plaintiffs' experts, shorter as to the defense experts. I'm obviously, you know, if need be will allow people to have some additional time, although I'm really hoping that we don't end up using all of the time. I think, as I was sitting down and calculating this this morning, it is a lot of time, and believe it or not I have actually read all of this stuff. There are many large notebooks strewn around this room, and because I -- I have to read things in hard copy. So we killed a lot of trees here.

I would appreciate, and I think we said this in the procedures, if there are particular points that you think might be unappreciated from the -- the papers, that you emphasize those, but other -- otherwise, you know, I don't -- you don't need to rehash everything that's in the papers because I've read them and my partner Andy has read them, and so, you know, I think -- I think maybe we could not spend all day together, as delightful as I'm sure that will be.

One thing -- one thing I wanted to raise just in the way of full disclosures upfront, there is -- I don't know any of these experts personally except one who I did meet years ago, somewhere between 15 and 20 years ago, and that's Mary Ann Mann, and I think I had one meeting with her in connection with a case I was working on at the time. Not surprising, I've been doing this for 37 years. Honestly, I would have thought more of them might have crossed my path, but -- but I just wanted people to know that in the interest of full disclosure.

So with that, let's get started and somebody should raise their hand, whoever is going to address the motion.

I think Wells is the first one?

Okay.

MS. DU PONT: Good morning, Special Master. My name is Julie du Pont. I'm going to be speaking on behalf of AstraZeneca.

And if I have your permission, do you mind if I share some slides to assist with my argument?

THE SPECIAL MASTER: Sorry, I'm not the most technologically sophisticated. Yes, it is fine for you to share some slides. Okay.

MS. DU PONT: Can you see those?

THE SPECIAL MASTER: Yes, I can.

MS. DU PONT: Good morning, Special Master. Defendants' brief on Dr. Wells, I think, clearly sets forth the defendants' argument as to why Dr. Wells should be excluded under Daubert, and consistent with what the Special Master just said, I'm not going to belabor and repeat all of those arguments that were set forth in our motions. I think my point today is simply to briefly underscore a few key issues for the Special Master. And that's what I will be doing.

First, the central issue in both Rieder and in Bales that the jury will need to decide is whether PPIs caused each of these plaintiffs' chronic

kidney disease. Tellingly here, we know that Dr. Wells is not offering an opinion about whether PPIs cause chronic kidney disease.

At his deposition he was asked:

"...are you offering an opinion that -- that your calculation and the change in eGFR establishes to a reasonable degree of medical certainty that PPI use can cause kidney injury?"

His answer: "No."

And plaintiffs acknowledge in their motion that they are not offering causation -- that he is not offering causation opinions with respect to PPIs and CKD.

They likewise state --

THE SPECIAL MASTER: Can I ask you a question, can I interrupt and ask you a question?

MS. DU PONT: Sure.

THE SPECIAL MASTER: Are you saying that any expert who says they are not offering causation opinions should be excluded?

MS. DU PONT: No, that's not what I'm saying. What I'm saying is that Dr. Wells' testimony needs to provide -- needs to be relevant to the issue and the issues in this case, and I will add that not only is

he not offering causation opinions, he admits he is not doing any hypothesis testing and that he admits that his opinions don't offer any clinical significance.

THE SPECIAL MASTER: But aren't there a lot of -- I mean, there are other experts, I mean, I've been through all of them now, who are -- who are offering opinions that do not reach the ultimate conclusion of whether a PPI product caused the plaintiff's CKD and they are still providing relevant and admissible evidence, I believe.

So I'm not -- I'm not sure why that would be an -- especially given his field, he is a biostatistician, and they often don't provide causation evidence, they just tell you about the data.

MS. DU PONT: Well, Dr. Wells has in other cases provided causation testimony before, but as you can see, he has not offered that here. And not only is he not offering any causation testimony, as I just mentioned, he is -- he is not even testing any relevant hypothesis through his metaanalysis, including the -- the particular hypothesis that PRAC looked at, and that was plaintiffs' argument, was that he was offering some sort of rebuttal to PRAC's --

PRAC's opinion, but, in fact, he repeatedly admitted that he wasn't doing any hypothesis testing whatsoever, and that he had no knowledge of what PRAC really does generally or specifically did with respect to PPIs here.

So not only is he not offering causation opinion, he doesn't provide any fit to the relevant issues in this case whatsoever.

THE SPECIAL MASTER: Well, one question I had, in the plaintiffs' papers, I think they said that the analyses that he is performing were ones that had been requested by PRAC and not done by AZ, is that correct?

MS. DU PONT: I don't believe that is correct.

What -- what Dr. Wells did was he first conducted the meta-analysis doing what essentially AZ did and PRAC reviewed, which was including the four-week studies. He then did an analysis where he excluded those less than four-week studies, and finally got the opinion that he wanted, that there was a decline in eGFR.

THE SPECIAL MASTER: And so are you saying that there was no legitimate scientific basis for him to exclude -- to exclude the four-week studies and that's -- and is that the basis -- I know in your

papers you say that his methodology was result driven.

Is that the basis for why you say it was result driven?

MS. DU PONT: I mean, I think that -- that Dr. Wells offers the explanation that he spoke with some of the plaintiffs' expert nephrologists and they believed that the four-week studies -- the less than four-week studies, I should say, would not add anything, but that is at odds with what PRAC itself said, first of all. And the fact of the matter is the way in which Dr. Wells conducted his analysis suggests it was with -- it was results driven. And what I mean by that is he -- he says -- he puts in his report only the metaanalysis where he excludes the four-week data.

When asked after the fact at his deposition whether he had conducted analyses including the four-week data, he explained that he actually did that analyses first and that then didn't find a significant decline in kidney function with that analysis. So he did the second analysis excluding those studies and actually found a decline in kidney function.

What is bothersome about that approach is if you thought he was going to conduct the

metaanalysis with his -- the intent to exclude those four-week studies, shouldn't he have done that first and then pressure test it by adding them back in? He did not do so. So his after-the-fact explanation sort of defies common sense.

If it is okay, Special Master, I can move on to our second argument in the brief?

THE SPECIAL MASTER: Yes, go right ahead. Thank you.

MS. DU PONT: And here, and I'll just stop sharing my screen, I just want to emphasize the two courts that have recently excluded Dr. Wells for similar results driven meta-analyses. The first is the In Re Incretin case in the Southern District of California decided just last year, where the court found that he had no adequate scientific reason for his metaanalyses, that his method was arbitrary and not scientifically sound. The second case is In Re Byetta, California Supreme -- Superior Court, also decided last year, again, the court found no scientifically reliable basis for Wells' litigation decision-making where he arbitrarily changed his analysis by excluding certain data from his metaanalysis and got a different result.

Here we know that Dr. Wells arbitrarily excluded several four-week studies after first conducting an analysis that included them. It was only after excluding those studies that he got the significant decline in kidney function. He then only presented that second analysis in his report.

The Special Master should follow the reasoning of In Re Incretin and In Re Byetta and similarly exclude Dr. Wells' opinions here.

And I'll reserve the rest of my time.

Sorry. Do you have another question?

THE SPECIAL MASTER: Okay. Yeah. I assume that you expect to be offering the PRAC data at trial, is that right?

MS. DU PONT: That -- that is not necessarily true. I think the part -- that AstraZeneca intends to move to exclude foreign regulatory. Now, whether or not we win that motion is a -- is a decision yet to be decided, but, no, I would not assume that we will be relying on PRAC at trial.

THE SPECIAL MASTER: I don't think I have any other questions for you. Thank you.

MS. DU PONT: Thank you.

THE SPECIAL MASTER: Who is up next?

Okay, James.

MR. MIZGALA: Good morning, Special Master. I just want to just emphasize a point about PRAC. Takeda did not put PRAC in their preemption and we did our own analysis, our epidemiologist has done his own analysis of the clinical trial data. So we won't be offering the PRAC data, but even if we were, the fact is, is that Wells can't tell you what his analysis mean in terms of the safety of PPIs and no other expert on plaintiffs' side has taken his analysis and said, This is what it means. So what's a jury supposed to do with that when he can't even tell you what the clinical significance of his data is. And I'll reserve the rest of my time unless you have a question.

THE SPECIAL MASTER: Okay. Thanks, Jim.

Who from plaintiffs' side is going to be responding?

Stephanie. Hi.

MS. O'CONNOR: Hi, Ellen. Hi.

THE SPECIAL MASTER: Okay.

MS. O'CONNOR: Stephanie O'Connor for the plaintiffs. And I will be arguing in opposition to both AstraZeneca and Takeda's joint motion, as I

understand it to preclude or exclude Dr. Wells.

First of all, let me say that all Dr. Wells did was take the same data that -- with regard to AstraZeneca, that AstraZeneca produced to PRAC and conducted a metaanalysis that the PRAC actually asked about in the incident of signal CKD detection back in September of 2016. They asked to receive data on all clinical trials that had looked at kidney function data, gave as examples estimated glomerular filtration, or GFR, and asked for a metaanalysis if available.

Now, what the companies did was they provided essentially summary arithmetic measures, summary statistics. They didn't provide individual patient-level data. They provided summaries across studies.

In the case of AstraZeneca, who has conducted over 1600 studies, perhaps even 2,000 studies, up to that number, they submitted 22 studies in response to Question No. 3 from PRAC seeking information on kidney function.

Takeda has conducted hundreds of studies across the three products that they submitted data for, that being lansoprazole, dexlansoprazole, and

pantoprazole, submitted a total of seven studies. All right.

So to the extent that we hear that there was cherry-picking or selection of studies, it is the defendants actually who have engaged in cherry-picking and selective process in providing information to the PRAC.

And the reason it is relevant, not having to do with whether or not PRAC is a foreign regulatory agency, but they cannot use it as both a shield and a sword. They can't say that Dr. Wells can't talk about his statistical interpretation of the same data that was submitted to the regulatory authorities in Europe and yet hold that data up, including in communications with the FDA, to say that the clinical trial data is clean.

In the preemption motion they do talk about the significance of the clinical trial data. I heard your question and answer from Ms. DuPont, and as we sit here today, we don't know what the answer is to that. But Dr. Wells should be able to and the plaintiffs should be able to rebut claims by the manufacturer defendants that their clinical trial data is clean and that there is no problem.

We've heard it throughout this litigation. It started on science day and it has continued through the depositions of practically every expert that I have defended in this case.

THE SPECIAL MASTER: Can I -- can I ask you a question, Stephanie?

So they've made the point that, you know, he is not going to talk about, you know, whether PPI's cause CKD in a particular case or more generally and -- and that I think Mr. Mizgala made a comment that he wouldn't be able to tell what the safety data -- what the data mean for safety purposes.

What exactly is the testimony that you envision this witness offering and how is that relevant to the case.

MS. O'CONNOR: So basically, as we know, and you pointed out in your questioning, Dr. Wells is not a medical doctor. He has conducted a biostatistical analysis, as biostatisticians do, on data, again, submitted by both the manufacturers to PRAC in support of their claim that there is nothing in the clinical trials to be concerned about.

By the time Dr. Wells would testify at trial, we will likely have heard from at least two

nephrologists, board certified nephrologists, and the jury will have learned through the course of the plaintiffs' case what estimated glomerular filtration rate means, or eGFR. And we all know, sitting here, that a reduction in eGFR is associated with renal disease, all right, a reduction of, I believe it is less than 60 milliliters per minute squared for a period of greater than three months.

By the time Dr. Wells gets on the stand, the jury will know what GFR is and he would present the forest plots that are attached as Exhibit A to show where it is the reductions are seen. It is a statistical analysis.

He will explain that everything to the left of 1 as seen in every one of the forest plots for both AZ and for Takeda shows a statistically significant reduction in glomerular filtration rate.

Now, he is not going to, as a nonmedical person, testify about the significance of that. That will be left to the plaintiffs' nephrology experts of whom two have been designated in Mr. Rieder's case.

THE SPECIAL MASTER: I thought I heard one of the -- either Julie or James say that none of the other experts are going to rely on his testimony, his

data.

Is that -- is that correct?

MS. O'CONNOR: I think it is a misstatement of the situation. All of the experts had Dr. Wells' report on their materials considered list.

Dr. Ross discusses, because his report was due about a month later, discusses in detail at Pages, I believe it's 363 and 364 of his report, discusses in detail the Wells' metaanalysis, pointing out that while the defendants could have done it, they didn't, and Dr. Wells did the very type of statistically sound, methodologically sound metaanalysis of their clinical trial data.

The experts have reviewed Dr. Wells' data, they didn't dispute the data, they formed their own opinions, of course, as experts must and do, but they did consider Dr. Wells' analysis.

THE SPECIAL MASTER: Okay. Before we run out of time, I wanted to ask about those two cases where he was excluded. And I don't remember which was which, but one of them did involve, I think, one of the same criticisms the defendants are making here, which is that data were arbitrarily excluded from -- from an analysis and, you know, it seems -- we looked at those

cases as well, and it seems somewhat analogous, frankly, to the facts here.

Do you have any response to that?

MS. O'CONNOR: Yes, I do.

First of all, both of the decisions that they cite to concern Byetta, also known as incretin or vice versa. The first of those two cases, which is the incretin decision, came out in March of 2021 followed within a month by the Byetta decision. The incretin decision is a District Court of California trial court, and the Byetta decision, again, it's the same product or -- same product, is the State Court in California.

So first and foremost, neither of these are Circuit Court cases, appellate-level cases.

I think that there is a difference, if you read -- essentially they are saying the same thing, both the State Court and the -- and the Federal Court.

First and foremost, the claim that there was no scientific basis for the exclusion of the studies that Dr. Wells excluded in that case, all right. Here we have a much, much different situation. As Dr. Wells described, all right, he did three -- basically three things.

First, he reviewed the Signal Assessment report by the rapporteur as well as comments by the member states. That is attached as an exhibit to -- Exhibit 4 to the Wells opposition.

And what I'd like to do, Ellen, if I may, since I think I do have some time left, is read from Page 13 of 26 of Exhibit 4, which is an assessor's comment in a dialogue box in which they are looking at the Takeda data, which is the 12-week or more studies in terms of the duration. And they note that there is a difference, that they submitted studies no less than 12 weeks of duration, and the statement, and I read from that document in the dialogue box:

"It is reasonable to suppose that shorter trials would tend to be less likely to detect events of interest or evidence of changes in kidney function than longer trials because of their shorter duration. It is unlikely that excluding such trials would bias the results of the analysis away from detecting an association between lansoprazole and CKD or kidney dysfunction."

Obviously it includes by definition the four-week studies, the shorter duration studies that Dr. Wells ultimately excluded from his analysis in

arriving at his opinions.

So he saw this information, then he saw that Takeda itself, in submitting its data and its response to the PRAC, indicated that it was relying upon the KDIGO definition of CKD, which I mentioned earlier, that being a GFR less than 60 milliliters per minute squared for a period of greater than three months. By definition, the four-week studies have no relevance.

And finally, the third thing that Dr. Wells did as distinguished from what occurred in the Byetta and the incretin cases is he consulted with two nephrologists who told him, and he disclosed it, they had the opportunity to ask him about it, they asked very little, but they told him that the four-week studies were unlikely to yield any change in GFR that would inform a nephrologist or anyone looking at data like this as to whether there really was a change in renal function.

THE SPECIAL MASTER: Okay. Thanks, Stephanie. I think your time is up, but thank you.

Julie or James, do you want to respond?

MS. DU PONT: I would like to respond, if that's okay.

THE SPECIAL MASTER: Yes, go ahead.

MS. DU PONT: I first just want to point out that Dr. Ross was specifically asked at his deposition whether he was relying on Dr. Wells' analysis and he specifically answered no.

Plaintiffs seem to suggest that Dr. Wells is offering a rebuttal opinion about the kind of analysis that the defendant should have submitted to PRAC, but Dr. Wells has repeatedly admitted that he is not doing any sort of hypothesis testing, including whether he was testing the hypothesis that PRAC was looking at. And, in fact, he has admitted that he doesn't have specific knowledge about what PRAC actually did here or general knowledge about what PRAC does generally.

I'd also add that the preemption issue is a legal issue for the court to decide and does not provide a basis for Dr. Wells to offer any opinions to the jury. The Supreme Court held in Albrecht that:

"We here decide that a judge, not the jury, must decide the preemption question.

"In those contexts where we have determined that the question is 'for the judge and not the jury,' we have also held that 'courts may have to

resolve subsidiary factual disputes' that are part and parcel of the broader legal question."

Simply put, the jury will not be addressing preemption and so what Dr. Wells said about PRAC has no relevance here.

And then, finally, just -- just with respect to -- I'll -- I'll stop there. Thank you.

THE SPECIAL MASTER: Okay. James?

MR. MIZGALA: Just quickly.

Ms. O'Connor mentioned that Wells is going to get up and talk about his analysis and then the jury is going to hear that and somehow the jury is going to know what the clinical significance of an -- of his findings are, because these nephrologists, which she didn't name, but the two at issue are Fine and Powers, and I'm looking at Dr. Powers' deposition transcript, and he says that Dr. Wells' report is not one that he had reviewed in connection with this case.

So there -- those opinions have never been disclosed, that any one -- any one of their experts has relied on Dr. Wells' analysis. It is not in their response. You'll notice there is a footnote that starts going down that road, but it is incomplete, and so they can't point to any affirmative evidence that

any of their experts have relied on Dr. Wells' analysis.

What they want to do is throw it out there and let the jury speculate as to what it means, and that's -- that's just not right.

THE SPECIAL MASTER: Okay. Thanks.

MS. O'CONNOR: Ellen, I'm sorry, may I just address one thing?

THE SPECIAL MASTER: Sure.

MS. O'CONNOR: Please allow me. Thank you. I appreciate it.

With respect to -- I'll just address AZ's argument, I think I've already said what it is that we would prepare, how we would present Dr. Wells. I've heard more than once and I've seen in the papers this business about hypothesis testing.

Dr. Wells -- first of all, the EMA didn't ask for hypothesis testing. They asked for a metaanalysis and a metaanalysis includes significance testing, the calculation of confidence intervals. That is something that neither AZ or Takeda did, but Dr. Wells did it.

And why did he do it? Because you just can't, to use an analogy, have a jigsaw puzzle with a

thousand pieces, put it on the table and say here it is. What you have to do is you've got to connect the dots, you've got to put the pieces together, present the picture and show what it means. And you do it in a statistical interpretation and analysis by doing calculations of confidence intervals by doing significance testing, none of which was done by either of the defendants in this case.

THE SPECIAL MASTER: Okay. Thank you.

All right. Let's move on to Gilbert Moeckel, and I think there are two motions pending with regard to him. One is the qualification motion and one is a motion to exclude his testimony.

And who is going to argue that one?

Okay. Katherine, go ahead.

MS. ALTHOFF: Hi, good morning, Special Master. My name is Katherine Althoff. I don't think we've met before. So I am pleased to meet you today.

THE SPECIAL MASTER: Nice to meet you.

MS. ALTHOFF: Nice to meet you. I am representing AstraZeneca on these motions and my colleague James Mizgala from Takeda is also going to be, I think, speaking on these motions as well.

As you saw, the motion to disqualify

really relates to AstraZeneca, but the motion to exclude addresses both defendants. So I actually have a few slides that I'm going to share as well here.

THE SPECIAL MASTER: I'd like to start with the --

MS. ALTHOFF: Sure.

THE SPECIAL MASTER: -- the motions to disqualify, if we can, because I think, you know, that obviously is -- is -- well, I'd just like to start with that one.

MS. ALTHOFF: I agree, because if the -- you know, if he is disqualified then in fact there is not much to talk about on a motion to exclude. So I think you should -- do you have it in front of you, can you see it?

THE SPECIAL MASTER: Yes, we see it.

MS. ALTHOFF: Okay. Great.

So, your Honor, again, with regard to -- Special Master, with regard to the motion to disqualify, this one relates to AstraZeneca, and I'm not -- for some reason it is not wanting to -- let's see if I can get it to go down here. Well, it worked this morning. There we go. All right.

And specifically here with regard to the

motion to disqualify, Special Master, what I tried to do on this opening slide was really say for you really why this should be granted.

And here we have Dr. Moeckel's own statement, which is: "I am very interested in working with Ice Miller and Katherine," that Katherine is me, "on the interesting Astra[Z] legal cases."

And this, of course, statement was made by Dr. Moeckel a very long time ago at the very inception of this litigation when we were starting to look for general causation-type experts in this litigation, not knowing who our particular plaintiffs were, there was no bellwethers yet, we did not know about Mr. Rieder yet or Mr. Bales, but we were looking for general kidney pathologists and in particular human pathologists, and that's why I was reaching out to Dr. Moeckel.

So it's important here, I think --

THE SPECIAL MASTER: Okay. Can I --

MS. ALTHOFF: Yes, go ahead.

THE SPECIAL MASTER: You may have this already, but, I mean, we've looked at some of the case law, and, I mean, I guess one of the key issues is I saw in, I guess it was your papers, a consulting agreement

that he sent over to you.

MS. ALTHOFF: Yes.

THE SPECIAL MASTER: Was there ever a consulting agreement -- I mean, I assume in cases like these you have a standard consulting agreement that you sign with all of your experts.

Was such a consulting agreement ever signed by both parties or was -- did you ever sign the agreement that he sent over?

MS. ALTHOFF: So, that's a good question, and what happened here was Dr. Moeckel, and actually if we go to this next slide we should be able to get it here. So, in fact, that consulting agreement I think is up on the screen right now, and --

THE SPECIAL MASTER: Yeah.

MS. ALTHOFF: Yeah. And so Dr. Moeckel sent that to us and we responded with an e-mail that said, Yes, we absolutely would like to engage you as a consultant.

So did we sign the same document that he sent us, no. Instead we responded with an e-mail and it actually came from me. And then, thereafter, you know, in reliance on that we went forward and met with him.

THE SPECIAL MASTER: Do you have a copy of your e-mail in the PowerPoint here?

MS. ALTHOFF: Not in the PowerPoint, but it would be an exhibit to our motion, Special Master, because it would be attached to my declaration.

THE SPECIAL MASTER: Okay. And -- okay. Keep going.

MS. ALTHOFF: Yeah, sure.

So what happens next. Let's see here. I don't know why this is not advancing correctly. All right. There we go.

So I met with Dr. Moeckel. This was not simply a case as some of the ones that have been cited in some of the motion with regard to a single phone call or where you blast a bunch of experts with materials. This is not that case.

I actually flew to New Haven, Connecticut and met with Dr. Moeckel. I spent two hours in his office and I had a roadmap of things I wanted to talk to him about and met with him for two hours. We talked about everything from his background and expertise as a human kidney pathologist, not working for the plaintiffs in this case, but then also talked with him about who we had retained, who we were

thinking about retaining. These were not only experts that would ultimately be disclosed in this case but also consulting experts.

We talked to him about the plaintiffs, what we expected to be their mechanistic theories, we talked to him about our mechanistic theories, and at the end of that two-hour meeting, I asked him again if he continued to want to meet with us and he said he did.

And so I asked him what next steps would be, and he said, Please send me some materials, which I did. I sent him two binders of materials of literature, medical literature and scientific literature from this case, which ultimately I would say showed up on his materials considered list.

THE SPECIAL MASTER: Okay. Can I ask you a question?

MS. ALTHOFF: Absolutely.

THE SPECIAL MASTER: Was he paid? Have you ever -- has AstraZeneca ever paid him for any of the time he spent meeting or reviewing that literature?

MS. ALTHOFF: That's a good question. I mean, I will tell you no, we did not send him payment. He told us he would expect payment. He sent us his fee

schedule, which is in our papers, told us how much he would charge us.

As is the case often with these experts, until they get closer to writing their report they don't send a bill and he didn't. He didn't send a bill, he didn't tell me he didn't want to, he didn't tell me that he didn't expect to be paid. He told me he expected to be paid. He just never sent a bill.

THE SPECIAL MASTER: Did you ever ask him for a bill?

MS. ALTHOFF: Not that I recall. No, not that I recall.

THE SPECIAL MASTER: Okay. Okay. I mean, I'm just trying to go through the criteria that I think a lot of the case law has looked at.

Let me ask you, there is a long period, and I can see it on your -- on your timeline from '17 to '20. That's a long time not to be in touch.

Was there any contact between anyone on your side of the table with him in that roughly three-year period checking in with him, that kind of thing, any of that?

MS. ALTHOFF: No, and here is why. Dr. Moeckel was not going to be someone who looked at particular

bellwether cases and looked at medical records or even biopsies. We only have one case in the initial bellwethers that has a biopsy. And so really we wanted him to look at medical literature and give general testimony, if called, from a pathologist's perspective.

And so there really was no reason during that period of time to check back in with him. We had talked with him, we knew what his preliminary opinions were, and the parties were busy in the bellwethers taking depositions, looking at particular plaintiffs and that really wasn't going to be his role.

And I think the questions that your Honor -- that, Special Master, you are asking, really, go to the Syngenta factors or, you know, whichever type of case you want to look at, and whether we had an objectively reasonable belief that we had retained him.

And what I would say to that is, I think the best piece of evidence there is not only the consulting agreement that he signed, but also the fact that I reached back out to him in November of 2020. If I didn't think I had retained him, why would I reach out to him again and ask him to, you know, start

meeting with me to put together an expert report.

THE SPECIAL MASTER: Um-hum, okay. I think we found Exhibit D. And is this the e-mail that says:

"We thank you for your e-mail and fee schedule. Please do not hesitate to contact me or Katherine for any questions. We look forward to working with you and will be in touch."

Is that what you're -- I just want to make sure that's the document?

MS. ALTHOFF: I think so. There were several e-mails around that time, but that was -- yeah, that works.

THE SPECIAL MASTER: And when did you first -- maybe you have this in your timeline. When did you first find out that he was working with plaintiffs' counsel? I guess the expert report was submitted in 2021, right?

MS. ALTHOFF: Correct. Yeah, in April of 2021 we got his expert reports and I was as shocked as anyone to see his report in their stack.

We had reached out to him, you know, in November of 2020 and received back, I guess you would say a cryptic e-mail, which is only really cryptic in hindsight where he said he is not available for legal

consultation in the foreseeable future. But if we take ourselves back to November of 2020, I will tell you we were hearing that kind of thing from lots of healthcare providers who were busy with COVID or their organizations were limiting, you know, their contact outside of the hospital because of COVID. And so when I got it, I was disappointed because we were interested in working with him as a human renal pathologist, but I was -- it didn't tell me, Boy, I think he has switched sides. It never, never crossed my mind until I got the expert report.

THE SPECIAL MASTER: Okay. And then at that point what did you do?

MS. ALTHOFF: Well, we noticed his deposition along with, you know, all of the other experts, and I took his deposition.

THE SPECIAL MASTER: Okay.

MS. ALTHOFF: And asked him about it.

THE SPECIAL MASTER: And did you reach out to plaintiffs' counsel at that time to say, What's going on here or anything like that?

MS. ALTHOFF: No. We took the deposition and, frankly, I wanted to hear what the expert had to say with regard to, you know, was he going to say I told

them all along or any such thing. It was a bit of an awkward situation.

THE SPECIAL MASTER: Okay. I think we are down to about 15 seconds according to my timekeeper here.

Is there anything else that you wanted to add, take another minute or two?

MS. ALTHOFF: No. I think, you know, if you look at the situation, I do think we have an objectively reasonable belief that we had a confidential consulting relationship based on the facts here, and this is just not the type of behavior that this -- that the court should countenance. We think he should be excluded on this basis because this is -- you know, it's not going to look good to the jury when you see this and it looks poorly on the judicial process.

THE SPECIAL MASTER: Okay. Thank you.

Who is going to respond for plaintiff side?

MR. PENNOCK: Good morning, Special Master. Paul Pennock for the plaintiff.

THE SPECIAL MASTER: Hi Paul, how are you doing.

Katherine, we still have your screen up, I think.

Still up. There we go. Okay.

All right. Go ahead, Paul.

MR. PENNOCK: Thank you.

First, I probably -- I probably should say and remind the Special Master, at least, as you saw in the papers that we -- I did not know that this contact had taken place, so -- in terms of her -- in terms of her going to meet in Connecticut or anything of that type. I never had, therefore, any conversations with them about those discussions, neither did Bess DeVaughn or Tracy Finken who had been working with him. We knew that a reach out had occurred years earlier and that's it and we didn't question him about it.

THE SPECIAL MASTER: When did you start meeting with him, Paul? When did your team start meeting with him and did you ask him about, you know, whether he had been contacted by any other party?

MR. PENNOCK: So it was in November of 2018 that we first started having contact with him. I was not a part of that at that time. And there was -- as I understand it, he did say the other side reached out to him a couple of years earlier and that's the extent of it from what we knew.

You know, the further exposition of the contact all happened at the deposition. You know, I was surprised by it, on the one hand, but on the other hand I'm glad I hadn't had any discussions with him about it.

So he had really no recollection of it. He didn't even recognize counsel that had been at this meeting. I mean, counsel has testified that it was a two-hour meeting. You know, I don't know that that's borne out. But in any event, he had really no recollection of it, any materials that were sent he did not have, and as far as he was concerned it all ended almost as fast as it began.

And to -- so that's sort of just the context that we were not understanding what had occurred with respect to that until the deposition took place.

I -- you know, we were not told when the report came out what had happened. I can't really lay too much fault at that. You know, I'm just, like, look, she wanted to come him and question him cold on it, take me by surprise, well, that worked, she did.

And I don't lay a lot of blame there, but I think the fundamental issue, at least the first

fundamental issue is whether or not there was this contract. I suppose someone, particularly lawyers, somehow could read into that responsive e-mail that there was a meeting of the minds to form a consulting relationship. I mean, I would suggest it's ambiguous at best, sending that to a doctor saying, he says I'm very interested in going forward and then -- and working with Ms. Althoff and then they respond, We look forward to working with you.

You know, I can tell you that certainly from Dr. Moeckel's point of view, he did not have a consulting relationship with them. They had left it there. They never went forward and they did not sign the document that he sent to them asking them to sign, which to him, you know, you can see why to him that would indicate they don't want me. I've sent them my deal. They've not signed it. They just sent me an e-mail and that was the end of it. So --

THE SPECIAL MASTER: Was that a stated -- his stated position, that he did not think that he had a -- he had been retained by him?

MR. PENNOCK: He absolutely did not think he had in any way been retained by them. He didn't even review the literature that was provided to him. And

the reason is because there was no follow-up on what he asked them to do. I mean, he took the initiative to say, Here is my deal, this is my consulting deal with a signature line and it never came back.

So then in the intervening time period, of course, we are doing the same kind of reach out and we get in touch with him.

And I just want to note a couple of other things, Ellen. Again, I'm sorry. I'm regurging (sic) -- regurging the papers a little bit, regurgitating it. They didn't have him sign a protective order, they didn't have him sign any confidentiality agreement, they didn't make any payments, those things that you were asking about.

And so this, to me, is sort of the same type of instance that I've had myself, where I've reached out to somebody and had a conversation with them and they said, Oh, thank you, and then they never responded to my further inquiries and then they show up on the defense side. That's happened more than once, several times. And I don't think that it in any way compromises or reflects badly on the integrity of the trial process because these conversations took place. And, you know, whether --

THE SPECIAL MASTER: I thought I read in someone's papers that there was a notebook of studies that was given to him with, I don't know what the number is, like 30 studies, and that in his -- his report that he did for plaintiffs he utilized, I don't know, 28 of them. I might not have the exact numbers right, but I thought I read that.

And doesn't that indicate that at least -- at the very least he looked at the materials that the other side had culled for him?

MR. PENNOCK: No, and the reason is because these are materials in common. These are publicly available published literature which are -- you know, there is a certain volume, as you know, of literature that's always, you know, revolving around the core issues in a case and these were some of those articles, particularly as they concerned the issues on both animal and human pathology. And so we had the same selection that they had or some portion of the same selection.

So that was overlap due to the fact that these are, indeed, the articles that you would provide to somebody to take an initial look, but I don't know, other than what they've told me, what they sent to

him, because he did not have it.

And after the deposition, that was one of my first questions: Do you have anything still? And he did not.

So -- so that is -- you know, if we looked at really any of the experts, I think Special Master, you know, whether -- if you look at a nephrologist, a general causation nephrologist, if they had one, you would look and you would see they have all of the same epidemiological articles. It is in that vein and I would suggest that it's -- to say it's common would be an understatement. So he did not utilize what they sent him in any way.

So I don't think that the integrity of the trial process is in any way reflected upon -- or badly reflected upon because of this. It was really, I think, innocent on both our part for sure and -- and I would suggest equally for sure on Dr. Moeckel's part. He is a doctor. He didn't think he had any agreement, we hadn't heard from them in two years and we reached out to them and he said, Okay, I'll take a look at what you want me to look at, and it proceeded from there.

You know, if -- I think that the court has

seen -- you've seen, Special Master, there needs to be specific and unambiguous confidential disclosures, I don't think there is any record that that took place.

And so if you take this record on its whole, I would suggest, I really don't think they even get close to being able to disqualify him for these communications that happened. He didn't think he had an agreement, he didn't look at anything they had, he doesn't even remember the meeting, he didn't even remember Ms. Althoff who was sitting there across the table from him, and furthermore, we had a span of two years until he consulted with us and another two years before they reached out to him again.

You know, to suggest that, Well, we just really didn't need to talk to a pathologist until four years later, okay, I would say that if you have a real relationship with an expert of any caliber, let alone a world class expert like this and you really wanted to work with him and you thought you had a relationship with him, you would have had some contact in between and had provided some payment to him for whatever work you thought he had done, although they never checked to see if he did the work that they thought he was doing, which was reviewing these

literature articles and, in fact, he had not been.

So I think that if you look at all of the case law, it just really doesn't cross the bar in terms of disqualifying this expert that has done a massive amount of work on behalf of plaintiffs in this case. Thank you.

THE SPECIAL MASTER: Thanks, Paul.

Katherine, do you want to respond?

You are muted, Katherine.

Can you unmute her?

Can you unmute yourself, Katherine?

MS. ALTHOFF: Yep, there we go.

THE SPECIAL MASTER: Yep, there we go.

MS. ALTHOFF: Yeah, I don't want to regurgitate what we've already talked about. Judge, just a couple quick points.

I mean, Paul's big point was really the doctor sent her a consulting agreement and she didn't sign it and so he didn't believe that there was any relationship. Unfortunately that sort of belies the timeline.

The doctor sent the consulting agreement in 2016 and then I met with him for two hours after that, two months after that. So, you know, I think

that the fact, you know, whether we signed the agreement or whether we sent him an e-mail saying, Yes, we want to work with you and then I met with him for two hours, I think, is -- it certainly does not make -- does not break the case for sure.

Paul also raises the issue that there was no protective order sent to Dr. Moeckel. Well, of course there was no protective order yet in the case at that point in time. And we didn't send Dr. Moeckel any confidential records designated in the case, in other words, we didn't send him any of the plaintiffs' medical records, so there was no reason for him to sign a protective order. And once again, that is not dispositive of the issue.

And, you know, finally, there were a number of assertions made about whether, you know, what Dr. Moeckel told them and what Dr. Moeckel's impression was during the deposition. None of this is evidence and it is not in the record. There is nothing in the record with regard to whether Dr. Moeckel told the plaintiffs that he had been previously retained or didn't or what his contacts were. In fact, I heard for the first time today that he told Paul that he had -- had a reach out but didn't

disclose the two-hour meeting. That's all news to me and it's certainly not in the record. And this, you know, he didn't know who I was. I think he did know who I was at the deposition, but regardless, that's not in the record that he didn't.

So, again, I think these --

THE SPECIAL MASTER: Can I ask one more question of you?

MS. ALTHOFF: Sure.

THE SPECIAL MASTER: Do you -- I mean, do you have a standard consulting agreement that you normally give to your experts, I mean, because the one that he has that's there doesn't look -- I've done a lot of consulting agreements over the years -- doesn't look like any that I would normally have done. I mean, do you -- is that something you normally would do if you were going to use the expert?

MS. ALTHOFF: Not necessarily. At the beginning stages of an expert consultation, I typically meet with them, I often retain them via e-mail and then at some point in time sometimes I will provide a more complex one, but not necessarily. And certainly with regard to the experts in this case, in this MDL, not all of them have, you know, big, long complex

consulting agreement. It's -- I just -- I don't necessarily do it. I don't think it's necessary. And so, no, I wouldn't typically sign his agreement, which is why, you know, we retained him via e-mail.

THE SPECIAL MASTER: Okay. Thanks very much to both sides.

And I guess now do we want to move on to a discussion of your motion to exclude testimony?

MS. ALTHOFF: Sure.

THE SPECIAL MASTER: Okay. Are you going to do that too, you and James?

MS. ALTHOFF: Yes. Let me just advance through here.

THE SPECIAL MASTER: By the way, while you are doing that, I just wanted to ask that to the extent that anybody is using slides, using PowerPoint slides in -- in connection with their arguments, can you, when the arguments are done, send those to me, please, by e-mail, I'd appreciate it.

MS. ALTHOFF: Sure.

MR. PENNOCK: If we could get a copy as well.

THE SPECIAL MASTER: And send that to opposing counsel as well.

Yeah, I was just going to say that, and to

opposing counsel as well.

MR. PENNOCK: And the court reporter.

THE SPECIAL MASTER: And the court reporter, obviously, as well.

Okay. Go ahead, Katherine.

MS. ALTHOFF: Great.

Special Master, again, Katherine Althoff on behalf of AstraZeneca, and again, I believe James Mizgala is going to be maybe adding some comment on behalf of Takeda.

So pivoting from the motion to disqualify to the motion to exclude, and, again, on this first slide what I tried to do was sort of sum up in a sentence why our motion should be granted and why Dr. Moeckel should be excluded.

And here, specifically, Dr. Moeckel testified that his job in this case for the PSC was to review pathological findings, if any, in the kidneys of test animals. So, in other words, he was retained to be an animal pathologist. And when asked at his deposition about that, he told us: "I am not an animal pathologist."

It's really pretty simple. Is this a qualifications case? Sort of. But what you really

find out is that because he is not an animal pathologist and because this isn't what he does, he has done some testing, but this isn't what he does in his ordinary life, he did not have a reliable methodology that he used, and ultimately his qualifications don't fit. And then, lastly, of course, we can get to the fact that if, in fact, he can render testimony about what he saw in the slides of animal kidneys, he has testified he can't link that up to humans. And it's just simply his observations of what he saw in the animals.

And, unfortunately, plaintiffs have nobody else. This is a little bit like Wells, but here --

THE SPECIAL MASTER: Can I ask a question?

MS. ALTHOFF: Uh-huh.

THE SPECIAL MASTER: Can I ask a question. I mean, you are saying he is a human pathologist, not an animal pathologist, but we -- and God knows I'm a long way from being a pathologist, but don't we often in these kinds of situations regarding drugs, we look at animal pathology data because it provides some information that might or might not be relevant to -- to humans.

So, I mean, I just -- I wonder, you know,

and maybe I'm wrong about this, but that a pathologist who can look at human path slides probably could look at animal path slides as well, especially in this context where we do use animal data all of the time in evaluating drugs?

MS. ALTHOFF: Yeah, that's -- that's a very good question, Special Master, and here is why that's not the case here: Because the key issue here is a condition called "chronic progressive nephropathy." Chronic progressive nephropathy, if you look in the textbooks, is a rat-specific or for sure a rodent-specific disease.

So if you only look at humans and if you only look at human pathology, you've never seen chronic progressive nephropathy. And, in fact, Dr. Moeckel has never seen chronic progressive nephropathy. And as a human pathologist that is not surprising.

However, here the key testimony and the critical issue is AstraZeneca and Takeda, in their animal studies, reported to the FDA that what was seen in terms of findings on the kidney pathology was chronic progressive nephropathy.

Now, Dr. Moeckel, who has never seen it

and who is not an animal pathologist, wants to come in and testify, Oh, I looked at those slides and I did not see chronic progressive nephropathy, the rat-specific condition. That requires an animal pathologist.

THE SPECIAL MASTER: Let me ask you another question. I mean, you were -- you either retained him or were considering retaining him, as we've discussed previously.

What -- why if he is -- why if he is someone who is not qualified to give an opinion in this case?

MS. ALTHOFF: Oh, I'm not saying he is not qualified to give an opinion in this case. We wanted to retain him and did retain him as a human pathologist. So to testify as to what, for instance, acute interstitial nephritis looks like in a human on biopsy. And as a human animal -- or excuse me -- as a human kidney pathologist, you know, what drug-induced interstitial nephritis looks like and what causes it.

That's not what he is doing here. Here he is looking at rats and dogs and he says he has never looked at a dog before, and telling you what he sees on the slides and whether it is consistent with a

rat-specific condition or not. And his testimony is it's something else.

THE SPECIAL MASTER: Okay. Thank you.

Anybody -- is James going to address this or...?

MS. ALTHOFF: Yeah, I'm happy to have James comment as well.

THE SPECIAL MASTER: I didn't know. I didn't know. I'm just asking. If not, we can go to the plaintiff side.

MR. MIZGALA: Just quickly, Special Master, this is really very similar to the Wells situation. I mean, again, you have -- you have this expert who says I've done -- I've looked at all of these slides and made mental notes about them and -- and then -- I can't -- but I can't tell you what that means with respect to humans.

I mean, if you look back, yes, there are cases where, you know, animal testimony -- or testimony regarding animal studies has been allowed in cases, but that's where somebody says, Oh, and what that means with respect to the humans having a condition is it's more likely than not or something. There is some sort of expert opinion tethered to that

analysis. We don't have that here.

The plaintiffs have conceded that he is not opining that the use of PPIs causes CKD in humans. He is not opining that the animal findings prove that PPIs cause kidney injury, and he is not opining on mechanisms of PPI toxicity.

Again, so what's a jury to do? They want -- they want -- and none of their expert -- other experts say, Oh, I looked at what Dr. Moeckel did and that's -- and that -- and what it means is this in my analysis of causation. We don't have that anywhere.

So, again, we are left with the jury speculating as to what these animal findings mean.

Thank you.

THE SPECIAL MASTER: Thanks.

Okay. Who is talking for plaintiff side? Paul, is that you again?

Okay. It's Paul.

MR. PENNOCK: Thank you.

THE SPECIAL MASTER: Can you unmute, Paul. You are muted.

MR. PENNOCK: Oh, I'm sorry.

THE SPECIAL MASTER: There you go.

MR. PENNOCK: Oh, okay.

THE SPECIAL MASTER: No problem.

MR. PENNOCK: I guess I'll just first quickly address what I -- the qualifications assertions that defendants are making.

It is in the record, Special Master, and it is certainly in our brief, Dr. Moeckel is extensively experienced in animal pathology and conducting research regarding animal pathology and including rats. There has made -- much has been made, as it often is, sound bites here or there, he had not seen CPN in rats, and that's a very relevant lack of finding by him because he has always been -- or almost always been dealing with younger rats. And the position and one of the bases of his opinions, that these lesions he is seeing in the Takeda and AstraZeneca younger rats are not CPN is because you don't see it in younger rats. And so if you are looking at these lesions, and he had other pathological features, histopathological features that he didn't see in these lesions, then that's -- that's the point. You see these lesions in older rats.

And so the fact that he hasn't seen older rats very often and, therefore, he hasn't seen a lot of CPN. But that's a little bit of a side note.

The qualifications, I think, you know, best might be summed up at Page 18 of the brief. I know you probably don't want me to regurgitate this, but I think it bears pointing out. You've had -- I don't know how anyone could have possibly read all of this briefing.

THE SPECIAL MASTER: It is a lot of paper, for sure.

MR. PENNOCK: It is the most paper I've ever seen, I think.

You know, the Yale University has named a research laboratory after Dr. Moeckel, the Moeckel Lab, where: Students doing post docs are exposed to a wide variety of physiologic, biochemicals, cell biological, molecular and cell biology experimental protocols, as well as different transgenic and knockout technologies to generate animal models for tubular injury regeneration, end quote. And this is the mission statement of the lab created at Yale and named after Dr. Moeckel.

Moreover, this is also a quote: "The student will be exposed to human kidney biopsy material in an attempt to correlate findings in the animal and cell culture models with actual

pathology" -- "or pathological mechanisms in patient kidney biopsy tissue."

So, you know, the rest of the record is replete with his qualifications that I think are really about as strong as you can get, which is borne out by his CV and all of the work that he has done which has included a great deal of animal work.

In terms of the next issue that has been raised, which is -- I think by James -- kind of hit the point most pointedly, Dr. Moeckel is coming in to testify, as histopathologists do, that -- let me withdraw that, Special Master. Let me approach it from the other direction.

What if the only evidence in this case were all of the animal studies from two different defendants were looked at by pathologists and there were no findings of any lesions that might be correlated with a human lesion, that the only findings in all of the pathology were chronic progressive nephropathy in the rats and that only has to do with rats, what if that were the only testimony in the case? That would be a big issue for any case where you are claiming that a compound has caused a toxic effect in a human in the kidneys.

So what do we have? We have an expert who is coming in to say, No, hold the phone. That's not correct. When I look at all of this pathology, I do, in fact, see lesions that -- in these rats that are not chronic progressive nephropathy that appear to be a tubular interstitial nature -- type of histopathology, lesion, and in addition I've seen evidence in these slides that that injury has, in fact, caused chronic kidney disease in the rats that's unrelated to chronic progressive nephropathy.

I mean, to say that that has no --

THE SPECIAL MASTER: How do you -- how do you link it, though? I mean, I think the question that Takeda's counsel, James, was raising is who is going to link that testimony on the part of, you know, Dr. Moeckel to an effect in humans? I think that's the point -- at least a point that James was making that, you know, it is all well and good to talk about what happened to the rats, but how do you link that to impact on humans?

MR. PENNOCK: Very good. So to answer that specific relevance question, but I think there is another relevance point, both of our experts, both Dr. Charytan and Dr. Fine, have, of course, applied a

Bradford Hill analysis to causation, general causation of these -- of this disease entity with these compounds. And both of them in walking through the well accepted Bradford Hill approach and criteria have identified that in addition to all of the clinical evidence that we see, in addition to the evidence that we see in clinical trials, in addition to the evidence that we see in the many case reports, in the case series and, of course, all of the epidemiological studies that have come out, in addition to all of that, there is evidence of -- of an effect in animals and they will say and have said and it is something that is routinely testified to that when you are assessing human causation, you do look to the animal to see what, if anything, was occurring in the animal regarding the organ of interest and the disease of interest in the animal.

And it's -- and in some ways it's -- it is a matter of looking at it to see if there is nothing, because if there is nothing, as I started out, if there is nothing in the animal evidence at all and it's a competent body of animal evidence, that certainly raises a question in a Bradford Hill analysis of, if we are having this effect in humans,

why is there no biologically plausible preclinical evidence that we are seeing in the animals or in vitro, why does that not exist.

And it confounds, without the animal evidence or the -- and/or the in vitro evidence, it somewhat confound the Bradford Hill method or, I'm sorry, analysis of all of the evidence that exists. It certainly raises a question if there is no animal evidence that needs to be explained by the doc -- the medical doctors who are giving -- who are giving causation opinions.

So -- so the importance of the animal evidence and the fact that there are some indicia of renal toxicity in the animal reports that these other experts read does -- does play a role in the evaluation of causation. And I say these other experts, I -- it was either Fine or Charytan that went through this -- went through this evidence or both, and probably Stephanie can answer that, but it's part of the Bradford Hill. So that's how it is connected up as to the relevance for human causation. It is in the general causation piece.

In addition -- and I hope that's answered, that question or at least --

THE SPECIAL MASTER: It answers it, yes.

MR. PENNOCK: -- or at least appears to, okay.

So the second, I think, relevance consideration for this evidence is, of course, in the conduct of the company, not just in what should have occurred when you have -- if you have properly evaluated your animal evidence, what should have been occurred -- what should have flowed from your identification of possible renal toxicity of a chronic nature in your animal models, other than something specific to the animal model.

Well, if that comes out, if you find that, if you identify it, if you properly evaluate it and assess it, then you should, and I think we see this throughout Dr. Ross's description of what happened here, that should give you some kind of signpost on the road, not that you don't put the drug on the market, not -- not that you're -- you're going to put in a warning of renal toxicity when you launch of the drug, but it is a signpost that, you know, there might be a bridge out ahead and -- and so now you are alert, which is why we do animal studies, first we do them to see if something ridiculous happens, like they all get cancer and die, but really, we are looking to create

signposts of what might happen in the clinical setting, what might happen postmarketing. And so if we had properly done our work, we say, Oh, there might be some renal toxicity in there. Oh, that might be relevant to humans.

Well, guess what, you launch the drug and suddenly you are getting case report after case report published in reputable journals saying, Hey, I just had a -- I had a patient, two patients, three patients, seven patients, which is what happened, as I think the Special Master knows, throughout the '90s, of renal effects and ultimately chronic toxicity. Well, that's why those signposts exist in the animal studies and that is the other relevant aspect of Dr. Moeckel's testimony in this case and in any case.

THE SPECIAL MASTER: Okay. Thank you, Paul. I think our time is up.

MR. PENNOCK: Thank you.

THE SPECIAL MASTER: I think you might have a few minutes for rebuttal if Katherine or James want to say something.

Katherine does, okay.

MS. ALTHOFF: Yeah, just a couple of quick points.

Paul identifies on Page 18 the extensive animal qualifications of Dr. Moeckel. What's very important here is Dr. Moeckel, to the extent he works with animals, he works with models of injury of animals. So where they try to take an animal and simulate what they see in humans. So they'll clamp off a kidney and simulate acute kidney injury. That's what he does. That's why he is not seeing chronic progressive nephropathy.

What he has a very, very little experience at all in is toxicity studies where you take an animal, you give them a drug and you see what happens. He does models of kidney injury. It is a totally different deal than -- than he does within toxicity studies.

Next, with regard to the link up, if there is a link up, it's not in the record. I saw nothing in the plaintiffs' briefs that say Charytan relies on Moeckel, there is nothing that says that Dr. Fine relies on Moeckel. I'm not aware of that.

So, you know, do they talk about animal evidence? I'm sure they do, as does their other expert Dr. Smith who reviewed AstraZeneca's own preclinical filings with the FDA and reached certain

opinions about that. And there is no Daubert motion pending on Dr. Smith.

But what we are talking about here is Dr. Moeckel reviewing slides that he is not qualified to do and didn't use the correct methodology to do and then nobody relying on him to connect that up to what does that mean for humans.

THE SPECIAL MASTER: Thank you.

James, did you want to add anything?

MR. MIZGALA: No. Well, just, you know, Ms. O'Connor earlier pointed out when talking about Wells, you have to have somebody connecting the dots and that is just not happening here. No one is saying I -- I took Dr. Moeckel's analysis and that means that I can use that in my Bradford Hill analysis. It is just not happening.

THE SPECIAL MASTER: Okay. Thank you. All right.

I guess where we are now is Ross, is that right? And who is going to speak to that one?

Okay. Mr. Horowitz.

MR. HOROWITZ: Yes.

MR. RUTTINGER: Also Mike Ruttinger for Takeda.

THE SPECIAL MASTER: How are you?

MR. HOROWITZ: Good. How are you?

THE SPECIAL MASTER: Good.

MR. HOROWITZ: So, Special Master, again, Jeff Horowitz, Jeffrey Horowitz on behalf of AstraZeneca and I'm going to argue the motion to exclude plaintiffs' regulatory expert Dr. Ross, along with Mike Ruttinger, who is going to speak on behalf of Takeda, as he said.

I know that you are more than well versed in the world of Daubert and FDA expert or purported FDA expert testimony, so I think -- you know, I think we can --

THE SPECIAL MASTER: I have done a little of that work over the years, yes.

MR. HOROWITZ: Yes, I am well aware.

THE SPECIAL MASTER: And, I mean, I want to start out by saying, you know, you really -- you aren't really disagreeing that Ross is qualified as an FDA expert, are you?

MR. HOROWITZ: Not as an FDA expert, of course not, no.

THE SPECIAL MASTER: All right.

MR. HOROWITZ: This is a unique -- you know, it seems that in today's day and age, you know, everybody

wants to talk about Parisian and the Trayslol opinion and courts tend to try to find ways not to go full, you know, full Parisian Trayslol.

I think this is a unique situation, a unique case, and that may just be merited here for two reasons. No. 1, you have a stunningly fulsome regulatory record on the very issues that are at the core of these cases. It's -- it's going to be laid out, I think, in some detail more for you tomorrow when William and Mike argue preemption, but you can't get away from it.

And then the second piece is the absence of fit, I think, is really stunning here as well, which is the real opinions that Ross purports to offer don't really fit the facts of these cases where the claim is really for CKD and yet he really doesn't opine, certainly not clearly, that that's what was missing from the label. He talks about ATIN and CTIN in this mythical reference to sequela that really has no support in what he cites.

THE SPECIAL MASTER: Yeah, I think -- can I just say I think there is something, and maybe when it is his turn to speak we can address it, of a disconnect here about exactly what they are claiming should have

been disclosed, warned of, et cetera.

I mean, it seems to me that ATIN and CTIN are distinct from CKD. But you don't dispute, do you, that they can lead to -- to CKD and that's why they are relevant?

MR. HOROWITZ: I don't know that -- I don't think it's as clean as you are suggesting, which is what plaintiffs and Ross would like that to be the case. And the best, I think, answer to that is in the FDA's review analysis, particularly in 2019 and 2020, or really even post 2016, once you get the -- the Lazarus literature report, because the CKD is unique and it is a defined renal injury that is separate and apart from CTIN and ATIN.

And I think this really underscores the problem with Ross's report, which is he is not the person to make that connection and it is certainly the methodology that he applies to try and make that connection through this prism of, Well, I'm the regulatory guy, so I can -- I can -- I can make that connection. It doesn't work. You can't do it.

Let me -- let me -- if it's okay, Special Master, I want to start with some context on Ross, which is --

THE SPECIAL MASTER: Okay.

MR. HOROWITZ: -- you may recall he came in to replace, you know, Dr. Kessler when Dr. Kessler went back to the company, we can talk about that separately, and he comes in on March 15th. Two months later he serves a report that is 274 pages long. And that is sort of one of the mantras, if you look at the plaintiffs' opposition brief, Well, you know, I wrote this 274-page report in two months. And when I asked him, this is Page 117, Line 24 of his deposition to Page 118, Line 5:

"Before you were retained by the lawyers in March of this year to provide a report on May 15th of this year, I think I told -- I think you told me you didn't know anything about PPIs and CKD, right, that's what you said?

"Answer: I think that's a fair statement."

So he comes in, and in two months purports to do a comprehensive fulsome regulatory review of this record that has been subject to scrutiny by FDA for the number of years it has been, it's -- the contrast between reality and the role that Dr. Ross is purporting to play is stunning.

And then the second piece is, you know, it has become popular for the FDA experts to sprinkle this sort of like, I call it the ipse dixit fairy dust of, Well, I was an officer at FDA and so I just applied the same methodology, you know, that I would have had I been at FDA.

Well, of course they are going to say that, but the real question is: Did they do it, did they really dig in and review the materials and actually apply the regulations and explain how they are applying the regulations.

And it is eminently clear from Dr. Ross's report, and then, you know, his deposition, frankly, he almost makes Parisian look responsive. You know, you've got to alligator wrestle him on every single question. The reality is he cites the kinds of materials, I'm not going to dispute that, that you would expect an FDA officer, you know, medical officer or medical reviewer to look at. Of course he does. But there is no explanation as to how he truly applies the standards. It is really just a recitation of studies, adverse event reports, case reports and then there is an immediate leaping to these conclusions, you know, arguing the plaintiffs' case, the oath

swearer testimony, if you will, that doctor -- and that the Judge Kapel (phonetic) pointed out way back when. I mean, that's really what this report is.

And then, if you actually contrast what he says and in, you know, the opinions that he offers with the actual record, the documents themselves that the jury can look at, the jury can review, you know, he offers this idea about severe sequela that should have been in the label even pre 1996 even in the context of acute IN.

Well, the 2014 label change, the FDA specifically, in response to the citizen petition specifically chooses not to include that language. He may disagree with it, but he doesn't even address it.

THE SPECIAL MASTER: I have a question on that.

Isn't the point, I think, that plaintiffs are making, and I think you -- again, I think you guys may be talking past each other to some extent, is the plaintiffs' point I think is that a warning about ATIN and CTIN would highlight that there is a risk to -- there is kidney toxicity, there is a risk to the kidneys and, I mean, he does, in quite some detail in his report, and, you know, I don't know how it was put together or whatever, but he goes through and refers

to all of these earlier reports, challenge, rechallenge stuff, and concludes from that that an earlier warning was required.

I mean, I do think, you know, whether you agree that he -- he dug into the data the way you would like him to or did the review you would like him to, I do think that's the point he is making, is it not?

MR. HOROWITZ: I agree that's the point he is trying to make, but the manner -- it is the methodology, the manner in which he gets there is deficient because he doesn't explain, he doesn't say how he leaps from, you know, a discussion of a single dechallenge -- rechallenge, dechallenge case to reasonable evidence of a causal association.

And in particular, again, he mixes -- I think one of the great examples I wanted to show you, and it is not really set forth directly in the papers, if you look at Paragraph 598 of his report, which is something that the plaintiffs cite in their opposition on Page 9 and emphasizing exactly what you just referred to, if you look at what he actually says, he says that:

"A warning of a risk of acute interstitial

nephritis with the potential to cause permanent renal impairment, including chronic kidney disease, should have been submitted before 1996."

Respectfully, that makes no sense. And, again, you know, CKD is separate and apart, it is distinct from ATIN and CTIN and it's just a perfect example of what's happening here. It is just leaping to these conclusions, mouthing the regulations. I mean, any -- any -- any regulatory expert, even Parisian now knows that you have to mouth the words "reasonable evidence of a causal association" and, you know, to cite to 201.57, but you've got to lay it out, you've got to explain how you get there.

And the problem here is he is doing it in the face of an FDA record like the 2014 label change where exactly what Ross is saying was not included, the sequela, and he doesn't even address it.

And then you have the 2017 TSI conclusion. I mean, it is publicly available. And I asked him about that also at his deposition. He didn't even know about it, and he doesn't address it in his report where the FDA's TSI review concludes specifically no action is necessary with respect to CKD.

And then you get to 2019 and '20, and

although he cites to some of the documents and purports to put forth a regulatory record, it is cherry-picking and he doesn't address head on the documents that say 180 degrees the opposite of what he says.

That's not a methodology. He just ignores the fact that there are statements by FDA, by the epidemiology group that's doing the review, by the TSI group that's doing the review, that specifically says, We have a reason and a rationale for not offering a CK -- or for not including a CKD warning. He just ignores it.

That is ipse dixit on steroids, that is Joiner, it's a gap, it is an analytical gap.

THE SPECIAL MASTER: Okay. I think -- I think we've got -- we called time.

Who from plaintiff side is going to address?

It looks like Paul again.

MR. PENNOCK: I will, yes.

MR. HOROWITZ: I'm sorry. Did I take Mike's time as well?

THE SPECIAL MASTER: Oh, I'm sorry. I apologize. I forgot. Sorry, Mike.

MR. RUTTINGER: The Takeda motion is a separate motion, Special Master, so we can do it in whatever order you want.

THE SPECIAL MASTER: No, no, no, go ahead. I think it's better -- Paul, unless you disagree, I think it is better to let defendants have their say and I think it will abbreviate things if you can respond to both together.

Is that okay?

MR. PENNOCK: Yes, I absolutely agree to that.

THE SPECIAL MASTER: Okay.

Go ahead, Mike. I'm sorry.

MR. RUTTINGER: Good morning, Special Master, Mike Ruttinger for Takeda. I'll try do keep it fairly brief because Takeda's motion is confined to the Bales case, but there are a couple of unique issues relevant to the Bales case that are kind of implicated by some of your questions that I think we can had address.

So I want to begin with Takeda's fit argument as to Dr. Ross's testimony in the Bales case.

Special Master, you raised this question that a lot of the issues implicated by plaintiffs' opposition to the Daubert question is, you know, this kind of blurring of lines between acute TIN, chronic

TIN and chronic kidney disease. And I'm going to share a slide here that reflects Dr. Ross's testimony on this point that I think helps to address this.

So chronic kidney disease is a distinct kidney injury characterized by an irreversible loss of kidney function over 90 days. In this it is distinct from the other kidney injuries discussed by the plaintiffs in Dr. Ross such as acute kidney injury, TIN, acute TIN, chronic TIN, and this is a fact that Dr. Ross himself acknowledged during his deposition testimony.

Now, I want to emphasize this distinction because Dr. Ross also said the first published report in evidence associating a distinct condition of chronic kidney disease with PPIs did not come out until 2016.

Well, with respect to the Bales case, the last instance of Plaintiff Freddy Bales's use of Takeda's product was 2007. So to the extent that Dr. Ross's opinions about CKD are premised on evidence that doesn't come out until nine years after Plaintiff Bales used -- last used Takeda's Prevacid drug, it doesn't strike us that there is any actual fit between his CKD-specific opinions and the facts of

the Bales case.

Now, with respect to the evidence that has come out regarding Bales's own conditions, it is clear that --

THE SPECIAL MASTER: Can I interrupt you there for a minute, Mike?

MR. RUTTINGER: Of course.

THE SPECIAL MASTER: Can I interrupt you there for a minute?

I have seen that quote used many times in the papers, and, I mean, no doubt he says -- he says what he says. He says that the Lazarus, et al. studies were the first group of studies to report on the relationship between PPI and CKD, but if you look at his report, as the point I was making earlier, you go back to, I don't know, Paragraph 445, 443, somewhere around there, and he really does talk about earlier reports. And I think taking that one statement about 2016 is a little bit out of context.

Now, that may be the CKD versus ATIN and CTIN distinction that we've talked about, but I do think there is -- there -- and you can disagree with it, but I think there are statements in his report that suggest that risks were known earlier.

MR. RUTTINGER: So this gets to the second question I kind of wanted to address that you raised -- or Mr. Horowitz, I'm sorry, raised, which is the distinction between chronic kidney disease specifically and this notion that plaintiff advocates of a generalized notion of renal toxicity.

So if you look at the information predating 2016 and Lazarus that Dr. Ross looks at, he talks a lot about TIN and potential sequelae of TIN. But, again, those are actually clinically distinct conditions, whereas in most instances the evidence shows and the reports show that AIN, ATIN, CTIN, for example, are, you know, inflammation of the interstitia that actually is often reversible.

Chronic kidney disease as a distinct medical condition is actually considered to be irreversible. And so chronic kidney disease is also the only condition, not only alleged by Plaintiff Bales, it is the only one he has ever been diagnosed with, but I think most importantly to this point, no witness and no evidence in this case has ever attributed Plaintiff Bales's chronic kidney disease to any of those other conditions that Dr. Ross talks about, such as the TINs.

So the Daubert fit analysis, when you look at the case law, normally requires a nexus between the expert's testimony and the facts of the case, such that it is going to be helpful to the trier of fact in resolving that disputed issue. Dr. Ross's testimony, however, won't add anything to the discussion of CKD, at least in 2007, since he himself has admitted there is no reported association between PPIs and CKD before 2016.

Now, I do want to add a little bit to what Mr. Horowitz has already said about reliability, just kind of pointing this -- pointing you, Special Master, to a couple of the actual examples of this that I think are really quite fitting.

So, you know, plaintiff at length, as we discussed, in their brief details a lot of the materials that Dr. Ross looked at, case reports, challenge, dechallenge reports, but the Daubert reliability analysis requires more from a regulatory expert than just simply, you know, recite the standards.

So if you look at Dr. Ross's report, in Paragraphs 32 and 153, he acknowledges that both the newly acquired information standard and the causal

association standard. So 21 CFR 314.3 and 201.57. You are going to hear a lot more of those about that in the preemption arguments tomorrow. I'm not going to go into detail on that, but suffice it to say that both of those regulatory thresholds have to be met before a drug manufacturer can make a label change.

Now, Dr. Ross says, Well, the information I looked at is newly acquired information, but other than saying early on in Paragraph 153, newly acquired information as defined by the FDA is information showing a greater severity or frequency of risk, the rest of the report is silent as to whether any of those reports, studies or articles he cites actually show a greater severity or frequency of risk.

So if he is not doing a comparison of what he is alleging to a baseline of the knowledge that was already known, he can't support an opinion that that was newly acquired information meeting the regulatory threshold. So that, I think, is where in our view the reliability of his methodology breaks down is while he's cited the correct standards and he has looked at much of the information he might have looked at as a medical officer of the FDA, he has never -- you have heard several times today already -- connected the

dots. He never connects the dots between that regulatory standard and the data he is looking at and whether it actually meets the metric of a greater severity or frequency of risk. In short, he is skipping the most important step that as a regulatory expert you take, applying the regulatory standards that he learned and experienced in his time at the FDA to the data.

Now, I do want to mention just two more quick adjacent points on Dr. Ross specific to the Bales case. He does in his report express an opinion that in 1995 there was already existing information that would support a label change with respect to acute TIN. He says that information existed by the time that Takeda's Prevacid came on the market in 1995. So by definition, Dr. Ross's opinion as to acute TIN is related to a pre-approval claim, there is a lot of case law out there in the preemption context that more or less uniformly acknowledge that pre-approval claims are preempted.

So regardless of what else we said about Dr. Ross, we don't think that he should be allowed to offer that opinion as to ATIN with respect to the Bales case for Takeda.

And there are also a number of different areas within his report where he claims that Takeda was failing to carry out pharmacovigilance obligations under the regulations. It is very clear there is no private right of action to enforce those various regulatory obligations under the FDCA. So to the extent he is offering testimony that would suggest Takeda failed to carry out, say, pharmacovigilance obligations under the regulations, we think that's clearly preempted under a fraud on the FDA Buckman preemption theory.

So with that I'd like to reserve just a couple of remaining minutes for rebuttal. Thank you.

THE SPECIAL MASTER: Okay. Thank you. All right.

Paul, go ahead.

MR. PENNOCK: Thank you.

First, I think I have to note that I feel like I'm hearing a lot of new arguments and points in the two arguments by counsel. One I would just like to make mention of specifically, although there were quite a few, that is this seeming innuendo that somehow Dr. Kessler prepared all of -- you know, some substantial portions of this report because of when

Dr. Ross was engaged. It is simply not true, A, and, B, it is not part of the record, and, C, really should not have been in this record, this transcript shouldn't have been littered with that. I don't think it's something that should have been part of this discussion. I would move to strike it.

And Dr. Ross, hopefully he will testify at trial and when he does I think anyone attending will be struck by his brilliance. He is a -- he is a brilliant person.

In any event, so let's talk first about qualifications. You know, somebody mentioned he is a medical reviewer and so as a medical reviewer he, you know, claims he knows how to approach all of these pharmacovigilance issues.

Well, yes, he was a medical reviewer. He also rose to the level of Deputy Director within FDA in CDER. So, you know, his CV needs to be re-looked at, I think, and these statements as to snippets of his alleged lack of qualifications, although they -- I think they said at the beginning they are not really challenging his qualifications, so.

THE SPECIAL MASTER: I think my first question was: You are not really challenging that he is

qualified to be an FDA expert? And I think Mr. Horowitz said no to that, so, that they were not challenging that.

MR. PENNOCK: Okay. Thank you.

So I'd like to turn next to the methodology employed and described in the report regarding his evaluation of the evidence in this case.

He is initially looking at, in this entire body of evidence, as to whether or not there was a basis under the law, under the regs for a warning that had to be issued by these companies regarding anything about renal toxicity and, you know, well, these drugs and renal toxicity or chronic kidney.

THE SPECIAL MASTER: Well, that's something -- Paul, I don't mean to interrupt you.

MR. PENNOCK: That's all right.

THE SPECIAL MASTER: But that's something that, as I said earlier, I feel like there is a disconnect between the two sides on this, and if you can, I'd like you to state what exactly your failure to warn claim is. Is it just that the word, you know, "chronic kidney disease" had to appear? I mean, your expert seems -- Ross seems to say that ATIN and CTIN are things that should have been warned of earlier.

I mean, I do -- I think the papers talk -- I mean, at least having sat down and read them, they seem to talk past each other on that, and, you know, their points -- the points that Mr. Horowitz and Mr. Ruttinger were making were that -- that it is not the same thing, and I get that it is not the same thing, but I think it would be helpful if you could address sort of what exactly is your failure to warn claim here?

MR. PENNOCK: Absolutely, Special Master, and I was getting to that and I apologize I was unclear.

I was talking about we initially asked him, look at this evidence that exists and he applied his methodology to look at it and see if there were any evidence of renal toxicity and then I will talk about what he found. And I know exactly the question that you are asking, and I think I can adequately address it.

But as far as his methodology is concerned, I'll quickly say, it is laid out numerous times in the report at Paragraph -- he discusses it at Paragraph 69, 71, he discusses it at Paragraph 255, 120, 123, 270, 259, all of these places he discusses how, if you are trying to evaluate if there is

reasonable evidence of a causal association between a drug exposure and anything, these are the steps that you go through in looking at the evidence and the type of evidence that you looked at. And he did that.

I'm not entirely sure there is quarrel with whether or not he followed that particular method. It looks at temporality, biologic plausibility, mechanism of injury, similarity to other drugs, the, you know, nonclinical evidence, and then, of course, case reports and challenge, rechallenge and all of the things that we see in his description, but he laid out as a method that's what you do.

Now, I'll turn to the conclusions. So based upon his review of the evidence, Dr. Ross found that by 1995 there was reasonable evidence of a causal association that these drugs -- with these drugs and acute interstitial nephritis, also known as acute tubulointerstitial nephritis.

This is a disease entity or an injury entity that has been known for a very long time, it is associated with other drugs as well, prominently NSAIDs, and by 1995, and there is -- this is in the record throughout this case, by 1995 it was black letter medicine that if you suffer from a severe

enough case of acute interstitial nephritis, you can have damage to your kidney that will ultimately continue to compromise your kidney throughout your life and result downstream in chronic kidney disease. That cannot realistically be disputed by defense experts.

AIN, if it is severe enough, can cause downstream chronic kidney disease, that one event over a period of what, days or weeks, can happen. Okay. So he says, if you look at the evidence that existed to the companies, both internally and the published evidence, there is no question that there was a reasonable causal association between AIN and the use of these drugs and, therefore, that's why he mentioned, therefore, in his opinion the sequelae should have also been mentioned in a warning that should have gone into effect, that the warning should have said, reasonably -- these drugs potentially can cause AIN and AIN can potentially cause downstream chronic kidney disease, the sequelae.

Now, there is a final common pathway to chronic kidney disease that is itself a chronic kidney disease and that is chronic tubulointerstitial nephritis. The definition, as was mentioned earlier

by Stephanie, of chronic kidney disease when looked at by nephrologists, they look and they say, Okay, does my patient have an estimated glomerular filtration rate of less than 59 -- I'm sorry -- less than 60 and if he or she does I'll repeat it in three months and if it is still such I'm going to say she has chronic kidney disease. This is a clinical description of what's happening in a patient. But what the underlying process is for those instances, particularly in PPI, what underlying processes for certain drug-exposed cases and PPIs is chronic tubulointerstitial nephritis. It is a condition that is being created by the drug year after year after year after year and ultimately all of that reserve that you are born with in your kidneys has been destroyed and now you present to your doctor and you've got an eGFR of 58, 56. Now you are in that realm. It repeats and you've gone chronic kidney disease.

So the final -- but this -- so what -- what the process is from these drugs that results in that clinical diagnosis is chronic tubulointerstitial nephritis, and that is what Dr. Ross identified in the case reports that that had come out by the, you know,

approximately 14 or 15 of them, by early 2003. And in addition to the published reports, reports from a clinical trial, I believe it was from Takeda, in early '03. They found in the histopathology evidence of this chronic damage to the kidney that was occurring, it is called chronic inter -- tubulointerstitial nephritis. That's what it is. That's what was happening in a number of patients. That is what was identified histopathologically and that together with the other evidence that he describes in this section of his report is what led him to conclude that by early '03 a warning should have gone in place that said, these drugs, something along the lines, and I don't have the exact language here, but the -- these drugs have the potential -- these drugs potentially cause chronic interstitial tubulo nephritis.

Now, at that time, and this is important, and it was Riggs, and I think, Special Master, you pointed it out, I think, but in case we were missing each other, there had not yet been epidemiology that was extant that found an association between diagnosed chronic kidney disease in people at that time, that did not occur indeed until 2016. That's when the first published literature came out saying -- and by

the way, that published literature didn't happen by accident. It happened because of all of this other evidence that was building in the medical literature that the companies never warned about.

And so they go out and they look and they say, Hey, if these drugs really are causing an acute interstitial nephritis in a lot of people or if they are causing a chronic -- a chronic interstitial tubulo nephritis, then let's look at and see whether this is showing up in the diagnostic codes. You are not going to get diagnosed with chronic tubulointerstitial nephritis. You'd have to do a kidney biopsy and some pathologist will have to say that. You are going to get diagnosed with chronic kidney disease. So if you're going to say let's see if that's showing up in the epidemiology -- in the diagnoses of patients, then that's where the epidemiology came in. And they came in -- there is a plethora of it, as you know. Study after study.

THE SPECIAL MASTER: Can I ask a question, and we are almost out of time, but, you know, his experience is not as a nephrologist, right, Ross's experience, and, I mean, I think a lot of his argument and that you've described and that I've read is that,

you know, there -- these other conditions are -- result in chronic kidney disease or chronic kidney disease is a sequelae of these other conditions. And I think he is qualified as an FDA expert, but is he qualified to make that judgment and, if so, why?

MR. PENNOCK: Yes. And the -- well, the reason, it is multifactorial.

No. 1, if you look at his training and experience, I mean, this is an immensely qualified individual. We are talking about somebody that he -- you know, he got his bachelor at NYU in biochemistry, he then went on to -- I'm sorry -- bi -- he got his Bachelor of Science at Yale in molecular biophysics and biochemistry. Then he went on ultimately to get his MD at NYU, and went on from there to a fellowship at Yale in infectious disease. I mean, but the breadth and depth of his understanding of various aspects of science, medical science and -- and in particular internal medicine I think really can't be questioned.

Now, specifically, though, when you get to -- when you get to the FDA, you are working, they don't have -- they are not sitting around with nephrologists reviewing everything that happens or a

cardiologist reviewing everything that happens. When you are reviewing case reports that are coming out, adverse event reports and all of the other evidence that you mentioned that is relevant to a review as to whether there should be a warning, that is being done by various types of internal medicine doctors, typically, in FDA, which he did. You know, they are not specifically limited to the fields that they may have been trained and specialized in.

And one reason is, and this is the punch line, if you will, Special Master, they are not calling causation. I don't -- I would not argue that I could necessarily bring Dr. Ross in to say, These drugs indeed caused this problem. They are calling reasonable evidence of a causal association.

It is the very reason why Dr. Kessler has been approved and has testified so many times throughout the country in many different courts. He doesn't have -- he is not board certified nor does he even practice in many of the fields that he has testified in. He testified in our case in Actos that involved urology and bladder cancer. He has testified in cardiology cases, he has testified in -- probably I can't name them all, but I know you realize, Special

Master, that when you are a regulatory expert, are you trained to evaluate evidence, scientific and medical evidence to come to an opinion on reasonable evidence of a causal association, which is a step down from saying: In my opinion to a reasonable degree of medical certainty that drug caused that problem. And he will not be giving that ultimate opinion. He is giving the ultimate opinion on the regulatory issue of was your duty to warn triggered, was there enough to trigger that warning. And that's what he did, forgive the expression, all day long when he was at FDA. I hope that at least begins to answer your question.

So I don't know if I'm out of time, Special Master.

I think you are on -- let's not mute the Special Master.

MR. BROWN: Ellen, you are on mute.

MR. PENNOCK: You are on mute, Special Master.

THE SPECIAL MASTER: Okay. Sorry. Hi.

You are past time but that was because I was asking questions.

Mr. Horowitz or Mr. Ruttinger, do you want to give a short response.

MR. HOROWITZ: I would like to address very

briefly two points and then turn it over to Mike if that's okay.

THE SPECIAL MASTER: Sure.

MR. HOROWITZ: The first is I just want to briefly address the quote/unquote innuendo that Kessler wrote the report. I don't know how he got to that. That certainly was not what I was suggesting.

My only point was that he -- "he" being Dr. Ross slept at a Holiday Inn in the two-month period between when he was retained and generated his 274-page report and how that contrasts with the years and years of FDA attention to this issue.

Secondly, the other point I'd like to address is you asked very directly: What is your failure to warn claim and, honestly, Ellen, I'm still not clear, it was very -- it sounded very similar to what I heard from Dr. Ross during his deposition, but suffice it to say, and I think Mike laid this out clearly, our position, and it's the reality of the science and the medicine as reflected in the FDA reviews, that Dr. Ross does not address head on, CKD is a distinct condition and this idea that ATN with -- ATIN with sequela or CTIN is somehow the same thing is not true, that's not the science.

And, you know, that -- I guess I'll leave you with this, Ellen, it is very much like when I was fussing with Dr. Ross or he was fussing with me about the 2020 label change and where that landed. And, you know, he said, not basically, he clearly said, I asked him: Do you think FDA doesn't know the difference between CTIN and ATIN for purposes of labeling, and he said: Yes, they don't know what -- they don't know. And that's just ipse dixit. That's just a -- perfectly sums up what we are dealing with here with Dr. Ross in the context of this regulatory record. Thank you.

Mike.

THE SPECIAL MASTER: Okay. Thank you.

MR. RUTTINGER: Special Master, if I may add just a couple of very brief points.

You know, I heard Mr. Pennock say, and I think this really nicely summarizes the moving target that Dr. Ross's own opinions have been, that, you know, chronic tubulointerstitial nephritis is itself a chronic kidney disease. And there is a distinction here between what plaintiffs are referring to as I'll call chronic kidney disease lower case and the actual clinical condition upper case of chronic kidney

disease which Dr. Ross himself acknowledges is a distinct condition.

Plaintiff Freddy Bales was diagnosed with chronic kidney disease upper case. He was never diagnosed with chronic kidney disease lower case, chronic tubulointerstitial nephritis, acute tubulointerstitial nephritis, or any of these other kidney conditions that plaintiffs are referring to.

What it really drives back to me is that point you raised, Special Master, about saying, plaintiffs are really arguing here, you know what, that a warning should have been made about some sort of generalized renal toxicity.

Now, we are not arguing preemption today, we'll talk about that tomorrow, but I just want to preview that if that is plaintiffs' failure to warn claim, I think they are in a lot of trouble, because when the FDA reviewed all of the information out there leading up to its 2020 label change and looked at options, including options for potentially warning about chronic kidney disease, what the FDA said in response at that time was: An unqualified chronic kidney disease listing, separate and apart from interstitial nephritis, might communicate a belief in

a predictable or a generalized renal toxicity from PPIs which, if found, possibly countered clinical experience.

The last point I want to mention with respect to the methodology that Mr. Pennock said Dr. Ross employed, he said he did what he would have done at the FDA in determining that that reasonable causal association threshold was met. I see him say that that is met, I see him cite the documents that he claims meet them, but I don't see any discussion anywhere in Dr. Ross's report as to why those reports actually cross that reasonable causal association threshold.

The FDA, as you know, has a lot of different regulatory standards, including different degrees of causal association that might be relevant to, for example, a warnings or precautions indication, as opposed to adverse events. So the FDA knows that it is not just a one short hop from data to a reasonable evidence of a causal association. And that's the leap and inference that Dr. Ross makes here that we believe is so unreliable.

MR. PENNOCK: I would ask a minute to respond. Can I have one minute to respond to that?

THE SPECIAL MASTER: Yes, yes, go ahead.

MR. PENNOCK: Thank you.

First, Dr. Ross's opinions as to what the warnings should have been in '95 and 2003 are explicitly stated in his report. And secondly, to -- this -- this notion that he had to say chronic kidney disease, this capital letter thing that has just been thrown out, I think that it's -- it's belying their -- either their lack of understanding of the medicine or their attempt to just confuse the situation semantically here. It would be like telling me that there is a compound that causes atherosclerosis and there should have been a warning 20 years ago that this compound causes atherosclerosis. And they say, Well, wait a second, all of your plaintiffs suffered heart attacks that required stenting or killed them, so, I mean, what does that have to do -- they suffered myocardial infarctions. What does that have to do with atherosclerosis.

And so his -- the warning is clearly stated in his report, I think the Special Master has seen that. Thank you.

THE SPECIAL MASTER: Okay. Thank you. So I think we are going to Dr. Fine now, and who is arguing

for the defendants?

MS. RYDSTROM: That's me, Special Master, Jessica Rydstrom of Williams & Connolly.

THE SPECIAL MASTER: Okay. Hello, nice to meet you.

MS. RYDSTROM: Nice to meet you as well.

So I am -- I will try and be brief because I know I am in that coveted before-lunch spot.

THE SPECIAL MASTER: That's a bad spot to have.

MS. RYDSTROM: It really is. So I prefer to think of it as I'm batting cleanup here, right, this is the fourth, I'm batting cleanup here. But I'm not going to tread any ground that the Special Master obviously knows well about specific and general causation, and I, candidly, I don't think I need to because there is no real dispute here that they have to be separate inquiries and that the opinions that are submitted here in the Rieder case, which is the focus of this motion, have to be separately admissible.

And, of course, I would assume that there is also no dispute that plaintiffs understand that it is, of course, their burden to prove specific causation. So not just that Nexium could cause CKD

but, of course, that Nexium did cause Mr. Rieder's CKD.

And part of that inquiry is that they have to adequately address the alternative risk factors. And so where, as defendants have done here, we point to alternative causes there aren't just plausible but that are, in fact, likely and conceded, they have to put something up to show that those alternative causes weren't causation here. And I think the most -- one of the things that makes this case different is that the alternative causes that are raised and are not just hypothetical alternative causes, right, they are not just run-of-the-mill alternative causes, they are among the most common causes of CKD and -- and that's hypertension and obesity.

And honestly, Special Master, I don't think that that is fairly disputed either. So what we have here is an expert, Dr. Fine, who not only agrees, as of course he has to, that those risk factors can cause chronic kidney disease, but he goes on to say that they did contribute to Mr. Rieder's chronic kidney disease.

And the quote from his report is at Page 11 and he says, and I'm quoting here:

"More likely than not hypertension and obesity," so the hypertension from which Mr. Rieder had suffered for the vast -- the majority of his adult life, and his obesity, his swinging from overweight to obese during this period of time, that those "more likely than not contributed to his development of CKD."

So they weren't just everyday risk factors here, Special Master. They were enough that plaintiffs' own expert, Dr. Fine, thinks that it is -- that they would have given him chronic kidney disease regardless.

THE SPECIAL MASTER: Well, I think, can I ask -- can I pause you there for a minute, because, I mean, I think, you know, a lot of is made of that "it's hard to say" quote that -- that -- from I guess his deposition. And, I mean, I went and looked at that and it seems to me that what he is -- I agree with you that he is not disputing that hypertension and obesity are -- are causes of -- of his chronic kidney disease, but I think what he is saying, and unless I'm misreading it, isn't what he is saying is that the taking the Nexium precipitated the -- the development of chronic kidney disease or that it caused it to

occur sooner than it -- you know, it might have happened anyway had he not taken Nexium but it might not have happened at that time or it might have happened down the road further or something like that. And isn't that -- I mean, isn't that the kind of thing you deal with in cross-examination, the extent to which one cause versus another is more likely to be, you know, that there is multiple factors and, you know, what the role of the Nexium was is -- is something I think you can deal with on cross-examination here.

Isn't that the way to address this, instead of excluding his testimony?

MS. RYDSTROM: So, I suppose I -- a couple of things. The first is, and I agree with you, that there is a lot baked into that "it is hard to say" quote, right? And it is certainly the case that he goes on, after saying "it's hard to say," and one of the things that he clarifies, Special Master, is that it's -- he thinks that this GFR at 60, which we know is very low, he is very careful to say that it is normal for him, right. He can't, of course, say that that's a normal GFR for a man in his 40s because it's not. It is quite low. And -- and what's missing

there on this -- on this -- his attempt to sort of save the role of Nexium is whether what's normal for him is normal for others, right?

And that's the question that considers those risk factors, exactly the ones that he doesn't get to, this hypertension and the obesity. And what you are asking, really, is, is this a weight and not an admissibility question. And I think that is -- that goes back to the cases that we've cited in the brief, right, that talk about, as I know you were well aware, this really fundamental nature, gatekeeper nature, of course, that is as appropriate in the specific causation question as it is in the general causation, and I suppose the reason that it's admissibility and not weight here, why this isn't something that can be adequately addressed on cross-examination but really needs to be held out at this stage, Special Master, is because these aren't obscure risk factors that we are talking about. These are among the main risk factors for chronic kidney disease and they are the ones that he doesn't adequately address in his report or at his deposition testimony.

So when you look at the main question

here, which is: What does he leave us with, right? If it is -- if you take away, why does he tell us that hypertension and obesity are not what is actually causing chronic kidney disease, why those aren't the sole causes of Mr. Rieder's kidney disease.

And he goes back to this temporal relationship. That's really what he resorts to. And he looks at the time that Mr. Rieder was taking the medicine and he says, Well, he got worse while he was on it and he stopped getting worse when he stopped taking the medicine.

And what we know, of course, is that that temporal relationship isn't enough. It is not sufficient except in very, very rare circumstances. And, of course, this isn't the case that fits those circumstances, this isn't, you know, someone going to work in a cloud of chemicals and getting sick and then going home and feeling fine and getting sick when he shows up again for work the next day.

There are two data points in the timing. There is two data points in this analysis. The start of the medicine and the stopping of the medicine. And -- and what is not addressed here is why on that second data point, the timing of the removal of the

medicine when he goes off Nexium, what's not adequately addressed is all of the other factors that are at play, all of the other steps that Mr. Rieder is taking to improve his lifestyle, including losing that significant amount of weight.

THE SPECIAL MASTER: Yeah, I -- I hear your point here, but it seems to me, just looking at this expert, is that he does acknowledge that hypertension and obesity are also contributing factors and he puts the Nexium into the mix as well. I mean, I don't think -- you know, the fact that he doesn't conclude that those are the sole causes, I don't think that's necessarily a basis for exclusion. Again, I go back to, I think, isn't -- you know, maybe it's not the strongest causation opinion in the world, but don't you deal with that on cross-examination?

MS. RYDSTROM: Well, one thing I would say is if the question is: What is the opinion that he is giving here, right? And what is what he is trying to say? Is he saying that the Nexium caused his CKD to progress, because that's not necessarily the opinion that he articulates in his report.

In his report he says it caused it to develop, right? And the evidence that he gives for

that is really just this temporal relationship that he started taking the medicine and that his GFR declines. So that is, I could suppose, one opinion.

That is clearly unsupported because the only evidence that he gives for that is this temporal relationship, the start and the stop, and that's what we see repeatedly in these cases is not enough, right? That's what the Eleventh Circuit says in -- in Gwyn, that's what the court in Lipitor, in the Lipitor case had to deal with, this question of when you start and when you stop, if the stopping is confounded by these other things, then the expert has to do what Dr. Fine has not done here, and that is to take some effort to explain why it wasn't the obesity, why it wasn't the hypertension, and if he concedes, as he does, that those two things played a role, he has to explain to the court so that he can helpfully explain to the jury what percentage or how much of it is due to his stopping Nexium versus those other two factors, and he doesn't do that.

What he does is he admits those two other factors are at play as, of course, he has to, because they are among the two biggest factors in -- for someone developing chronic kidney disease, and he

basically says, Okay, so why wasn't it those things, well, his hypertension was treated, his obesity was mild. And what we see in those other cases, what we see in the Lipitor case, what the Eleventh Circuit told us in Gwyn is that you have to do more than hand wave at the other two -- at the other factors, you have to explain why it is that those aren't the sole cause.

And as, Special Master, as you pointed out earlier, he can't even really do that. He struggles with this, and that's what that "it is hard to say" quote is about, right. He is struggling to explain and really provides no explanation for why in the absence of his hyper -- in the absence of taking the medicine he wouldn't have gone ahead and developed that -- that chronic kidney disease in any event.

And so what we have here is -- is a question where courts who have been presented with these similar situations, what they tell us is that the experts have to do more than what Dr. Fine has done here in order for their opinions to be helpful. And that's particularly true where we aren't dealing with these obscure risk factors, we aren't dealing with having to rule out some very hypothetical risk

factor, but these are -- this is a disease that has clear and well articulated risk factors that no one, of course, not even Dr. Fine, denies were at play and they are not just any risk factors but they are among the most prominent ones, and Dr. Fine ought to have known that in order to get past causation here he needed to meaningfully engage with those risk factors and he did not.

So with that, I'll reserve the remaining time for rebuttal. I'm happy to take, of course, any questions that you might have.

THE SPECIAL MASTER: Okay. Thank you.

Okay. I'm guessing, Stephanie, are you doing this one?

MS. O'CONNOR: I am.

THE SPECIAL MASTER: Good guess, right.

MS. O'CONNOR: So I think one of the first things I want to say is I'm less interested in what the Eleventh Circuit has to say than I'm interested in what the Third Circuit has to say. And I think the Third Circuit is a lot less dogmatic, if you will, about what it is that the plaintiffs need to show. And I would point out that the Heller case relied on by the defendants actually supports that Dr. Fine did

a proper analysis, a proper differential diagnosis that rests on, I believe the expression might be "good grounds."

But let me go back a little bit, if I may, Ellen. I want to address some of the more specific issues that were raised by counsel.

First of all, Dr. Fine, as I think you know, is a board certified nephrologist. He is at the Johns Hopkins University and is most recently an associate professor of medicine there. He has been treating patients for 30 years, nephrology patients in particular, and is absolutely qualified to offer opinions here from the outset.

In terms of how he approached the differential diagnosis, he reviewed all of the records that were available to him, the same ones as the defense experts reviewed, he mapped out, very significantly, he mapped out certain parameters that he thought were key to arriving at his differential diagnosis and ruling in Nexium, ruling out other factors and ruling in certain factors as contributing. And the two facts, he ruled in PPIs definitively and he also states at Page 11 of his report that both hypertension and obesity may have played a role.

Now, counsel is completely incorrect in taking the position or stating it, she obviously didn't read Dr. Fine's report, general report or any of the other experts, for that matter, hypertension and diabetes are the main causes of chronic kidney disease, not obesity.

And by the way, at Page 11 cited by counsel of Dr. Fine's report, he indicates under this section called Obesity, which is Section B at Page 11, that:

"While it's been implicated in the development of CKD, the role of obesity in the development of CKD is somewhat controversial."

All right. Now, he doesn't say it doesn't cause it, but he says it is controversial. That is far and away from being one of the most important or one of the two most important risk factors for CKD. And, in fact, diabetes has been ruled out both by Dr. Fine as well as his treating doctor, Dr. Stoycheff.

That being said, Dr. Fine at Exhibit D of this report that we have -- can we bring up Dr. Fine's report, and I would like to go to, if I may, Special Master --

And if we go to Exhibit D, all right, and just come down.

As you can see, Special Master, Dr. Fine mapped out Mr. Rieder's weight with all of the data that he had available to him at the time starting with April 25th, 2002, when we have the first note that he started Nexium, up through March 15th of 2021, which will be the last page, all right.

And you can see as we scroll through and Dr. Fine actually describes Mr. Rieder's weight as not being really bad, that he hovers, if you will, he is on the side of obesity at times and other times not, but basically, his -- and if we can just go back a little bit, his BMI, body mass index, hovers at the 30, sometimes above -- keep going, please -- sometimes below.

So the obesity that all of the hand waving is about is at best borderline obesity, sometimes obese, sometimes not obese. And given Dr. Fine's opinion that obesity itself is controversial, this is not the level of obesity that doctors, nephrologists are worried about when looking at causes for CKD, and I believe that Dr. Fine says that.

I'd also like to talk about hypertension.

Can we go to Exhibit E of this report. And let's come down. This is a chart entitled "Blood Pressure," and, Special Master, Dr. Fine has mapped out and, therefore, considered Mr. Rieder's blood pressures beginning as early as April of 2002.

And if we can continue going down all of the way through March of 2021.

He looked at all of these blood pressures, not just two or three snippets of blood pressures that were taken out by defendants' experts, but all of the blood pressures over time. And, in fact, in his deposition, counsel may remember, he referred to Mr. Rieder's blood pressure as being beautifully controlled at times and not being that high to cause such concern. And that is throughout his deposition and in his report.

Now, contrary to what counsel says, he does rule out the two causes that he admits may have contributed, but he does rule them out as the sole cause.

And how does he do that? He does it, for hypertension, by saying: Given the patient's continuous use, PPI use, in conjunction with the patient's underlying treated hypertension, in my

opinion PPI use is the, not are, is the substantial factor in causing the development of CKD, but his hypertension may have contributed in that it was an underlying condition.

He has clearly ruled it out as the sole cause.

The same thing with obesity, after telling us in the same page, at Page 11, after indicating that it is controversial, he also goes on to say it's more likely that it associates with diabetes and hypertension and that any association of obesity of renal injury is driven by obesity's impact on these two health conditions. And, again, I remind Special Master that he does not have diabetes.

He goes on in the same paragraph to talk about: "Mr. Rieder exhibited mild obesity that tended to wax and wane at times, albeit he weighed more in an earlier period of time when he was ingesting Nexium daily."

Now, this is very key.

"The stabilization of his kidney function after his discontinuation of Nexium is more consistent with the removal of that exposure than with the effect of his weight loss. His kidney disease is currently

progressing and weight loss does have a role in slowing that progression."

Mr. Rieder's weight is not that much different today or in 2015 or earlier years when he stopped taking Nexium.

What I'd like to do is, can we put up the graph from Page -- I think it is Page 4.

In addition to mapping out all of the parameters that address Mr. Rieder's health conditions, Dr. Fine in Figure 1 entitled "Estimated GFR Changes Over Time" shows us in a pictorial form, a picture is worth a thousand words, that prior to 2006 Mr. Rieder's GFR is in the normal range. Counsel may not like that. Their experts may not like that, but Dr. Fine has opined that it was within the normal range.

And, again, I spoke to this issue earlier, CKD as an entity, and I'm not going to talk about upper or lower case, but CKD as an entity is defined as a GFR less than 60 for a period greater than three months.

In this case we do not see this decline in GFR until 2006 where it is at 51, according to the graph, and this is fully four years after Mr. Rieder

began taking Nexium.

Now, his weight is pretty much the same, his blood pressure, there are some rises, there are some dips, but if you look at this graph, what you see is a downward trajectory, clearly, of his kidney function. There are a few dips here and there and the doctors will explain that these are physiological differences, but the redline that we get to is in 2015.

Now, Mr. Rieder was taking PPIs daily and continuously until his last prescription filled in January of 2015 for 90 pills, he ingested 79 of those 90 pills, as the deposition testimony shows, which took him to the end of March of 2015.

And then what happens? We see a stabilization, as Dr. Fine pointed out, of the GFR. Blood pressure, weight, yeah, there was some weight loss, yeah, maybe he is working a little bit harder on his hypertension control. Now he is under the care of a nephrologist.

But look at that as you go across, it is very, very stable until we get to about 2020 and now we are seeing a downward decline, nothing else has changed, his weight is pretty much the same, blood

pressure is pretty much the same, but by this point in time he has advanced kidney disease.

Dr. Fine explains that aging does cause loss of nephrons, but in someone who already has CKD, and in our position induced by Nexium, that person will get to the point of no return, and, in fact, that is where Mr. Rieder is today. He is on a transplant list at age, I think 63 years old.

THE SPECIAL MASTER: How do you square this with the -- the -- the testimony where he says, you know, "it's hard to say," because, I mean, they did -- he was asked sort of the, Okay, is it your position that but for the Nexium this wouldn't have happened to him. And he says, you know, "it is hard to say." And it is a lengthy and somewhat complicated answer, but it seems to me that, you know, there is an argument that by saying, I can't -- he does say, I can't say that he wouldn't have be here if he hadn't -- he wouldn't be here today perhaps if he hadn't taken the Nexium?

MS. O'CONNOR: One thing I would say is I'm not aware that the Third Circuit is a but-for state in analysis. I believe it is a substantial factor analysis.

THE SPECIAL MASTER: Substantial factor, yeah.

MS. O'CONNOR: I would also point out, I would also point out that Dr. Fine, in his comprehensive general opinion report, which by the way is not challenged by the defendants, so Dr. Fine's opinions on general causation come in no matter what if we choose to put him on, but what he does also do in his general opinion report is he addresses not only those studies, of which there are droves of them that find a connection between PPI exposure and chronic kidney disease, chronic renal insufficiency, other forms of kidney disease, including AKI, but there are several studies that he cites here at Page 11 of his report that show that in people that already have kidney disease or at risk of it, it will actually enhance or exacerbate the progression.

So Dr. Fine has given two opinions, one that it caused the development of CKD and that it may have played a role in the progression, more likely than not played a role in the progression of his disease. It is a pretty rapid trajectory for a man this age.

THE SPECIAL MASTER: Okay. Did you want to respond, Jessica?

MS. RYDSTROM: Very briefly, Special Master.

I guess I would start where Ms. O'Connor stopped, which is, it is true, we are not challenging Dr. Fine's general causation report here, but, of course, he has to do more than the general causation report to explain why it is that, if he believes that Nexium can cause CKD, why in this case on these facts with a plaintiff, Mr. Rieder, who had this particular health history and these preexisting risk factors, Nexium actually did cause Mr. Rieder's CKD.

And that's what he hasn't done. He hasn't explained why the other two -- it wasn't the hypertension and it wasn't the obesity that caused Mr. Rieder's CKD, and that's exactly what he is doing with this quote. That is the question that he is struggling with, that is the question that he can't adequately address.

So very briefly, Special Master, if I suggested that obesity was the most common risk factor for chronic kidney disease, then I misspoke. What I -- what I -- if it is, in fact, so controversial, it's presumably not so controversial, Special Master, that Dr. Fine didn't think it was necessary to say explicitly in his report that obesity was more likely than not contributing to Mr. Rieder's development of

CKD, not the progression of his CKD, but the development of his CKD.

And that's the question that you asked me earlier, is the opinion here that these risk factors were simply making the CKD worse or is it that they in the absence of Nexium wouldn't have led to his developing CKD anyway. And the opinion that he gives us in his report is that hypertension and obesity more likely than not contributed to his development of CKD.

And what he doesn't do, Special Master, is tell us, when he says: "Given the patient's continuous PPI use," and this is in the report at Page 11, "in conjunction with the patient's underlying treated hypertension, in my opinion the PPI use is the substantial factor in causing the development of his CKD."

So what does he give us there, Special Master? He only gives us two things, that he continuously used PPI, that's the temporal relationship, right, that's collapsing the general causation and the specific causation here, and that he had an underlying treated hypertension.

And that's simply not what we see when we look at the graph that Ms. O'Connor put up. That is

not what we see when we look at Dr. Fine's own data and chart. We don't see that this person, this Mr. Rieder who had suffered from hypertension since his 30s, so since he was a young man, who was being treated with multiple medicines for hypertension and who is still experiencing the blood pressure spikes that Dr. Fine records in his chart, what we don't see it treated hypertension. We see an individual who was struggling to treat that hypertension.

And so if you take out, as the cases say that we have to, that temporal relationship, we aren't left with an explanation as to why the hypertension would not in and of itself have been enough, given his long history of this and other risk factors for Mr. Rieder to develop chronic kidney disease.

THE SPECIAL MASTER: Okay. Thank you.

So I think, happily, we are at lunch break time, and I guess what we suggested is we'd come back at 1:20. I don't know if that assumed a 12:30 conclusion or not.

Okay. All right. Well, let's -- I don't know, should we stay with the 1:20? Yeah, does that sound okay? Does that work for folks? Does anybody have a problem with that?

Okay. All right. So let's get back on at 1:20, okay.

(WHEREUPON, a recess was had from 12:32 to 1:20 p.m.)

THE SPECIAL MASTER: Let's go back on the record. And I think the first thing up on our schedule is AstraZeneca's motion for summary judgment on other grounds for Rieder.

Who is going to handle that for AZ?

Hi Mike. Go ahead, Mike Schissel.

Is he on mute?

You need to unmute yourself, Mike, I think, I'm being told.

MR. SCHISSEL: Okay. I've done it.

THE SPECIAL MASTER: There you are.

MR. SCHISSEL: Can you hear me now?

THE SPECIAL MASTER: Yeah.

MR. SCHISSEL: Nice to see you, Special Master.

THE SPECIAL MASTER: It is nice to see you too.

Okay. Go ahead.

MR. SCHISSEL: Okay. So this is our motion on summary judgment based on the issue of proximate cause and we think that the issue has been adequately briefed, but there were just a few points that we

would like to highlight for you, and I can do that, I think, in a few minutes, and I have a PowerPoint that hopefully you can see. Okay.

THE SPECIAL MASTER: Yes, I can see it.

MR. SCHISSEL: Yeah, so just a few -- just a couple of foundational issues.

Obviously the plaintiff has the burden to prove that his ingestion of Nexium was proximally caused by an inadequate warning, and if the plaintiff can prove that the label was inadequate, and we, of course, disagree that it was inadequate, we believe that it was fully adequate, but if the plaintiff bears that burden then under Ohio law there is a rebuttable presumption that the failure to adequately warn was the proximate cause for the ingestion, and then we have an opportunity to rebut it if this so-called adequate warning would have made no difference in the decision -- the physician's decision to prescribe the drug, and we can do that with unequivocal testimony from the physician that he would have prescribed the drug despite the adequate warning.

Now, there are two doctors, two prescribers in this case that matter. The first one is Dr. Konold. He was the original prescriber. He

passed away before the litigation was filed and, therefore, by no fault of either party his testimony is unavailable to us.

The plaintiff argues that Dr. Konold's death would preclude us from the ability to rebut the presumption, and, therefore, summary judgment should be denied. And what they are trying to do, effectively, if that -- if that was to occur and if that was the law, then a rebuttable presumption under Ohio law would be turned into an unrebuttable presumption merely because the prescriber happened to pass away before the litigation was filed. And we think that would be an unfair result, particularly since I don't think anybody disputes that the -- that the ultimate burden of proof on proximate causation lies with the plaintiff. And of course the plaintiff doesn't have to --

THE SPECIAL MASTER: What do you do when -- when a doctor dies with the ceding presumption?

MR. SCHISSEL: So, you know, we don't have a lot of cases in this particular situation. We've cited a number of cases in, I think it was Footnote 6 of our reply brief, where the case is made clear if the prescriber's testimony is unavailable, either somebody

decides not to take his deposition, you know, he dies during the litigation itself and his testimony is unavailable, the cases do say that at the end of the day the burden to prove causation lies with the plaintiff and, therefore, they have to prove it somehow.

And, you know, different jurisdictions can deal with it different ways, reasonable doctor or some other standard, but in no -- and we haven't found a single case, and I don't think the plaintiffs have cited a single case that said in a burden shifting situation that just because the prescriber dies it somehow turns the rebuttable presumption into an unrebuttable presumption.

THE SPECIAL MASTER: Okay.

MR. SCHISSEL: And so that's the first doctor, and that's really very much, I think, an issue for the court.

The second doctor is Dr. Wallin, and he took over the prescription from Dr. Konold effectively. He began prescribing in 2008 until sometime in 2010. His deposition was taken. The plaintiff took it first and then we examined the doctor after the plaintiff took the deposition.

And his testimony, we think, is un -- is unequivocal. He says that he thinks that Nexium is -- was a safe and effective drug, it still is a safe and effective drug, and, you know, he was examined by the plaintiff and the plaintiff obviously, you know, in the questions was suggesting that Nexium caused kidney disease. And then we asked him when we had a chance to examine him whether there is anything that he has seen or heard today that would cause him to question his decision to prescribe Nexium and he unequivocally and affirmatively said no.

And so we think that, you know, based on this record, one, they can't carry the burden on the first prescriber and the second prescriber we think we have overcome the presumption based on the deposition of the prescriber, which is what the cases allows us to do.

THE SPECIAL MASTER: Am I correct that he also testified that if there had been a warning he would have communicated that to Mr. Rieder and that Mr. Rieder testified that if warned he wouldn't have taken Nexium.

Does that -- does that change things?

MR. SCHISSEL: I don't think so because even if

we go back to the rebutting -- or the rebuttable presumption -- or rebutting the presumption, the warning, we rebut the presumption if the warning, an adequate warning would have made no difference in the physician's decision to prescribe. It doesn't say that, you know, whether or not the patient would heed any information passed on by the doctor. The question is whether the doctor would prescribe, and that would be the law -- that is the law in these learned intermediary states.

So we think that that is a little bit of a red herring or very much of a red herring in this case because what you have to focus on is whether the doctor would prescribe, and that's what the cases talk about.

THE SPECIAL MASTER: Okay. So just to be clear, if Rieder did -- if Mr. Rieder did testify that, you know, if he had been given some kind of a warning he wouldn't have taken it, you are saying that's irrelevant given the learned intermediary doctrine?

MR SCHISSEL: Yes, that's our view.

THE SPECIAL MASTER: As long as the doctor says, I still would have prescribed?

MR. SCHISSEL: That's right. That's right.

THE SPECIAL MASTER: Okay. Okay.

Sorry. Go ahead.

MR. SCHISSEL: No, and really, you know, the third doctor, Dr. Oberlander, you know, the plaintiff concedes that that testimony is -- is not necessarily something that the court has to address, because at the time that that doctor prescribed, Mr. Rieder's CKD was fairly advanced at that point. And so both sides sort of agree that, you know, that's irrelevant.

Now, if you want to consider it, you know, that testimony, too, at the end of this long -- this long back and forth, at the end of the day he says that he would still prescribe the Nexium today.

So, you know, the testimony is there, but at that point in time the plaintiff is saying, you know, you don't even have to look at that one. Really what matters is Dr. Konold and Dr. Wallin.

THE SPECIAL MASTER: Okay.

MR. SCHISSEL: And I will save anything else for rebuttal at this point.

THE SPECIAL MASTER: Thanks, Mike.

Who is talking for the plaintiffs?

MR. AUTRY: I am. Good afternoon. Pleasure to meet you.

THE SPECIAL MASTER: Nice to meet you.

MR. AUTRY: And I also wanted to thank everybody, both defense counsel and yourself, for being accommodating with my schedule a couple of weeks ago.

THE SPECIAL MASTER: No problem. My condolences on your family as well.

MR. AUTRY: I really appreciate it. It means a lot.

Going straight into the argument here on proximate causation for Mr. Rieder, I don't think it's that complicated because we are in the State of Ohio which has a rebuttable presumption that requires defendants to produce evidence, unequivocal evidence if they want summary judgment in their favor to show that a stronger warning would have made no difference in whether Rieder ingested Nexium. That evidence just doesn't exist here. And, in fact, there is substantial evidence, especially viewing the evidence in the light most favor to Rieder, taking all inferences in Rieder's favor, that a stronger warning would have made a difference.

You know, starting with the first doctor, which is several years, Dr. Konold, defendants'

position is basically that the rebuttable presumption disappears if a doctor has passed away. There is no Ohio law to support that and they are arguing for a change in the law and they should be the ones that should produce cases to say that a death of a physician eliminates their rebuttable presumption.

The Ohio Supreme Court --

THE SPECIAL MASTER: Well, would you agree with what Mr. Schissel says, that you are basically arguing that it makes a rebuttable presumption irrebuttable because obviously you can't get testimony from him, or are there other ways you are saying that it could be rebutted?

MR. AUTRY: You could potentially rebut it with the testimony of plaintiff, you could potentially rebut it with other evidence from the medical records. The -- we are not -- a physician's testimony is not the only possible way for defense counsel or a defendant to present causation evidence. There is plenty of evidence that can go to proximate causation. And the issue right now, when we are talking about what's unfair or fair, is defendants are seeking summary judgment. They are seeking judgment as a matter of law in their favor that they have met their

burden of production to overcome this rebuttable presumption.

So in the sense of fairness, we are not seeking judgment in Rieder's favor on this presumption. We are asking for a trial. And trials -- they will be able to present their evidence to a jury. We are not seeking directed verdict on this issue at this moment. We are simply saying this is a jury question, viewing the evidence in the light most favorable to Rieder and taking the inferences in his favor, and that's especially true when you factor Rieder's own testimony.

You know, the record is not silent as to what would have happened between 2003 and 2008 were there an adequate warning that -- on Nexium's label. Rieder says, If that was conveyed to me from the beginning, I would not have taken the product. If it was conveyed to me after I had started taking the product, I would have stopped taking the product. His testimony is, in fact, unequivocal, even though it does not need to be because we are the party -- we are the non-moving party on a motion for summary judgment. That's just step one.

Step two is Dr. Wallin, although you don't

have to get there because they have to rebut the presumption as to all three physicians, Dr. Wallin's testimony is that he would have discussed all medications that had a risk of kidney injury when Rieder's GFR dropped. He says that after two distinct tests and he would have wanted to know whether Rieder's medications had a risk of kidney injury.

Unfortunately for Dr. Wallin and for Mr. Rieder, defendants did not warn about even acute kidney injuries until the FDA required them to do so in December of 2014, they did not warn about tubulointerstitial nephritis until the FDA required them to do that a year and a half ago. So at this point that Dr. Wallin was meeting with Mr. Rieder, he did not have the information at his disposal in the Warnings and Precautions section to see that this medication carried a potential risk, a reasonable causal association of kidney injury to determine whether or not to take Mr. Rieder off of that.

Further, you have, again, Mr. Rieder's testimony. If this information was conveyed to me, I would have stopped taking it.

And then you have Dr. Oberlander. And, again, you don't have to get to step three because

they have to prove, they have to rebut the presumption at all three steps. But if you get to step three, Dr. Oberlander's testimony is that he had no recollection of Mr. Rieder. His testimony was before -- in November, before the FDA required -- November -- sorry -- I'm getting the years mixed up. But at the point of his testimony, he was unaware of the potential risk of long-term kidney injury and would not have associated that with Nexium even at the point of his deposition.

When he was asked to assume that Nexium could cause long-term kidney injuries, he gave a very qualified response in which he said, Well, it was a long time ago, I don't really remember Mr. Rieder. It is not the unequivocal testimony that you would need to get judgment as a matter of law in your favor as a manufacturer, viewing the evidence in the light most favorable to the plaintiff, especially -- especially where that plaintiff says, If I was told about this risk, I would have stopped taking it.

And when you go to the learned intermediary doctrine, that is important, because defendants want judgement as a matter of law that Rieder's doctors would have said, No, I am going to

prescribe this to you anyway even though you don't want it. That is not a reasonable inference, but nonetheless it would be an inference in their favor which they are not entitled to at the summary judgment stage, that Rieder's doctors would have prescribed him Nexium even if Rieder says, I didn't want to take it.

This is especially true when you consider the fact that Rieder was able to change his eating habits in 2015 so that he did not need Nexium anymore. When Rieder stopped taking Nexium in 2015 it was because he decided to change his diet, he got his heart rate under control. That could have happened in 2014, 2010 or 2006 if Rieder knew that there was a risk of Nexium.

So the idea that Rieder's doctors would have continued to prescribe him Nexium when he said he didn't want it and even if he had got his heart rate under control is an unreasonable inference and, again, defendants at this stage are not even entitled to reasonable inferences in their favor.

I need to mention a little bit this Footnote 6 that defendants reference from their reply brief. I believe it was Footnote 6. But there is a footnote in their reply brief where they cite a lot of

cases to argue that the death of a physician goes against the plaintiff.

It's important to recognize that they are citing authority outside of Ohio and they are citing cases that explicitly reject a rebuttable presumption under various states' laws. Defendants conveniently ignore that from their footnote and ignore that from their argument today.

They cite a South Carolina case that says: "South Carolina courts would not apply causation presumption." They cite a Pennsylvania Common Pleas County Court decision from 2005 that says: "Pennsylvania courts have consistently declined to apply any heeding presumption." They site an Eleventh Circuit from Georgia, that says: "Deeds," referring to a prior Eleventh Circuit case interpreting Georgia law, "forecloses a holding that Georgia law provides a rebuttable presumption that shifts the burden to the defendant."

Defendants repeatedly cite authority in their reply brief that explicitly rejects Ohio law and rejects the rebuttable presumption that we are under in this oral argument.

And I believe that is the gist of

everything I had to say, but I would be happy to answer any questions, if you have them.

THE SPECIAL MASTER: Yeah. One thing, and I don't know if it is necessarily relevant for this motion, but, you know, you've characterized what the warnings should be in a variety of different ways.

I mean, for purposes of this motion, I guess, what is it, and I guess we talked a little bit about this this morning, I don't know if you were listening --

MR. AUTRY: I was.

THE SPECIAL MASTER: -- you know, what is it that plaintiffs in the Rieder case are saying the adequate warning would have been?

MR. AUTRY: Sure. And I'm going to give a caveat because under Ohio law we are not required to draft the label language. We are required to demonstrate that the label was inadequate.

THE SPECIAL MASTER: Okay.

MR. AUTRY: But we do give several examples of adequate -- of language that would be stronger that would have, viewing the evidence in the light most favorable to Rieder, changed the course of his -- of his treatment.

So Rieder's doctors say and Rieder says that if they had even -- and this is Dr. Wallin and Rieder himself, if there was even knowledge of the risk of kidney injury at the time, that he would have stopped -- that that would have been relayed to him and he would have stopped taking it.

So to the extent the defendants are arguing that to show proximate causation we need certain magic words in the label, viewing the evidence in the light most favorable to Rieder, that is not true. If Rieder's Dr. Wallin had been aware that there was a risk of kidney injury at all and had relayed that to Rieder, Rieder is pretty unequivocal that he would have stopped taking it.

But further, if you look at our Dr. Ross, and, again, this was gone into pretty extensively this morning, it will be touched on again tomorrow in preemption because it sort of bleeds through everything, there was reasonable evidence of causal association when it comes to chronic tubulointerstitial nephritis by 2003 and acute tubulointerstitial nephritis by 1995 and at that time there was also, at '95, evidence of downstream risk that acute tubulointerstitial nephritis could lead to

chronic kidney disease, and by 2003 there was evidence of the chronic kidney disease risk.

And, again, as Paul talked about earlier, chronic kidney disease itself is a term that we ascribe to the nature of results from the tests. So chronic kidney disease is basically a diagnosis that says your GFR has been below 60 for 90 days or more, whereas a lot of the medical literature will use the term "chronic interstitial nephritis" or "chronic tubulointerstitial nephritis" instead because they are more talking about the long-term degradation or deterioration of the kidney or permanent deterioration of the kidney. But when it comes to --

THE SPECIAL MASTER: Okay.

MR. AUTRY: -- the label language itself, in Rieder's case, viewing the evidence in the light most favorable to him, there was plenty of language they could have used that would have changed the course of treatment.

THE SPECIAL MASTER: Okay. Thanks. I didn't mean to take us down a, you know, a path that may not be all that relevant to this, but I was just curious.

Mike, did you have anything else you wanted to make?

MR. SCHISSEL: Yeah, very briefly just a few points.

First of all, the rebuttable presumption is rebutted by testimony from a physician that he would have prescribed regardless of this so-called adequate warning, whatever it is, and I think we still don't know what that is in this case.

But what counsel said is that we could rebut it by the testimony of the plaintiff. Well, there is certainly no law to suggest that a plaintiff can get up and say what a doctor would have done, okay. So that's completely inadmissible testimony. It makes absolutely no sense in this case.

Secondly, counsel says, Dr. Wallin would have discussed. Well, that's not the standard. The standard in these presumption cases is would he have prescribed it. Doctors discuss adverse effects and warnings with patients all of the time, but what the relevant inquiry is, would he or she have prescribed it.

And I think in this case Dr. Wallin's testimony was pretty unequivocal. And they had an opportunity at his -- they took his deposition first. They could have said, If you had the following label

in front of you. Well, they didn't do that because, frankly, we still don't know what that label would say, but they didn't even ask that question. So what we have is the un-refuted testimony from Dr. Wallin that he thinks it is a safe and effective drug and would prescribe it today. The same testimony from Dr. Oberlander if you get there.

And, you know, I think those are the points. I mean, the key points on the presumptions you focus on, whether the doctor would have prescribed. We know with first doctor, we don't have the benefit of that, and you shouldn't change the law, which is, at the end of the day, says that the plaintiff bears the ultimate burden for proximate causation and you need to focus on the conduct of the doctor and the second doctor says and the third doctor says I would have prescribed it in any event.

THE SPECIAL MASTER: You may not have asked this at the deposition, no one may have, but was Dr. Wallin asked whether he would have still prescribed it even if the plaintiff didn't want to take it.

MR. SCHISSEL: He was not asked that at his deposition. And -- no, he was not asked that. He just said he would have passed it -- I think he said

he would have passed on the information if there was this warning that nobody can really describe to him.

MR. AUTRY: Your Honor, if I could briefly respond in less than 15 seconds?

THE SPECIAL MASTER: Fifteen seconds or less, go for it.

MR. AUTRY: Sure.

Viewing the evidence in the light most favorable to Rieder, Dr. Wallin's prescribing habits would have changed. Dr. Wallin did not know even at the time of his deposition that this was a risk of Nexium and Dr. Rieder -- Wallin did change his prescribing habits of NSAIDs because he knew at the time that this was a risk of NSAIDs.

So there was a reasonable inference in Rieder's favor that Dr. Wallin would have changed his prescribing habits and he did not testify that had the label warned of CKD or kidney disease at all that he would have prescribed it anyway. That is nowhere in the deposition.

MR. SCHISSEL: Can I respond to that in a similar amount of time?

Yeah, the cases they cite on a doctor prescribing -- changing prescribing habits is very

different from this case. It is not would you have passed on a warning or would you have discussed a warning with the patient. It is things like, in the cases they cite, the doctor says, I would have been more cautious, I would have used maybe less of a dose, I would have eased this patient up to the dose that's prescribed, that's changing a prescribing habit, not passing on information to a patient.

So I think it is a very different situation, and there is no record here that any of these prescribers would have actually changed their prescribing habits.

THE SPECIAL MASTER: Okay. Thank you very much.

MR. SCHISSEL: Thank you, I appreciate it.

THE SPECIAL MASTER: So I think we are moving on now to plaintiffs' omnibus motion to exclude experts, and I don't feel strongly about which order we want to go in. I had Mann listed first but don't feel strongly about that if folks on the plaintiffs' side want to go in some other order? Anybody?

MR. AUTRY: I think that's fine. I'm going to handle the Mann argument for us.

THE SPECIAL MASTER: Okay. I mean, is there somebody who needs to go before you? I don't think

that there is any magic to the order, but... No?

MR. AUTRY: Speak now or forever hold your peace.

THE SPECIAL MASTER: Go for it.

MR. AUTRY: Special Master, I think Mann's opinion is a series of conclusions with no methodology. Mann repeatedly praises AstraZeneca, PRAC and the FDA, although testifying in her deposition that she did not review the things that AstraZeneca, PRAC or the FDA reviewed.

So she says that AstraZeneca's submissions to PRAC were very thorough and forth going -- forthcoming, that AstraZeneca's PRAC submissions were very good. A comprehensive report by AstraZeneca. But she doesn't know what AstraZeneca had at its disposable to submit to PRAC, she doesn't know what AstraZeneca left out, she doesn't know what the clinical trials say that AstraZeneca submitted in writing.

She reviewed AstraZeneca's own PRAC submission and said they must have reviewed everything to get to this point. That is like reading a book report and grading it without reading the book. It is not a reliable expert opinion.

As an expert, you have to have -- if you are going to have an opinion about an underlying document, you should review that underlying document, and that's what Mann repeatedly needs to do but doesn't do.

She says PRAC's review was careful, that PRAC's review was comprehensive and thorough, but she did not know what PRAC considered, she did not know what the records say that PRAC considered, she did not know what the clinical trials say. She ignored the lion's share of the medical literature. She took a head-in-the-sand approach to the record and then gave opinions that PRAC, the FDA and AstraZeneca adequately and thoroughly and well summarized that record. That is not a reliable --

THE SPECIAL MASTER: Let me stop you there -- let me stop you there, because I read your papers. And a lot of your arguments, it seems to me, seem to rely mostly on her -- her supposed failure -- either the failure to identify certain missing information, and what you are -- you are saying now kind of sounds the same way, that -- I mean, you don't know what you don't know, right. And so she is presented with reports and information that were submitted to the

FDA, and if I was reading the papers, they seem to be saying that, Well, somehow she -- she didn't take into account what wasn't there.

And I wonder if that's really the right standard to evaluate testimony. I mean, you can only look at what's there and evaluate whether that's adequate or not. And, you know, in her experience as someone at FDA, can only look at a report and say, Would I have found that sufficient.

Like I say, I feel like maybe your argument is kind of saying, Well, we have to look at what's not in the report and I'm not sure that's really what experts do.

MR. AUTRY: Special Master, I believe that's an incorrect statement of what Mann did at the FDA. When Mann was at the FDA, she reviewed the medical literature, she reviewed the clinical trials, she didn't just review a one-page summary of the medical literature by a manufacturer. She didn't just review a paragraph or two-paragraph summary of the clinical trials, she reviewed the underlying data. This is not what she did at the FDA. She had a methodology at the FDA. That's a reliable methodology. That's not what she did in this case.

In this case she reviewed a manufacturer's summary of the record and then said that's a good summary of the record. She says that's a thorough summary of the record, a comprehensive summary of the record. That is not a reliable opinion of praise. In order to say that AstraZeneca did a good job in reviewing the record, you have to actually review the record yourself.

THE SPECIAL MASTER: So you are saying that she has to review all of the raw data that went into any report in order to say that that report was adequate or sufficient?

MR. AUTRY: Not necessarily all. I mean, we are not talking about --

THE SPECIAL MASTER: Where do you draw the line? Where do you draw the line?

MR. AUTRY: Daubert says that it needs to be reliable. If you completely take a head-in-the-sand approach to the record, you can't have an opinion on what that record says. She is just regurgitating AstraZeneca's opinions and saying they are her on, and not only that, saying they are good opinions.

THE SPECIAL MASTER: So I guess what I'm trying to get to, you are describing it as a completely

head-in-the-sand approach.

What is that -- what are you saying -- where is the line that what the expert needs to look at in the way of raw data, underlying data, studies that support a report and what, you know, obviously they can't review every piece of data that goes into every report, and that's not what FDA reviewers do, but where -- where is the line, that's what I'm trying to understand.

MR. AUTRY: Well, when it comes to medical literature, we've identified about, I think, three dozen relevant pieces of published peer-reviewed literature. That's not an insurmountable burden to review those, but we would not be here and we would not be filing a challenge to her if she reviewed 30 out of 32, but that's not what she did. She reviewed a summation of the medical literature and then said that's a good summation. You just can't -- that's not a reliable opinion if you don't look at the underlying record being summarized.

This is not -- our Daubert is not against her because she should have spent 10,000 hours as opposed to 2,000 hours. You know, we are not going down that road. Her opinion is completely unsupported

and she is a mouthpiece for AstraZeneca to say -- I mean, like, look at her opinion that AstraZeneca appropriately labeled Nexium at all times. I cannot for the life of me determine how she reaches the conclusion that AstraZeneca could not have warned about acute interstitial nephritis before 2014. I have no idea how she gets there. I have read her report several times, I have read her deposition several times. How does she reach the opinion that in 2013 AstraZeneca's label was appropriate? How does she reach the opinion in 2002 that AstraZeneca's label was appropriate? I'm clueless. And I've read her report several times and I've read her deposition several times.

You need a methodology to get from Point A to Point B. Your methodology cannot simply be the manufacturer said it so I agree. That's just not a reliable opinion under Daubert. The manufacturer can say it to the jury just without an expert hired to say the same thing and say we did a good job. And if the manufacturer -- and if the expert is going to say we did a good job, the expert needs to review the same thing you were reviewing as the manufacturer to come to the conclusion that your summary was a reasonable

one.

I mean, she says it was correct, thoughtful, extensive, comprehensive and careful. I don't know how she is reaching those opinions without reviewing the underlying literature. She is just rubber stamping assessments without reviewing those assessments. Again, it is like saying a book report is good without reading the book and this is not what she did at the FDA.

THE SPECIAL MASTER: Okay. Let me ask you: Can she -- do you think she can testify as to what -- whether the process that FDA followed in certain circumstances was appropriate?

MR. AUTRY: I think her FDA opinions suffer the same flaw as her AstraZeneca and PRAC opinions. She did not look at the underlying data to determine what was being considered or not considered. So I don't think she can give a reliable opinion that the FDA thoroughly reviewed what was out there because she didn't and she didn't try to. Like, how can you give an opinion that the FDA conducted a thorough review if you don't even attempt as an expert to conduct a thorough review yourself. I mean, it is not like she made an effort and failed, it is not like she made an

effort and fell short, she just didn't try to conduct a thorough review herself. She just jumped straight to the conclusion that PRAC, the FDA and AstraZeneca conducted a thorough review.

THE SPECIAL MASTER: All right. Anything else?

MR. AUTRY: I believe that's it, your Honor.

THE SPECIAL MASTER: Okay. Thanks. Who is going to respond?

MR. MILLER: I'll respond to those.

Can you hear me okay, Special Master Reisman?

THE SPECIAL MASTER: I can. Nice to meet you.

MR. MILLER: And for the record, I am Jake Miller on behalf of AstraZeneca.

So there's a few things I'd like to say in response to Mr. Autry's presentation. The first is he did not even mention, from what I could tell, anything related to the first two arguments that are actually made in their briefing. So I will take from that that plaintiffs have conceded that those two arguments have been adequately and fully addressed and that they are appearing to now shift the focus of their arguments.

For Mr. Autry's presentation, you might be led to believe that Dr. Mann is somehow being put up

as an expert whose sole job is to opine on PRAC issues. And I just want to point out some context, right. Dr. Mann is offering a regulatory opinion about the appropriateness of FDA's decisions vis-à-vis the content of the Nexium label when it comes to kidney disease. PRAC is one piece of the data that goes into that analysis, it is just that, a piece of data. And I'm going to talk about that but I just want to make sure that we are talking about the correct context. You know, Mr. Autry's presentation seems to suggest or leave the listener with the view that this is somehow an auditing opinion or something, which it is not, it is a regulatory opinion.

Now, Mr. Autry said a couple of times that Dr. Mann is simply regurgitating opinions or rubber stamping opinions without doing her own analysis. Frankly, Special Master Reisman, this is an absurd position. I'm going to start just by talking about the FDA side of things and then I'll go into the PRAC.

Mr. Autry said that Dr. Mann essentially didn't do any of her own homework, so to speak, failed to review any of the relevant underlying information and simply just regurgitates what FDA concluded, and that is a gross, gross misrepresentation of the record

here.

So just as an example, if you look at both Dr. Mann's written report and importantly her materials considered list, it is littered, littered with the leading studies discusses a potential association between PPIs and kidney disease, the very studies that form the basis of FDA's own analysis. She reviewed the Lazarus study, which is MCL No. 103; she reviewed both the Xie studies, which is MCL Nos. 160 and 161; she reviewed the Attwood publication, which is MCL No. 14, which discusses the randomized Zofran and Lotus studies; she reviewed the Moayyedi publication, which discusses the randomized COMPASS study. And I don't mean to just make this a long list of things that she reviewed, but just because I think this was the focus of plaintiffs' presentation here, she reviewed Simpson, MCL No. 153; Tomlinson, MCL No. 157; Wu, MCL No. 159; Antoniou, MCL No. 1; Arora MCL No. 3.

Special Master Reisman, I can go on and on and on. I don't want to belabor the point. What I want to suggest to you -- well, not suggest. What I want to affirmatively say is Mr. Autry's assertion that Dr. Mann essentially didn't do any of her

homework and didn't review any of the underlying studies herself is simply a misrepresentation of the record and the report.

Now, in addition --

THE SPECIAL MASTER: How do you respond -- hold on.

How do you respond to plaintiffs' claim that -- where -- that she reached conclusions without supporting documentation for, I think some examples that I saw were the PRAC submission and data relevant to FDA's 2020 conclusion, and I think her deposition testimony was cited by plaintiffs with regard to those as areas where she did not -- or she said she did not review support documentation.

Do you agree with them, disagree?

MR. MILLER: I don't agree with plaintiffs' characterization at all. So there was a few -- there were a few things that you flagged there, Special Master Reisman. I'll try to address them all. If I forget one, please remind me to address it.

But you mentioned, for example, the FDA 2020 decision. So, you know, I started my presentation by talking about all of the underlying studies that she herself reviewed, not just FDA's

analyses but the actual studies themselves, and those leading studies are the very things that FDA itself was -- was primarily and principally focused on in its sort of 2016 to 2020 timeframe in evaluating whether there needed to be a label update in 2020.

Now, in addition to reviewing those studies, Special Master Reisman, Dr. Mann also reviewed internal FDA analyses themselves, right. She reviewed, for example, the FDA's internal analyses of the Lazarus study, of the Xie study, of the Antoniou study. She reviewed FDA's 2018 mechanism paper by Dr. Fanti, which by the way notes that FDA had and considered the PRAC analysis, which I'll get to. And, I mean, again, not to belabor the point, Special Master Reisman, but Dr. Mann reviewed copious materials demonstrating FDA's analysis of the kidney safety issues over many, many years. Just as an example, Item No. 66 on Dr. Mann's materials considered list consists of more than 500 pages of internal FDA analysis of renal safety issues spanning many, many, many years. And Dr. Mann's written report, which Mr. Autry gives very short shrift to, fully discusses the careful and thorough FDA analysis, again, over many, many, many years. I mean, we are

talking going back to, you know, the mid-'90s all of the way up through 2020, the FDA performed numerous internal analyses of these issues. And the materials that Dr. Mann reviewed clearly, clearly gives her an adequate basis to say that the FDA was appropriately and carefully assessing these issues and going over them.

Now, Special Master Reisman, I believe your question all touched on PRAC, and, okay, so let me address that now.

You know, Mr. Autry, I think, really ignores the scope of the information that is available from the documents that Dr. Mann herself reviewed. And I think it is important to mention those because, again, plaintiffs would have you believe that what happened is something completely different than what actually happened.

Now, Dr. Mann's report includes an in-depth discussion of PRAC's CKD assessment, the accuracy of which plaintiffs do not and cannot dispute. And the PRAC materials that Dr. Mann reviewed established the following undisputed facts, I want to underscore that point, Special Master Reisman.

Now, first, PRAC's review was prompted by

the publication of the Lazarus and Xie articles in 2016, again, both of which Dr. Mann reviewed and discussed in her report. The information that Dr. Mann reviewed establishes that AstraZeneca submitted renal safety data to PRAC on more than ten thousand patients and identified in that the number of renal events observed in that universe of patients.

Now, the information that Dr. Mann reviewed also shows that in addition to AstraZeneca, Takeda and Eisai also submitted renal safety data to PRAC. And in reaching its conclusion, PRAC, this is PRAC now talking, said that this is the information that we reviewed. And this can be found in the final PRAC report. I believe it is on Page 22 in Section 3.2.

PRAC says across all submissions for all PPIs 64 trials, 64 trials, including over two -- excuse me -- containing over 22,000 patients were included. They say 14 of these trials were more than a year long and they included over 3400 patients and four trials -- of those, four were more than three years in length or three years or longer and included over 1100 patients.

And PRAC went on to explain, Special

Master Reisman, that these trial timeframes are more than sufficient to reach conclusions here because the Xie study, which is one of the two studies that caused PRAC to look into this, said that -- or showed that the peak in the relative risk of renal outcomes, including CKD, occurred after one to two years of cumulative exposure.

So it was only after assessing all of this data that PRAC reached its conclusion. And this universe of information, again, all of which Dr. Mann had available to her and considered, it plainly and clearly provides sufficient grounds for Dr. Mann to offer her opinion here.

And, again, I want to underscore plaintiffs do not and cannot dispute the accuracy of the PRAC discussion in Dr. Mann's written report. Instead, you know, what they've done, Special Master Reisman, is they've sort of pivoted to this theory that plaintiffs have about AstraZeneca purportedly, you know, manipulating is the word they used, manipulating the data, and, you know, they claimed that essentially, as I understand it, it is tough to fully understand the argument, but as I understand it, they are basically saying that in order for Dr. Mann

to be able to offer any opinion at all, she has to essentially effectively audit AstraZeneca's submission in order to affirmatively rebut plaintiffs' manipulation theory, for which, again, there is no evidence or basis in the record.

And I just want to emphasize one or two other quick things, Special Master Reisman, with respect to this. The materials that Dr. Mann reviewed make clear that AstraZeneca enumerated the selection criteria it was using to identify responsive information to PRAC's request, and it is undisputed, undisputed that PRAC has never raised concerns with AstraZeneca's submission or AstraZeneca's selection criteria.

And Dr. Mann also made clear in her testimony that it is common for companies in response to broad requests for data like it to identify a universe of data in responding and that is precisely what occurred here. I hope that was responsive to the Special Master's question.

THE SPECIAL MASTER: Yes. Thank you.

MR. AUTRY: Your Honor, if I could briefly respond?

THE SPECIAL MASTER: I kind of thought you

might.

MR. AUTRY: Thank you.

Your Honor, I have no idea what AstraZeneca's counsel is talking about when he says that Dr. Mann reviewed the clinical trial data because she explicitly says in her deposition she did not. You know, on Page 300 of her deposition:

"I looked at the summary of those trials.

"Okay. You looked at the discussion of those trials in AstraZeneca's submission to PRAC?

"Correct, along with PRAC's review as well as their assessment of those data."

She did not look at the data. I don't care what's on her clinical trials list. She testified under -- or what's on her materials considered list. She testified under oath as to what she considered and what she didn't. And under oath she said she did not look at the clinical trial data.

Now, even though she didn't look at the clinical trial data, her report in her deposition is full of opinions about what the clinical trial data shows or does not show.

"In clinical trials no significant imbalances were observed for renal function and no

cases of interstitial nephritis were observed."

She did not look at the data to reach that conclusion. She looked at what AstraZeneca said about the data to reach that conclusion.

"No cases of interstitial nephritis have been observed in clinical trials."

She did not look at the clinical trials to reach that opinion about what the clinical trials showed. She looked at AstraZeneca's summary of the clinical trials to reach that opinion about what is in the clinical trials. That is not a reliable opinion.

THE SPECIAL MASTER: Hold on. I just want to ask -- I just want to ask you a question.

When you talk about clinical trial data, are you talking about raw patient-by-patient data? What exactly? I'm just trying to understand what the documents are that you think she really did need to review.

MR. AUTRY: Okay. So there are -- when you have a clinical trial there is obviously thousands of potential pages to review. All she reviewed was what AstraZeneca put in as their summary to PRAC of what those clinical trials show. She did not go even one step beneath that. And then she looked at what PRAC

responded to AstraZeneca in their letter response. These are summaries of summaries of summaries that -- and she is just taking them not only as face value. She is saying they thoroughly, accurately and correctly summarized the level beneath them. That is an unreliable opinion because she is not looking at the level beneath them. She looked at the summary.

THE SPECIAL MASTER: And the level beneath it is what? It's the actual patient data?

MR. AUTRY: Yes. And she is not even looking at how many trials were conducted. Like she is not even going a level above that, right. So a level above that and still relatively surface level would be how many trials AstraZeneca conducted to determine if AstraZeneca included all pertinent trials. She is giving an opinion that AstraZeneca included all pertinent trials, but she does not know how many trials AstraZeneca had. She is giving an opinion that AstraZeneca accurately summarized the trials but she did not know what AstraZeneca was looking at to reach those summaries.

And, you know, defense counsel is saying that this is unreasonable to expert their expert to audit their conduct. But that's the opinion their

expert is giving. Their expert is giving an audit opinion that I've looked at what they did and they did good. That has to be a reliable opinion.

THE SPECIAL MASTER: Thank you.

All right. I think we can move onto the next one. I think it's -- the next one on my list was Dr. Deo.

Hi. Jessica, are you going to do that one?

MS. RYDSTROM: I am not, your Honor, because I am opposing it.

THE SPECIAL MASTER: Oh, sorry.

MS. RYDSTROM: So I would rest, but I don't think -- I don't know if that would go over very well.

THE SPECIAL MASTER: I don't think so.

MR. PENNOCK: Everyone will be able to rest pretty quickly because my argument will be very short, Special Master.

THE SPECIAL MASTER: Okay, Paul.

MR. PENNOCK: You know, the papers lay it out I think pretty clearly and I think it boils down to this: If Dr. Deo wants to come to trial or I should say if his lawyers intend to try to put him on the stand to say that the causes, the only causes of the

chronic kidney disease in Mr. Rieder are the things that he outlines, he can't do it. He should be excluded. He should be precluded from offering that view, that opinion because what -- because he didn't rule in everything that he needed to rule in and then rule them out. This is sort of basic Daubert analysis by any expert giving a causation opinion about anything, whether it's a defense expert or a plaintiff expert. You have to rule things in. You can then rule them out.

You can say: Yes, I considered PPIs? And do you think that that played any role in contributing to his disease? No. Why not? I reviewed all of the literature, I reviewed everything that is out there, et cetera, et cetera, and I don't find that there is sufficient support that these drugs can actually cause chronic kidney disease and, therefore, I ruled it out. That's how he would do this.

THE SPECIAL MASTER: So, Paul, is it your position that Deo has to offer an opinion on whether PPIs contributed or not in order to testify at all?

MR. PENNOCK: No, and I was about to give that up, Special Master.

THE SPECIAL MASTER: Okay.

MR. PENNOCK: He could take the stand and he could take the stand to say, Look, I have reviewed his medical history and I believe that, you know, this -- his cardiac issues were a substantial factor in the development of his disease and whatever else he wants to throw in the mix. I think there are a couple of other things in the mix. He said, I think those contributed to his disease. But, you know, have at it. I mean, if he --

THE SPECIAL MASTER: So, I mean, you were anticipating my question. Doesn't that just go to the usefulness of his testimony to the jury, right?

MR. PENNOCK: Yeah, then I think it's like, okay, that's good. And what about PPIs? I don't have any opinion on that. Why not? Because you didn't read anything or review anything. Nothing. I mean, I almost would invite him to give that opinion, but -- you know, to come to the stand for that.

But the bottom line is, I think certainly if we put -- and they said this in their papers, and I don't really disagree, if we put up the cardiologist and say, Look, I looked at all of the cardiology here and I really don't think that his cardiac issues were substance or significant, and I don't think that they

in a meaningful way contributed to this kidney disease and here is why. Well, then they can put Deo up and I can't attest that, to say, Look, I looked at all of the cardiology stuff too and I do think it contributed. That's all fair game.

THE SPECIAL MASTER: So this is -- Rinder is the expert you are talking about, right?

MR. PENNOCK: Yes.

THE SPECIAL MASTER: And so, I mean, I think, you know, as reading over this stuff, it seems to us that the scope of his testimony is going to depend on what -- if Rinder testifies what he says, right?

MR. PENNOCK: I think that's exactly right. And that's why he could end up getting on the stand. But they are going to have -- they will have to be very careful and circumscribe because they can't lead, either deliberately give testimony or leave the impression that he is giving an opinion that these are the only causes of his chronic kidney disease, because if they do that, then he is clearly opening himself up to the cross of, like, Well, you don't have any idea because you didn't even consider all of this stuff that the jury now knows. The jury now knows more than you know about PPIs and chronic kidney disease because

they've actually heard it and you didn't.

So I think we are on the same page, Special Master, and maybe I am with the defendants as well. I mean, sometimes with all of this briefing, as you pointed out several times, we might be missing each other, but that's where plaintiffs stand on Deo.

Thank you, Special Master.

THE SPECIAL MASTER: Thanks, Paul.

MS. RYDSTROM: I will be similarly brief, Special Master.

I mean, from the amount of times that Mr. Pennock mentioned cross-examination, I think we are in heated agreement that that is the place to address any deficiencies in Dr. Deo's opinion. And, look, certainly if Rinder is in, he is in. There is absolutely no question about that. But he comes in regardless of Rinder because he actually has opinions that are -- exist separate and apart from the responsive agreements to Dr. Rinder, and those are, of course, that hypertension, the issue or the sort of disease with which he is so intimately familiar, is the likely cause of Mr. Rieder's CKD.

And separately, taking on two issues that Dr. -- that Dr. Rinder -- I'm sorry, the Rinder/Rieder

thing is really going to trip me up here, so I'll have to go a little bit slow. Two issues that Dr. Rinder raises in his report, Dr. Rinder says that Mr. Rieder's blood pressure was well controlled, right, that's obviously a very hotly contested issue in the litigation. It came up when I was talking to you about Dr. Fine, it comes up here. It is really the key risk factor that we believe explains Dr. -- Mr. Rieder's development of chronic kidney disease, and there is going to be a lot of discussion about that.

THE SPECIAL MASTER: Yeah, but to go back, to go back to -- and I'm glad you mentioned Dr. Fine, because I think in a lot of ways this is a mirror image of the argument we had on that. I mean, how -- how can Dr. Deo really address ultimate causation without taking a potentially relevant alternative cause into consideration? I think, and I think similar issues, as you will remember, came up in our discussion of -- of Dr. Fine. So, I mean, I think these two are kind of related.

MS. RYDSTROM: So here is the difference. The difference, Special Master, is that we don't have the burden of proving causation, right. We don't ever

have that burden, and that burden always remains with plaintiffs. And so what the cases say, and this is true about the Third Circuit cases that are cited here by plaintiffs with respect to Dr. Deo, all they say is that once defendants, right, in a case of plaintiffs who have that burden, once defendants have raised some alternative cause, that the burden shifts back to plaintiffs, right. And that's all those cases say. There are no cases that are cited by the plaintiffs here that talk about what happened when -- what happens when the defense expert does or does not pass an opinion on the agent at issue. And that makes sense, right, because that -- that burden shifting is one that is uniquely applicable to plaintiffs. And the only case that we found that's cited by either side that talks about our situation, right, where the defense expert has an opinion that is -- that specifically, and this is not a secret, right, he is open about it, that specifically is not passing an opinion on whether the medicine specifically caused the injury in this particular case is that Burton case from the -- from Wisconsin. And that case essentially says it's fine for a defense expert.

THE SPECIAL MASTER: What is the case relying on

for that proposition?

MS. RYDSTROM: It is the Burton vs. American Cyanamid case. It is cited in the papers. It is from the Eastern District of Wisconsin. And, of course, I expect that I'm going to hear in just a minute from Mr. Pennock that -- that that is not a Third Circuit case. Concededly, it is not. Wisconsin is very far from the Third Circuit, I agree. But I would also note that there is no cases cited by plaintiffs that specifically say in our situation, right, a defendant has to consider even all of the agent that's at issue in the case.

And, of course, that makes sense for a couple of reasons. One, because most defense experts are going to say general causation is not there, right. That's not this situation because Mr. -- Dr. Deo is not -- is not offering that opinion, but it also is because most plaintiff experts, unlike this case, right, most plaintiff experts don't try to -- to avoid giving an opinion about whether or not a particular agent has caused the -- the disease or the injury in this case. So it's actually you could see in that respect not something that might come up all that often.

Now, here, of course, Dr. Rinder doesn't himself offer that opinion, that PPIs were specifically the cause. So that opinion that Dr. Deo gives that it was hypertension that caused it is absolutely in, whether or not Dr. Rinder ever shows up at trial or not. And -- and that opinion is -- is separately admissible.

That's the issue here. It's not purely a responsive opinion, although, of course, it is, and I have no doubt that Mr. Pennock at trial is going to do exactly the cross-examination that he just did of Dr. Deo. Well, Dr. Deo, you know, what are you doing here if you are not giving an ultimate opinion. And the jury may or may not weigh that as against all the other information and all the other opinions that Dr. Deo offers about the interplay of Mr. Rieder's underlying CV disease, his longstanding hypertension, and the kidney disease that he ultimately developed.

MR. PENNOCK: May I reply, Special Master?

THE SPECIAL MASTER: Sure.

MR. PENNOCK: First, I just want to be clear, I guess I haven't been, I am not suggesting that Dr. Deo has to give an ultimate opinion on his evaluation of the contribution of PPIs to the disease here. He

could dispose of it by, as I would have expected, by reviewing all of the general literature and then the defense expert comes in and says, I ruled it out because I don't think that it can cause chronic kidney disease. So I did not have to incorporate it in my analysis of the individual factors that were involved in this -- this person's disease because I don't think he can do it.

So, but, again, I will say that other than that Eastern District of Wisconsin case, there is -- we agree, there is no case law we can find where going the other way or the way that that Eastern District case went, which is you can put an expert on the stand to testify to what caused something without ruling in everything and then ruling out those things that have to be ruled out.

Now, I do think it is different than the Fine situation. I think the Fine situation they are trying to parse out this issue with Dr. Fine that I think was addressed, but I don't want to start restating or getting into Stephanie's argument. Thank you.

THE SPECIAL MASTER: Okay. Thank you. I think that's it on that one.

The next one I have is Palese, P-a-l-e-s-e.

MS. MARTINES: Dr. Palese.

THE SPECIAL MASTER: Hi, Buffy.

MS. MARTINES: Good afternoon, Special Master. This is Buffy Martines on behalf of plaintiffs, and I'm going to argue the motion to exclude Dr. Palese.

I took Dr. Palese's deposition last summer, and the truth of the matter is she is quite a puzzle to me. She is not qualified to give her opinions and her methodology is not reliable, so I'm not sure exactly what she offers, but let me take each of those piece by piece if I can.

She is not -- Dr. Palese is a gastroenterologist. She is not a nephrologist. She is not even a primary care physician for kidney patients. She has no experience evaluating patients with CKD to determine if PPI is a cause. During her deposition she conceded to me that she often works in one of these cross-functional teams where nephrologists are used for -- for patients with kidney disease. So I'm not exactly sure why she was selected for this, other than she is a big fan of PPIs, big fan.

The defendants response to that is you don't need to be the best qualified expert to testify. I agree with that. I think that's what the case law says, but you've got to be kind of qualified. You don't just get to pull anybody out and say, This is pretty close, so we are going to put her up.

In support of her qualifications, the defendants also say she routinely treats patients with multiple comorbidities, including kidney disease, and she is comfortable doing that. Again, not the standard to qualify an expert. I'm glad she is comfortable treating these patients. I hope they are comfortable with her, but, again, that doesn't qualify her to take the stand and testify as an expert in this litigation.

Now, even if for some reason that you are to determine that she is qualified, in the second prong of this analysis, her opinions are not reliable. And let me just kind of walk you through my experience and what I gleaned from Dr. Palese during her deposition.

Her big opinion is that Mr. Rieder's CKD was preexisting to the time he took the PPIs. She says that on Page 17 of her expert report. During her

deposition she said she knows this because she did some calculations. I asked her about those calculations and she couldn't tell me a whole lot about -- I asked if she had documentation of the calculations, and she said no, she did it on a website. I asked her what website she used and she didn't remember. She said she had to Google it. When I pressed her on that and continued to ask her about documentation or the name of the website or any detail about this calculation, she told me it doesn't matter, she just knows.

Take that a step further. The lab report that she relies on to make these mystery calculations don't show CKD. And earlier this afternoon in your -- when we were talking you mentioned in another argument, you said you don't know what you don't know, and I've heard you say that before, and I'd add on in the case of Dr. Palese, we are never going to find out. We are never going to find out what we don't know. We are never going to be able to test these calculations or how she got to where she got.

During her deposition she repeatedly stated that as part of these calculations she needed to use his age, Mr. Rieder's age, and she said over

and over again that he was 30 years old. Over and over again. Finally, I pushed her on that and asked her what his birth date was and asked her to do the math and she conceded that he was 44. But she said that mistake didn't matter either. Well, we don't know if it mattered or not because we don't have the calculations.

So I'm just not sure how reliable it is and how we can possibly depend on her analysis in support of this opinion. She -- you know, she says that she did these calculations and that for a 44-year-old man the GFR shows that he has CKD. I guess we are just going to have to take her word for it because there is certainly no paper to back that up. In fact, when plaintiffs counsel went back and actually did the math with the one website she could remember, not that she could confirm that she used, but that she can remember, when plaintiffs counsel went back and did the math, the GFR was fine.

So when you add all of this up, Dr. Palese has no business testifying in front of a jury.

Now, in their brief I believe defense counsel said in different pieces, Well, she briefly misspoke. Well, it is just like when you switch

Fahrenheit to Celsius. Well, it is just like this.

I don't disagree that if you took any one of these components and looked at them in a vacuum, maybe it's just an honest mistake, maybe you just briefly misspoke, maybe it is common sense, but not when you take them all together. You can't look at each little piece in a vacuum and say, That's okay. You look at it all together.

And you have an expert that's not qualified, she is not a nephrologist, she is not even close to a nephrologist. She doesn't analyze CKD and determine causation. And her methodology, she can't even remember how she came to the conclusion she came to. And for these reasons we would ask that she be excluded, and I would like to reserve the rest of my time for rebuttal.

THE SPECIAL MASTER: That's fine.

Jessica?

MS. RYDSTROM: Thanks, Special Master. So let me tell you why Ms. Martines raised the question why is she here. Let me tell you why she is here.

Dr. Palese is here because she is clearly qualified to determine what caused Mr. Rieder's CKD. She is a gastroenterologist, she is here in town at

Georgetown Hospital, her -- she is as terrifyingly credentialed as most of the rest of these folks, right. She -- she teaches at Georgetown Medical School, she went to Mt. Sinai School of Medicine, did an internship and a residency at Georgetown, and her -- her specialty there, your Honor, and her former board certification was in internal medicine, right. That is exactly the type of training that she received. She now specializes in gastroenterology.

Now, what she said and what I think I heard in the briefs was that Dr. Palese is somehow not qualified to know whether PPIs caused -- caused Mr. Rieder's CKD, and that's not what Dr. Palese said at all. What she said is that of course, as one would hope any treating doctor would do, and that's one of the main distinguishing characteristics of Dr. Palese here, is that she is seeing patients all of the time like Mr. Rieder, right, and she may not be seeing them for their chronic kidney disease. That is not the disease state that she is treating, but she is treating them for things like what Mr. Rieder had, which is GERD, right, the kinds of diseases that cause people to start taking medicines like PPIs.

And what she said, of course, was what you

would expect any doctor to do, which is all patients should be evaluated for all causes of their kidney disease or other diseases and if she needed help in a particular case or a particular consult, she would bring that in.

THE SPECIAL MASTER: Can I stop you for a minute?

MS. RYDSTROM: Sure.

THE SPECIAL MASTER: Leaving aside her qualifications for a minute and, you know, I think the crux of her testimony is supposed to be that his chronic kidney disease was preexisting to his taking Nexium. And the basis, as I'm understanding it, the basis for that conclusion is a calculation, a GFR calculation. And I think what I'm understanding from the papers and what Ms. Martines says, no one can, as we sit here today, know exactly what numbers she put into that calculation, right.

And so if his, as I understand the science, if the GFR is 60 or less, that's -- that's an indicator that he has got chronic kidney disease. And I guess the question I have for you is: If she puts the right numbers in, you know, the -- I think creatinine goes into it, I think age goes into it. I

don't know what else goes into it. But if she puts the right numbers in, does she still come out with the same conclusion?

MS. RYDSTROM: Well, here is what -- we know what it's based on, right, we know what she put in because she says it was based on the fact that his creatinine was 1.4 and we know from her report that she had his date of birth, right? So those are inputs.

And Ms. Martines is right, she cannot remember the website that she -- that she -- to which she inputted, but what she says is that for, in her experience and, right, so combining her experience and with the calculations that she did, it results in an eGFR of 60. And I should stop myself here --

THE SPECIAL MASTER: Let me stop you.

How does experience come into this?

MS. RYDSTROM: Because what she says --

(Indiscernible due to simultaneous talking.)

THE SPECIAL MASTER: -- doing the calculation?

MS. RYDSTROM: That is the Fahrenheit to Celsius is that Dr. Palese says is, Look, I see patients like this and I have a sense, right, given my clinical

experience that when you have a creatinine of 1.4 and you are roughly in, you know, a certain age group, that she believes that gives you a -- that she would know what someone's eGFR is.

But I'm going to stop right here because it's not actually just Dr. Palese that says it. Dr. Fine, you'll remember Ms. O'Connor put up the chart, right, you'll remember Dr. Fine's chart with the zigzags that she put up that show his eGFR and lo and behold, right, at around the same time as we get that 1.4 creatinine reading, Dr. Fine lists on his chart an eGFR of 61.

So -- so here -- I guess I am surprised at how hotly we are disputing two experts on opposing sides who fundamentally come up with a very similar number. And I guess what I would say is all of this question, if we are talking about testability, they tested it, right. The reply that was submitted to the Special Master reproduced the plaintiffs' -- what the plaintiffs got, the different number that they got when they say they inputted into one of the websites that Dr. Palese potentially used, they put in those inputs and they got a different number.

And that, your Honor, is a

cross-examination. I mean, presumably that's an issue for cross. They tested it. It was a testable methodology, right. They attempted to recreate it and they got a different number.

THE SPECIAL MASTER: But they don't know they are using the same formula or the same calculator, right?

MS. RYDSTROM: And presumably, Special Master, that's an issue for the cross-examination as well. I mean, there is a lot of stern -- wrong about this, you know, this misstatement. And I read the transcript and, I mean, Lord help us all, as Ms. O'Connor pointed out earlier, I may have misspoken and I was talking for only 20 minutes. After five hours or however many hours of her deposition, Dr. Palese said, and I looked at it, and she -- she didn't say it just once, concededly, she said it and five pages later she fixed it, right. She fixed his age and -- and counsel, Ms. Martines, had the opportunity to ask her whether or not that error changed her opinion, had every opportunity to interrogate whether that misstatement, right, what she believed at the time and whether she believed he was in his 40s or whether she -- she believed he was in his 30s, that -- that was the time

to explore those, and I believe that Ms. Martines did.

And so what Dr. Palese answered about the work that she did, the calculations that she did, whether she could remember those calculations, those are all those are all potential fodder for cross-examination.

And ultimately, when you look at it, the numbers that she came out with are not all that dissimilar from what Dr. Fine concludes and puts in his chart.

MS. MARTINES: May I respond, Special Master?

THE SPECIAL MASTER: Yes.

MS. MARTINES: I wrote down a few things that defense counsel said. She is clearly qualified and a list of all of the great places that she went to school and she worked at. At the end of the day that's great. She did go to some really high-end schools and worked at some great hospitals. And I'm sure she is a fine gastroenterologist. She is not a nephrologist. She is not qualified to determine causation.

And by the way, on Page 17 of her report, that's exactly what she tries to do, and I'm reading a direct quote:

"In contrast, there is no evidence that Nexium caused or substantially contributed to Mr. Rieder's CKD."

That's exactly what she is trying to do in this report and she is not qualified to do it.

Defense counsel said we know what she put in the calculator. No, we don't. No, we don't. She said multiple times that Mr. Rieder was 30 years old when I corrected her, not when she corrected herself, when I corrected her. She said, Oh, I meant 44. And I said, Which number did you put in the calculator? And she said, I put in 44.

We don't know that for sure. She corrected herself. We are never going to know what she put in that calculator because she didn't keep any documentation of it.

Defense counsel said that kidney.org is the website she potentially used. Again, we are never going to know which one she used because she didn't document it.

These are things that an expert in litigation has to do. Maybe if we are treating patients we can do things a little bit different. Maybe when we are treating patients you can rely on

your sense of what's going on, but there are rules in litigation.

Daubert and its progeny laid out specific requirements, and I have a right to depend on that those specific requirements are met when an expert takes the stand. It's not a matter for cross-examination. Daubert is a gatekeeping function. If Dr. Palese can't meet the basic requirements to get through the gate, it is not a cross-examination issue. It is a she doesn't come to trial issue. She hasn't met those qualifications.

With regard to whether or not we've been able to test her hypotheses, we got as close as we could without knowing the specific age she used and the specific website she used, and you know what happened. The results were different than what she said happened. For those reasons we do believe that Dr. Palese should be excluded.

MS. RYDSTROM: Two points, Special Master.

The first is of course we allow experts to testify based on their clinical experience and their experience treating patients all of the time. We absolutely do that. Many, many an expert comes to trial and testifies just as Dr. Palese did about

things that they have learned over their years of practice.

And on the testability question, they tested it, Special Master, they got a different result and if Ms. Martines claims that she is unaware of what numbers that Dr. Palese put in, well, I don't know what more to give her except for her sworn testimony, which she said she put in 44. Now, if Ms. Martines thinks that that is not credible, then that is absolutely a jury issue and something that is for a jury to decide whether or not they believe Dr. Palese, but Dr. Palese testified under oath as to what she put into that calculation.

THE SPECIAL MASTER: Okay. Thank you.

So I think the next one that's -- that I have on my list is Lamsita, L-a-m-s-i-t-a.

And, Tracy, are you going to be arguing that?

MS. FINKEN: Yes. Good afternoon, Special Master Reisman. It is Tracy Finken from Anapol Weiss on behalf of plaintiffs.

THE SPECIAL MASTER: Okay. Go ahead.

MS. FINKEN: Okay. As far as Dr. Lamsita's testimony goes, there are three specific opinions that

plaintiffs seek to exclude, and I'm going to go through them briefly because there has been some concessions that have been made on behalf of AstraZeneca so I just want to make it very clear on what's been conceded and versus what we are still seeking to exclude.

You are muted. Sorry.

THE SPECIAL MASTER: I said that's helpful. Sorry. Go ahead.

MS. FINKEN: So I'll just go through the three one by one.

The very first opinion that we were talking about relates to the findings of chronic progressive nephropathy in the animal studies. And AstraZeneca has conceded that Dr. Lamsita will not offer an opinion on the pathological criteria of chronic progressive nephropathy in the animal studies or the significance of chronic progressive nephropathy in rats to humans.

However, plaintiffs seek to exclude any opinion by Dr. Lamsita as it relates to chronic progressive nephropathy because by Dr. Lamsita's own admission she is not qualified to offer such opinions. She has testified that she is not an expert in kidney

function and not an expert in kidney function across species. She has testified that she is not a pathologist and she doesn't feel qualified to speak to the details around the pathology relating to chronic progressive nephropathy. That's on Page 109 of her deposition.

She has testified that she is not comfortable describing any of the inflammatory components involved in chronic progressive nephropathy in rats, and that's on Page 109.

She hasn't looked at any of the findings under a microscope. She admits that she doesn't know whether her own description of kidney findings in certain studies of nephrocalcinosis are similar to other types of kidney injuries.

She opines, though, she doesn't just regurgitate the findings in the animal study reports that AstraZeneca created, she takes it one step further. So she finds that there's are nephrocalcinosis in some of the short-term rat studies but then she takes it one step further and opines that that's an early precursor of chronic progressive nephropathy. And she has already testified multiple times that she is not qualified to give that opinion.

She also attempts to explain away the findings of a dose-dependent increase in chronic progressive nephropathy in the treated animal groups, and that's on Page 117. But because she is not qualified admittedly to discuss the pathological findings of chronic progressive nephropathy and did not actually do that, she should not be able to testify as to the cause of those kidney findings in the underlying clinical -- or preclinical animal study reports.

Dr. Lamsita says that she relies on the expert opinion of Dr. Sandusky. However, the Third Circuit law is pretty clear that for an expert to rely on the opinion of another expert, they need to be able to assess the validity of those opinions and Dr. Lamsita could not assess the validity of the opinions of Dr. Sandusky because she is not qualified to do so and she admits that.

Because she did not assess the validity of Dr. Sandusky's opinions, it renders her methodologies unreliable in accordance with Third Circuit law and you can look at the citation in our papers to In Re TMI litigation which supports that.

The second opinion that plaintiffs seek to

exclude in terms of Dr. Lamsita is that she is not qualified to give opinions about the cost of drug development generally. AstraZeneca concedes that Lamsita will not testify on the cost of the development of Prilosec and Nexium or PPIs, but they oppose our motion to exclude her testimony as to the cost of drug development generally.

And first, as it goes towards drug development, putting the qualifications aside, defendants have not provided any evidence that Dr. Lamsita is qualified to give that opinion based upon the preclinical work and experiences that she has done. There is no evidence that she has done drug development soup to nuts to give that type of opinion.

She admits that she could not provide an opinion on the cost of drug development a long time ago at the time that Nexium and Prilosec were developed, and that's on Page 85 of her deposition, but she says that she may, may be able to offer an opinion on the cost of drug development today. That's also on Page 85.

So putting aside her qualifications to give the opinion of the cost of drug development today based upon a single trade publication article, it's

critical to recognize as a practical matter that the cost of drug development today is not relevant to any issue in this case whatsoever.

So besides the lack of qualifications, there is a lack of fit. And her opinion on this issue as to the cost of drug development today should be excluded.

And then just going to the third point, and that's about Dr. Lamsita's testimony as to whether Nexium or Prilosec will be approved by the FDA today, defendants concede that -- that Dr. Lamsita would not offer an opinion on whether Nexium or Prilosec would be approved by the FDA today but only offer an opinion as to whether the nonclinical studies would likely result in approval today. That's directly from their brief at Page 36.

And this is misleading for a couple of reasons. One, Dr. Lamsita admits that when you seek approval for a drug and drug development, I think everybody on this call would probably concede this, that there are multiple factors that the FDA considers in approving a drug, only one of which is preclinical studies. The clinical studies in humans, you know, Phase 1 through 4 studies are all highly relevant to

that inquiry. And Dr. Lamsita has testified on Page 144 of her deposition that the clinical studies are a really bigger part of the drug approval process than the preclinical studies. And then she says that she didn't review the clinical studies in this case and she can't offer an opinion about the clinical data.

So any opinion by Dr. Lamsita regarding whether these drugs would or would not be approved today based on preclinical studies is misleading to the jury.

THE SPECIAL MASTER: Would you agree that she could give opinions about the adequacy of the preclinical studies for FDA consideration? I guess what I'm saying is maybe even if she couldn't go to the ultimate decision, Oh, yes, it would have been approved, it seems like with her qualifications, could she not say I've looked at these preclinical studies and at least that portion of it would be fine -- found adequate?

MS. FINKEN: I think that there are opinions that Dr. Lamsita gives in her report that are appropriate for her area of expertise that we can cross-examine her at trial on relating to, you know,

good laboratory practices and things of that nature, the process generally of submitting preclinical studies to the FDA, you know, whether or not these -- these clinical studies complied with the laboratory practices or not.

But Dr. Lamsita should not be able to testify that the drugs would be approved based upon the preclinical studies that she reviewed because the FDA can't approve a drug based on preclinical studies. They would not, they could not, they cannot do it. They have to evaluate the entire package, including the clinical studies which Dr. Lamsita has not evaluated and she has admitted as much during her deposition. And that's on Page 144 of her deposition testimony.

And with that, Special Master Reisman, I will -- I will turn over the floor to Ms. Althoff and save any other time for rebuttal. Thank you.

THE SPECIAL MASTER: Thanks.

Hi, Katherine.

MS. ALTHOFF: Hi, Special Master. Yes, I'm going to respond on Dr. Lamsita.

Again, Katherine Althoff on behalf of AstraZeneca. I'm going to take these in reverse order

because I think it goes from the simplest to perhaps the most complex issue.

Dr. Lamsita said in her deposition, I'm not testifying regarding any clinical data. Dr. Lamsita is a toxicologist. She has years of experience at FDA, in industry, and consulting, in which she worked on helping companies get their drugs approved to put on the market. She only works with animal studies. This is what she does.

And taken into context, that's exactly what she is saying here is that the nonclinical studies would have been sufficient to have these drugs approved, not that everything, the entire package would have been approved, but purely that the nonclinical program was sufficient and appropriate. So I think we agree on that, so I'm not sure --

THE SPECIAL MASTER: I'm going to make a bold statement, I think you are kind of in agreement on that.

MS. ALTHOFF: Yeah, I think so too, and so I'm not sure why, based on your our agreement, that we are having this argument today. But in any event, I think she can testify to the level that she wants to testify to on that issue.

Secondly, with regard to the drug development costs, I think this one is also pretty simple. Again, Dr. Lamsita, this is what she has done throughout her entire experience is work as part of a team in helping to get drugs approved. She said she had not reviewed any documents that specifically addressed how much Omeprazole costs to get to market nor how much Esomeprazole, that being Prilosec and Nexium, costs to get to market, and so she has no intention of testifying as to those precise numbers.

But in terms of a general opinion, if asked, about how long does it take to get a drug to market and what does it cost, I think, you know, based on her years of experience on a variety of compounds, she has got the qualifications and the expertise and background knowledge to testify to that.

THE SPECIAL MASTER: Can I ask you a question about that?

I mean, she is a toxicologist, right? I mean, how -- I'm -- how does she know what it costs? I mean, she is not like in the finance group, has she worked for companies? I mean, how does she get that knowledge? And I think she was a toxicologist at FDA, right?

MS. ALTHOFF: Yes. She was a toxicologist at FDA for a few years, she has also worked in industry and she has also worked as a consultant. And so she is part of a team. She understands how long it takes and generally what it costs.

Again, this is -- she is not going to come in as some kind of an economist or something like that, but I think at the level in which she would be asked and at the level that she discusses it in her report, I think she is qualified and got the experience and background knowledge to testify to that.

THE SPECIAL MASTER: All right. And so the remaining thing I think is the CPN?

MS. ALTHOFF: Yes, chronic progressive nephropathy. Again, I think to some extent we are talking past each other, and as I think you mentioned in one of the arguments earlier today. She is a toxicologist, she is not a pathologist, and so when she would work at FDA, she would review pathology reports, as she did in this case, she would review nonclinical study reports, as she did in this case, and if she had a specific question about the pathology, she would go talk to one of the FDA

pathologists.

That's not really what she is doing here. I mean, she is reviewing the study report, she sees what's reported, she has familiarity, as she testified in her deposition, I think it was Page 176, that from her work at FDA she is familiar with chronic progressive nephropathy, not as pathological criterion, as we've conceded she is not going to testify to, but to the determination that that's in fact something that happens in rodents, she is aware of it and she has seen it before.

And so I think to the extent she is testifying about chronic progressive nephropathy, she doesn't plan to step on top of Dr. Sandusky who is an animal pathologist. She is going to testify with regard to what was seen and to the extent that AstraZeneca provided that information to the FDA. Again, I think we are talking past each other here.

THE SPECIAL MASTER: Tracy, do you want to respond?

MS. FINKEN: If I could, please, just very briefly.

Dr. Lamsita does not just regurgitate what the animal clinical study reports say about chronic

progressive neuropathy. That's not what she does. She does that. But she also takes it one step further and she attributes what the cause is of certain kidney findings in the animal studies. While admitting in the same breath that she's -- while she has heard of CPN, or chronic progressive nephropathy, she is not qualified to opine about it but yet that's exactly what she does in her report.

And you can see that on Page 114 to 115 of her report and 117 of her report where she talks about different kidney findings that she observed in some of the animal studies and this then she opines that those are evidence of early precursors of chronic progressive nephropathy, or CPN, which is the -- a pathological finding.

And yet she admits throughout her deposition that she is not qualified to evaluate the pathological findings of chronic progressive nephropathy nor did she evaluate them and she is not comfortable giving opinions about that. But that's -- you know, what she says in her deposition and what she actually does in her report in terms of making those leaps of just not regurgitating what's in the study reports but actually attributing cause to certain

findings are two different things, and she is -- she is simply not qualified to be able to give those types of opinions.

So plaintiffs seek to exclude any testimony by Dr. Lamsita about chronic progressive nephropathy because by her own admission she is not qualified to address that.

MS. ALTHOFF: May I speak just very briefly, Special Master?

THE SPECIAL MASTER: Go ahead.

MS. ALTHOFF: The problem with that is they don't disagree that she is qualified to analyze the reports and determine the adequacy of the preclinical study program. And in the preclinical study program AstraZeneca's own investigators identified chronic progressive nephropathy. So you leave us in a strange position if you say she can't utter the words "chronic progressive nephropathy" because it's in the study reports and she is familiar with it, she is familiar with that condition from having worked at -- at FDA, and if she had questions about it there, she would do the same thing that she did here, which is talk to a pathologist.

THE SPECIAL MASTER: Okay. Thank you.

MS. FINKEN: Can I just make one point, Special Master, in response to that?

THE SPECIAL MASTER: Oh, sure.

MS. FINKEN: She is not familiar with chronic progressive nephropathy. She says she has heard of chronic progressive nephropathy. That's a big difference and that's what she states in her deposition testimony. And hearing of chronic progressive nephropathy does not render you qualified to be able to evaluate findings of kidney toxicity and determine that they are chronic progressive nephropathy or attributed to chronic progressive nephropathy, and that's exactly what Dr. Lamsita attempts to do in her report if you look at it critically. Thank you.

THE SPECIAL MASTER: Okay. Thank you both.

Okay. So the last one that we have is Andrea Leonard-Segal, an FDA expert. I believe that this -- this expert is just as to Takeda. Am I correct about that?

MS. MARTINES: That's correct, Special Master.

THE SPECIAL MASTER: Okay.

MS. MARTINES: Actually, I have kind of a dual motion. There is a motion to disqualify and then

there is one to limit her testimony.

THE SPECIAL MASTER: Yeah, I'd like to take up the motion to disqualify first, if we can.

MS. MARTINES: Of course.

THE SPECIAL MASTER: Okay. Let's do that.

Can you identify yourself?

MS. MARTINES: Okay. Yes, ma'am. Buffy Martines on behalf of plaintiffs on their motion to disqualify Dr. Andrea Leonard-Segal.

Special Master, to make a long story short on this one, in the interests of time, I know you've read all of the papers, the fundamental issue is that this expert was a long-time employee of the FDA who now purports to be an expert on the very matters that she worked on at the FDA. And under Federal law that is prohibited under the code section that we have cited, and I believe it's 18 USC 207.

THE SPECIAL MASTER: Buffy, can I stop you there for a minute?

MS. MARTINES: Of course.

THE SPECIAL MASTER: That's a criminal statute, correct?

MS. MARTINES: Yes, ma'am.

THE SPECIAL MASTER: And I guess the question,

the fundamental question that I had when I was reading through all of these materials is where is the authority to use that statute to exclude an expert in a civil case? In other words, I mean, they might be running afoul of a criminal statute by testifying and not something most people would want to do, but where do you get the authority from that statute that you can exclude in evidence -- disqualify an expert from a civil case?

MS. MARTINES: I believe the case that we cite you to is US v. Coleman, which is a Third Circuit case from 1986, 805 F.2d 474. And in that case they talk about the fact that these revisions, these provisions and then revisions to the provisions that Congress made are used in order to vent even the appearance of impropriety in these types of matters, that a former public official cannot use their position for private gain, personal or private gain. And then we also cite a couple of other cases within that same section of our brief.

THE SPECIAL MASTER: Yeah. We looked at them. I guess I didn't think, and I'll go back and look again after we have this argument, I didn't think any of them were exactly right on point here, and maybe

this is sort of a first impression issue. I don't know.

MS. MARTINES: And that could be. There is a grouping of cases that we cite that go to this. And I don't know if they are -- you know, if they are just absolutely on point, but they certainly go to the proposition that this statute -- in this statute Congress forbids the exact kind of testimony that's going to happen here or that's anticipated.

Dr. Leonard-Segal, as I said, from 2002 to 2013 worked for the FDA and was involved in -- with PPIs, including the FDA's approval of Prilosec OTC, of the OTC version of Prevacid, she oversaw labeling, adequacy of the warnings, label changes, on each product she considered renal failure as a risk, she reviewed the safety and efficacy of those products, she considered the adverse events, and she gave opinions on all of those matters with regard to both Prilosec OTC and the Prevacid OTC version.

She also oversaw the Prevacid switch from Rx to OTC versions. She discussed efficacy and safety on that product as well, part of the labeling.

Importantly, with regard to Prevacid, which is the product we are talking about here, during

her testimony in her deposition, she discussed the fact that as part of the Prevacid switch she did a comprehensive -- the FDA did a comprehensive review of all safety data and that that included Prevacid and, in fact, all of the PPIs. So she was involved -- I know that there is going to be an argument that, Oh, she was just involved on the OTC side and that makes it a lot different. I'm going to talk to you about why OTCs aren't different, which is a whole another issue, but the fact of the matter is that during the course of this work she did review Rx information, she did review safety and efficacy labeling issues, adverse event reports, and those were comprehensive reviews. And that is the very specific subject matter that she is it going to try to talk about in this litigation and that is the specific type of testimony that the statutes preclude.

THE SPECIAL MASTER: Have you made any effort to contact FDA or the Department of Justice or anybody and see if they are complaining about this?

MS. MARTINES: I have not done that personally, and I would -- I do not -- I am not aware that the USC has done that either.

Again -- oh, go ahead.

THE SPECIAL MASTER: Well, because as I read the statute and some of the cases, they are the ones who have the gripe about this, right, if she is out there, you know, doing -- engaging in this conduct, aren't they the ones who really have standing to complain?

MS. MARTINES: Well, I think they certainly -- I mean, obviously they certainly have standing to complain. I think plaintiffs also have the same issue, because part of the reason why, and the cases talk about this, the reason why this statute exists is to limit this kind of revolving door concept from governmental work to making your living off of kind of the fruits of your labor, so to speak.

The plaintiffs' issue is going to be that Dr. Leonard-Segal is going to come in, and this is included in our Daubert motion as well, she is going to come in and say, I was part of the FDA, I looked at this stuff, this is what the FDA decided, everything is great, fine and wonderful, let's go drink coffee. And that is the exact type of testimony that this -- these code sections and the cases talk about is improper. And it leaves the jury with the opinion that it is almost the FDA that's in there saying it because this woman, this doctor has been doing this

all of this time and she is going to rely on her experiences in the FDA. And the supposition, what the jury is going to be left with is, Oh, well, the FDA is in here telling us that everything is fine.

And in our Daubert motion we discuss the fact that she is relying strictly on what the FDA says about this drug. She hasn't done any of her own work on it. She is just going with all of that. And that's the exact kind of testimony that -- that the code sections and the cases discuss is improper.

The other item I would want to pick up, and then I'll reserve the rest of my time for rebuttal, is in Takeda's briefing they discuss the fact that Takeda is off the hook, so to speak, because it was actually Novartis that was applying for all of these -- for the OTC version of Prevacid and those types of things, and I just want to remind the Special Master that the code sections and the cases discuss that it doesn't have to be the exact party that -- that it's -- there is no identity of parties necessary. This isn't some kind of gotcha regulation where if you can sneak by because it is a different name, you are okay.

The fact of the matter is that when the

applications for the Prevacid OTC products were being put in, yes, Novartis was the representative on behalf Takeda and Takeda was actually listed as the supplier and manufacturer. So there is no escaping this issue simply by saying, Well, we weren't the ones that specifically were involved with Prevacid OTC application. They were certainly involved, and the statute defines them as any other person that was participating. So that is not a means of escape, so to speak.

And with that, I will reserve the rest of my time for rebuttal.

THE SPECIAL MASTER: Okay. Thanks, Buffy.

Hi, Mike.

MR. RUTTINGER: Good afternoon again. Just for the record, this is Mike Ruttinger on behalf of Takeda.

Just to clarify, are we going to argue the Daubert issues separate to Dr. Leonard-Segal following this or do you want me to address those as well?

THE SPECIAL MASTER: I think we are going to argue them separately. I don't think -- Buffy, I don't think you argued all of your Daubert issues, did you?

MS. MARTINES: I did not. I think it is a very short argument on Daubert, but we can certainly separate them up.

THE SPECIAL MASTER: Let's do it separate.

MR. RUTTINGER: Perfect.

So focusing on the disqualification issues, Special Master, you hit the nail on the head here. This is a really unprecedented argument for plaintiff to make, to request a disqualifying Takeda's regulatory expert based on an assertion that she has committed a crime when it is undisputed that there has been no charge or pending proceedings or even a request by plaintiff to the FDA to look into this.

If you look at the cases plaintiff cites, there are some that come up in the context of a motion to permit expert testimony under the exception that's built into the statute when the regulation applies, but we think that this case is a different one because the regulation, Section 207(a)(1) doesn't apply in the first place. So plaintiff hasn't identified any other case quite like this one where a court has disqualified a former FDA expert from testifying just based on her experience regulating what we believe are different drug products.

THE SPECIAL MASTER: Okay. Can I stop you for a minute there.

MR. RUTTINGER: Of course.

THE SPECIAL MASTER: You say that it doesn't apply, and I think you are going to talk about why you think that, right, but if it did apply, you would have to -- she would have to go seek permission under that regulation, correct, from FDA or from the court?

MR. RUTTINGER: Correct. The regulation exception built into the statute specifies that if those initial three criteria that are required for a finding disqualification under the statute apply, then there is an obligation to affirmatively seek permission from the court to testify.

THE SPECIAL MASTER: Yeah, from the court, you are right. And to be clear, you have not done that, right?

MR. RUTTINGER: That is correct, yes.

THE SPECIAL MASTER: She has not done that, okay.

MR. RUTTINGER: Now, we don't think that you need to get into the question of whether or not this statute can apply to disqualification when raised by a plaintiff, in the first place, because, as I've

alluded to, we don't think that plaintiff has identified that they can prevail under any of these three requirements for the statute to apply. And to be clear, the statute requires proof as to -- or I suppose to persuade the court that it applies as to all three of those elements.

So I do want to address one item quickly from plaintiffs' briefs that I believe to be a misrepresentation before we get into those three elements, and that's this repetition in both their motion and their reply brief that Dr. Leonard-Segal admitted she couldn't represent Takeda before the FDA.

If you actually look at her testimony, and it is even quoted in plaintiffs' brief, she says she couldn't represent Takeda before the FDA on the same matter on which she worked at the FDA. As I go through those elements, one of which is the particular matter requirement, I think you'll understand our position as to why we don't believe that her testimony there is at all inconsistent with the statute because it is not the same particular matter.

THE SPECIAL MASTER: This is the argument that she worked on OTC, not on -- not on prescription?

MR. RUTTINGER: In part, yes, that's correct.

So I think it makes sense to start with that particular matter issue, and so the first requirement under the statute is that, you know, the United States must be a party or have a direct and substantial interest in the particular matter at issue.

Well, the United States was not a party, so let's think about what does direct and substantial interest in a particular matter at issue mean. And there are two components to that, right. So the regulations here interpreting the Ethics in Government Act, the 2641.201, it confirms the United States is neither party to nor does it have any direct and substantial interest in a particular matter, merely because a Federal statute is at issue or the Federal Court is serving as a forum for resolution of the matter.

So our position is that the United States doesn't have a direct and substantial interest for purposes of this statute just by virtue of the fact that this is litigation involving, you know, failure to warn claims, particularly when it's brought by a private entity and not by a governmental entity.

It's also worth noting, I think, and

Special Master, you raise this question of, you know, what's sort of enforcement provision for the Ethics in Government Act. Well, that regulation, 2641.201(j)(2), actually sets for a procedure for an agency to follow when it is unclear whether or not the agency has a direct and substantial interest in a matter. And it states forth a process by which there is actually a government procedure and a little bit of a hearing process to determine is this an issue in which the government has a direct and substantial interest.

So the fact that there is no pending proceeding here suggests to me that that first element, the direct and substantial interest test, can't be satisfied.

THE SPECIAL MASTER: Hold on. Who would be bringing such a procedure? The FDA, right?

MR. RUTTINGER: So it could also be brought by -- actually, if you'll bear with me for a moment, 2046 -- 2641.201(j) specifies that the proceeding must be brought by, one moment here, coordination by designated agency ethics officials.

So the ethics department has designated ethics officials for the former employees's agency, so

the FDA has these officials, who have the primary responsibility for coordinating the determination of whether a substantial interest is at issue. So it would be brought by the FDA counsel.

THE SPECIAL MASTER: Yeah, stop for a moment. So they would have to know that she was intending to give such testimony, right, and then decide if they were going to do anything about it. And I guess the question I have for you is, you know, has she made the FDA aware that -- that this is something she is going to be doing or wants to be doing?

MR. RUTTINGER: The record isn't clear on whether there has been any correspondence with the FDA, as far as I am aware, Special Master. The regulations themselves are also silent as to what the obligation is to provide notice to the FDA or any agency and how that information is followed up upon.

THE SPECIAL MASTER: Yeah, but, I mean, I guess just as a practical matter, how are they supposed to know about it?

MR. RUTTINGER: Right. And the regulations are silent on this, I think probably because this is, as you noted, something of an unprecedented issue.

Now, this is also wrapped up in the particular matter issue, though, and here is why I don't think this has to be resolved on just the direct and substantial interest. When you look at the same regulations for how to define a particular matter, particularly this is Paragraph (h)(2) to that regulation, the FDA provides -- or sorry -- the Ethics in Government Act regulations provide an example that we think is quite applicable to this situation. And the example they provide is one in which a former government official while working at the FDA was involved in promulgation of a rule applicable to a category of a particular type of medical device made by multiple manufacturers. And the example goes on to say, If the regulation was not limited in application to the particular companies already existing but it is, for example, open-ended, it would not be a particular matter involving specific parties.

So an issue of a former FDA official having spent time at the FDA regulating an open-ended class of a drug or medical device does not arise to the level of particularity required by the act to be a particular matter on which the government has a direct or substantial interest.

So we think that under either prong, under either category of that first prong of the test, plaintiff cannot show that it is applicable.

There is also the second category, and the second prong of the test is the OTC issue that plaintiffs counsel alluded to. And essentially their argument is premised on Dr. Leonard-Segal's involvement in the over-the-counter switch of Prevacid 24-hour. And plaintiff has taken the position in their briefs that because Prevacid 24-hour involves the same active ingredient as prescription Prevacid it is functionally the same matter.

And you heard Ms. Martines refer to Dr. Leonard-Segal as having worked on the same labeling and same issues as she's opining on in this litigation. That is just unfortunately not true and it, I think, it shows a misunderstanding of the Durham-Humphrey Act under which over-the-counter drugs are regulated.

So under the Act, the FDA actually requires for an over-the-counter drug to be marketed that there be meaningful differences within a regulatory sense, "meaningful difference" is a term of art in this context, from prescription drugs. In the

case of Prevacid 24-hour versus prescription Prevacid, that includes different indications for use. Prescription Prevacid has I believe ten different indications for use versus just a couple for Prevacid 24-hour, different patient populations, different labeling, and fundamentally different NDA numbers. So they are, within all respects regulated by the FDA, different drug products.

So Dr. Leonard-Segal's involvement with prescription Prevacid is simply not the same prescription drug product or not the same drug product at all that she is testifying on in this litigation.

As to the third criteria involving specific party or parties, it is not our position, as Ms. Martines suggested, that the parties have to be identical for purposes of whether or not the statute applies. The fundamental issue here, and if you look at the cases cited on Page 20 of plaintiffs' motion to disqualify where they talk about cases of limited expert testimony and other testimony in these cases, all of these cases talk to the fundamental concern underlying the statute of side switching. It is the idea that former FDA official or a former government official of any kind has left government employment

and is switching sides and offering testimony against the government or against the government's interests on the exact same issue. When the government isn't a party here, isn't involved in private failure to warn litigation and the work that she did is on a different drug product than is at issue in this case, different warnings and different labels than are at issue in this case, the whole side switching burden simply isn't met here.

So as a result, we don't think that either the first, second or third criteria of the Ethics in Government Act are satisfied here, and if even one of those doesn't favor disqualification of Dr. Leonard-Segal, then plaintiffs' motion should be denied as a whole. They have to prevail on all three of those prongs of the statute to even argue that disqualification can occur, assuming in the first place that this court can use a criminal Ethics in Government Act statute as a basis for excluding expert testimony.

THE SPECIAL MASTER: So a couple of other questions.

I mean, if -- if she -- if we said okay, she can testify, does that expose the court, this

process to any kind of risk? I mean, should the court seek FDA approval, input on the question here?

MR. RUTTINGER: I don't -- I believe the answer to that is no, Special Master. The statute itself, assuming that there -- the application of these three provisions is kind of a mixed question of fact and law, right. So the court's determination of that will, you know, in any potential appeal or something of that issue, be subject to the same kind of standards where it will be a, you know, an abuse of discretion standard as to whether disqualification is appropriate and a de novo standard as to any of the legal issues underlying that. But there is no, you know, sanction for the court in determining this. It should be ultimately decided under the same discretionary standard for admission of evidence that would normally apply with the application of the ethics in government issue being a legal issue that the reviewing court would need to decide.

THE SPECIAL MASTER: And I guess I might have asked this before, but maybe not clearly, I mean, are you aware of whether she has ever raised this with the FDA?

MR. RUTTINGER: I am not aware of that based on

the record that I have seen, but I can't speak conclusively to that.

THE SPECIAL MASTER: Okay. All right. Because, I mean, in some respects, you know, if you were right about all of this, then what's the harm in going to FDA and, you know, saying this is what I'm doing, I just want to make sure you're okay with it?

MR. RUTTINGER: I guess I would say, in response to that, that the harm it could extend is, it is not unique to this case, it is that what plaintiff is really suggesting here is, you know, an unnecessary procedural obligation that doesn't have a basis in law that could really quickly roll out of control.

A lot of the issues that Ms. Martines identified as her concern for this, this notion of a revolving door between the FDA and the government and an expert stepping in, saying, Well, I worked at the FDA and here is what the FDA would say about that, I'm not sure I understand how that's really different from someone like Dr. Ross coming in and offering testimony when he is going to say I'm talking on my basis of a -- on the basis of my experience at the FDA and the imprimatur that brings.

Now we are not arguing that Dr. Ross is

disqualified under the statute. We don't believe it applies here and we don't believe it applies there. But you can quickly see how this might get out of control.

THE SPECIAL MASTER: Yeah, but I think the question is, here, is you say OTC and prescription are very different matters. And Ms. Martines says, no, they are not. You know, they are certainly a whole lot closer than what most FDA experts that I've seen over the years are willing to testify about based on their experience. So, I mean, I think -- you know, I think that's the difference. That's why it doesn't apply to Dr. Ross or Dr. Mann. I think it's -- you know, you've got an expert here who undoubtedly was involved with the OTC products and their labeling and their adverse event review at FDA and I guess the question is, as you've already discussed, you don't think it is the same particular matter, but, you know, I can see why someone would raise that question certainly.

Anyway, Buffy -- or Mike, do you want to add anything else?

MR. RUTTINGER: Oh, I was just going to add a single sentence there, which was, you know, I think

the similarities are misleading in this case because ultimately this case boils down to labeling, right. It boils down to failure to warn claims, at least in the Bales case which is the only one in which Dr. Leonard-Segal is being disclosed as an expert, and the labeling issues between a prescription drug and over-the-counter drug are fundamentally different because they are different labels and different products.

So I think that the dissimilarities here are more pronounced when this court looks at the labeling issue and that they are labels for different products. That's all I have.

THE SPECIAL MASTER: Okay. Thanks, Mike.

Buffy, did you want to follow up?

MS. MARTINES: Yes, please. Let's start with switching sides, Item No. 1.

Dr. Leonard-Segal is absolutely switching sides. Her work at the FDA was on behalf of the government, and as everyone on this call knows, the process of getting a drug approved with the FDA is inherently an adversarial process with the manufacturer. There are negotiations, there are discussions, there are all kinds of things. During

that process, while she worked there, she worked for the government and she represented the FDA.

And she represented the FDA on a lot of issues. One -- a couple of things I forgot -- I neglected to mention. The 2011 citizens petition, a very important issue, and the 2012 tracked safety issue regarding PPI-induced AIN. Dr. Leonard-Segal testified that she more than likely would have been involved in both of those issues, which are class-wide issues. She would have worked for the government during that time on behalf of the FDA in opposition of the manufacturers.

So now she has left the FDA, she has switched sides, she is working for the manufacturers now in a United States District Court. She testified that she wouldn't be able to be in front of the FDA representing Takeda. She cannot go in front of the United States District Court either. The government is a single entity. We've cited that in our brief. The government is a single entity, whether it is the FDA or the court, she can't do it. She cannot switch sides, which is exactly what she is trying to do.

Now let's talk about OTCs. You just heard the party line on prescription versus OTCs when it

suits the manufacturer, and this is an issue that I have gotten into very deeply. You'll hear more about it in the next round of cases, but these manufacturers have a history, a history of marketing these drugs, whether it's a prescription drug or an OTC, however they want. They are interchangeable when they are marketing them or when they are trying to steal somebody else's market share. When studies come out that say there is something wrong with PPIs, all of a sudden it is a big -- whole different issue, OTCs and prescriptions are completely different. When they want to bring an expert to court who has worked on this product who shouldn't be there, oh, all of a sudden OTCs are different than prescription. It is a distinction without a difference. We are talking about the same type of warnings, we are talking about the same injuries, we are talking about the same formulation, we are talking about the same manufacturers making money on these drugs, making money on these drugs. It is a distinction without a difference and they should not be allowed to play some kind of smoke and mirror games with whether these are the same products or not.

Dr. Leonard-Segal worked on this product,

this specific product while she was at the FDA. She worked on OTC issues, she worked on prescription drug issues, she did comprehensive evaluations, she looked at the citizens petition, she looked at the track safety issues. She is up to her neck in this specific issue and she -- under these statutes that we are citing and under the case law that we are citing, she is not allowed to do that and she should be disqualified.

Thank you.

MR. RUTTINGER: May I have a true 15 seconds?

THE SPECIAL MASTER: You may.

MR. RUTTINGER: Special Master, I'd encourage you again to look at that CFR 2641.201(h)(2), Example 5, about the former FDA official, that makes clear to me that involvement in class-wide class labeling and other types of issues is not involvement in a particular matter within the meaning of the statute.

THE SPECIAL MASTER: Okay. I will look at it.

Okay. So Daubert, did you want to -- do you have more to say about that?

MS. MARTINES: Well, just a little bit. I don't -- I don't want to belabor some of these points,

and the papers, this was a short motion on Dr. Leonard-Segal and I know that you've already taken a look at those.

Just very quickly, she has basically got two opinions, as best I can tell, that Takeda acted appropriately in its labeling and that there is no causal association between PPI use and the kidney injuries.

And I want to start by saying the doctor has already conceded that she is not qualified to speak about causation in her deposition testimony, Page 93, lines 18 and 19, she specifically says: "I don't testify as a medical -- as a medical officer expert giving my opinions about causation."

I'm not -- it's a little bit hard for me to tell in Takeda's papers, and maybe we'll get some clarification on this, I think that they concede that she is not qualified or she is not going to speak about causation, but I'll -- I won't speak for them, but she should -- she has conceded that she can't speak to causation issues, that she is not testifying as a medical officer or a doctor in that area.

So we believe at a very minimum she can only testify to regulatory issues. Now, I'm not

waiving my argument that she shouldn't be testifying at all, but for purposes of what we are talking about, at a minimum limited to regulatory issues.

THE SPECIAL MASTER: I think there was a stipulation that she is not going to offer a medical causation opinion.

MS. MARTINES: And that may very well be true. I hope so. I hope that's the case because that makes things a lot cleaner.

With regard to the opinions that she does give and her methodology and how she did that, she testified that she didn't review any underlying data, she has reviewed no published literature and that she relies strictly on the assessment or actions of the FDA and Takeda as support for her testimony.

In fact, she said in her testimony that she is not basing her review on any nephrology information and any medical evidence on anything related to kidney injuries and that she is only testifying with regard to certain regulatory items, including the label.

Now, with regard to those conclusions, the problem with those opinions I believe is that she -- they are all supported by -- only by assumptions. She

stated that -- she specifically stated in her deposition, again, at Page 119, Lines 11 through 22, that she comes to these conclusions because she assumes the FDA must have seen data or had discussions.

And you simply cannot base any kind of expert opinion on assumptions and speculation that you have no proof of. That's certainly not a reliable methodology that -- that she can bring to court under -- under the applicable Daubert standards.

So with that, I will -- I will reserve the rest of my time for rebuttal.

THE SPECIAL MASTER: Thanks, Buffy.

Mike.

MR. RUTTINGER: I will keep this very short.

So first off, to clarify, Dr. Leonard-Segal will not be offering medical causation or kind of regulatory causation opinions in this case. So that should make this all a little bit cleaner.

What she is going to offer is testimony based on her experience about what FDA did and what various interactions between the manufacturer and the FDA mean in terms of providing context for that, which

she can do as a former FDA official who has the experience of being involved in those kinds of interactions.

Now, what plaintiff has said is their main Daubert challenge here is a criticism of the fact that she didn't look at, say, some of the underlying nephrology studies and data. That's information that might be important if she was offering the kind of regulatory causation opinion that, say, Dr. Ross is offering. She is not. The opinions she is offering here, they are not based on assumptions. They are based on her experience at the FDA and having done this kind of job and having worked with the FDA and seen interactions between FDA and manufacturers and being able to tell a jury, because these are complicated issues after all, what it means when a manufacturer submits X to the FDA and what it means when the FDA reacts in such a way. We think that that's all based on her experience and qualifications which plaintiff here doesn't appear to be contesting, and we think that that's sufficient and that there are many other cases cited in our Daubert reply in which the kind of regulatory testimony that she is offering has been readily allowed under Rule 702.

THE SPECIAL MASTER: Okay. Buffy?

MS. MARTINES: Thank you very much for that clarification. We will certainly rely on that.

The problem is she is going to give an opinion that the label was inadequate and to do that she needs to base it more on what she assumes the FDA saw and what she assumes they should have discussed and what she guesses would have happened. She needs more than that if she is going to give an opinion on whether or not the label was adequate. And her testimony is that that's all she did was rely on assumptions and speculations and that's simply not enough for an expert opinion to be presented to the -- to a jury.

So with that I will conclude.

THE SPECIAL MASTER: Okay. I think we are done for today, unless I missed something. I hope I didn't. Thank you all very much, and we will resume at 10:00 a.m. tomorrow.

MR. BROWN: Ellen, one quick issue. I know we have a court reporter. This is Arthur Brown from Arnold & Porter. I'm hoping that you can circulate the rough, to the court reporter, as soon as you can. I'm happy if I need to sign anything, just to shoot it

over to my e-mail.

THE SPECIAL MASTER: Juliana, or whoever is on from Golkow, what's the process for that?

THE COURT REPORTER: I will shoot an e-mail over to him.

MR. BROWN: Thanks, Juliana.

THE SPECIAL MASTER: I'll forward -- maybe we can forward it around to everybody who wants it.

Okay. All right. Thanks everybody, very good. See you tomorrow.

Thereupon, at 3:33 p.m., on Monday, April 4, 2022, the hearing was adjourned.

CERTIFICATE OF OFFICER

I, JULIANA F. ZAJICEK, a Registered Professional Reporter, Certified Shorthand Reporter and Certified Realtime Reporter, do hereby certify that I reported in shorthand the proceedings had at the remote hearing aforesaid, and that the foregoing is a true, complete and correct transcript of the proceedings of said hearing as appears from my stenographic notes so taken and transcribed under my personal direction to the best of my ability.

IN WITNESS WHEREOF, I do hereunto set my hand on this 8th day of April, 2022.

Juliana F. Zajicek

JULIANA F. ZAJICEK, Certified Reporter

EXHIBIT 2

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: PROTON-PUMP INHIBITOR PRODUCTS LIABILITY LITIGATION (NO. II) **This Document Relates to:** ***Bales v. AstraZeneca Pharmaceuticals LP*, No. 2:17-cv-06124** ***Foster v. AstraZeneca Pharmaceuticals LP*, No. 2:17-cv-02475** ***Kersch v. AstraZeneca LP*, No. 2:18-cv-03159** ***Lee v. AstraZeneca Pharmaceuticals LP*, No. 2:17-cv-00212** ***Nelson v. AstraZeneca Pharmaceuticals LP*, No. 2:17-cv-13727** ***Rieder v. AstraZeneca Pharmaceuticals LP*, No. 2:19-cv-00850**	Case No. 2:17-md-2789-CCC-MF (MDL 2789)

JOINT REPORT TO THE SPECIAL MASTER RE *DAUBERT* MOTION ORAL ARGUMENT

Pursuant to section III.A of the Special Master's Amended Procedures Regarding Oral Arguments on Preemption, *Rieder* Statute of Limitations, *Daubert* Motions, and Related Summary Judgment Motions, AstraZeneca, Takeda, and Plaintiffs submit this Joint Report regarding the parties' meet-and-confer efforts to narrow the disputes raised in the parties' *Daubert* motions.

Counsel for AstraZeneca, Takeda, and Plaintiffs participated in three meet-and-confer calls and numerous emails. The first call took place on Thursday, March 17, and attendees included Stephanie O'Connor, Paul Pennock, Jonathan Sedgh, and Josh Autry (for Plaintiffs), Julie du Pont and Jake Miller (for AstraZeneca), and James Mizgala (for Takeda). The second call took place on Tuesday, March 22, and attendees included Stephanie O'Connor, Paul Pennock, and Josh Autry (for Plaintiffs), Julie du Pont and Jake Miller (for AstraZeneca), and James Mizgala (for Takeda). The third call took place on Thursday, March 24, and attendees included Stephanie O'Connor, Paul Pennock, and Josh Autry (for Plaintiffs), Julie du Pont and Jake Miller (for AstraZeneca), and James Mizgala (for Takeda). Each meet and confer session lasted approximately 25 minutes.

As a result of the parties' meet-and-confer efforts, the following agreements have been reached.

1) Plaintiffs agree to withdraw their motion to exclude Dr. Pinto-Martin, and AstraZeneca agrees to withdraw its motion to exclude Dr. Gerstman.

2) AstraZeneca and Plaintiffs agree to mutually rest on the papers with regard to AstraZeneca's motions to exclude Dr. Charytan and Dr. Mehal.

3) Plaintiffs and AstraZeneca agree to mutually rest on the papers with regard to Plaintiffs' motions to exclude Dr. Gibbons.

4) Plaintiffs and Takeda agree to mutually rest on the papers with regard to Plaintiffs' motions to exclude Dr. Hansen.

5) Plaintiffs and AstraZeneca agree to limit oral argument regarding Plaintiffs' motion to exclude Dr. Deo to the *Rieder* case.

6) To the extent Plaintiffs seek to prevent Dr. Lansita from offering an opinion on the pathological criterion or significance of chronic progressive nephropathy (CPN) to humans, AstraZeneca does not oppose Plaintiffs' motion. Plaintiffs still seek to exclude other CPN opinions by Dr. Lansita, drug cost opinions by Dr. Lansita, and any opinion by Dr. Lansita about whether PPIs would be approved by the FDA today, which AstraZeneca opposes.

7) To the extent Plaintiffs seek to prevent Dr. Lansita from offering an opinion on the historical cost of bringing Prilosec or Nexium to market, AstraZeneca does not oppose Plaintiffs' motion. Plaintiffs still seek to exclude other drug cost opinions by Dr. Lansita, other CPN opinions by Dr. Lansita, and any opinion by Dr. Lansita about whether PPIs would be approved by the FDA today, which AstraZeneca opposes.

8) To the extent Plaintiffs seek to prevent Dr. Hansen from offering an opinion on the biological plausibility of AIN developing into AKI or CKD, Takeda does not oppose Plaintiffs' motion. Plaintiffs still seek to exclude any other opinions by Dr. Hansen about biological plausibility as well as all other opinions by Dr. Hansen, which Takeda opposes.

9) To the extent Plaintiffs seek to prevent Dr. Leonard-Segal from offering a medical causation opinion on whether a causal association exists between PPI use and CKD, Takeda does not oppose Plaintiffs' motion. Plaintiffs still seek to exclude all other opinions by Dr. Leonard-Segal, which Takeda opposes.

10) To the extent AstraZeneca seeks to prevent Dr. Mehal from providing an opinion on the adequacy of the label in a regulatory

context, Plaintiffs do not oppose AstraZeneca's motion. AstraZeneca still seeks to exclude all other opinions by Dr. Mehal, which Plaintiffs oppose.

11) To the extent Defendants seek to prevent Dr. Wells from offering (a) an opinion that PPIs cause CKD, and (b) an opinion that his analyses establish that PPIs are harmful to the kidney, Plaintiffs do not oppose their motion. Defendants still seek to exclude Dr. Wells in all other respects, which Plaintiffs oppose.

12) To the extent Defendants seek to prevent Dr. Moeckel from offering an opinion that PPIs cause acute or chronic kidney disease in humans or from using animal evidence to prove general causation, Plaintiffs do not oppose their motion. Defendants still seek to exclude Dr. Moeckel in all other respects, which Plaintiffs oppose.

Dated: March 25, 2022

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: PROTON-PUMP INHIBITOR PRODUCTS LIABILITY LITIGATION

2:17-MD-2789 (CCC)(LDW)
(MDL 2789)

This Document Relates to:
All Actions

Judge Claire C. Cecchi

(PROPOSED) ORDER

Upon consideration of the Report and Recommendation of Special Master Ellen Reisman regarding *Daubert* Motions ("Report and Recommendation"), any objections thereto, and the entire record herein, it is this ___ day of _____, 2022:

1) ORDERED that the Court overrules all objections to the Report and Recommendation and adopts the Report and Recommendation in its entirety as the decision of the Court;
2) ORDERED, as to all six Bellwether Trial Cases, that Plaintiffs' Omnibus *Daubert* Motion to Exclude Defense Experts be and hereby is DENIED as to the testimony of Dr. Marianne Mann;
3) ORDERED, as to all six Bellwether Trial Cases, that Plaintiffs' Omnibus *Daubert* Motion to Exclude Defense Experts be and hereby is GRANTED IN PART and DENIED IN PART as to Dr. Janice Lansita, as follows:

a. The motion is GRANTED to the extent that it seeks to exclude Dr. Lansita from offering the following opinions:

i. The pathological criterion or significance of CPN to humans (per stipulation by the Parties);

ii. The historical cost of bringing Nexium or Prilosec to market (per stipulation by the Parties);

iii. The cost of bringing a drug to market generally;

iv. Whether PPIs would be approved by the FDA today;

b. The motion is otherwise DENIED, including but not limited to, as to Dr. Lansita's testimony as to the following:

i. Her opinions concerning the nonclinical studies relating to PPIs that she reviewed; and

ii. The sufficiency of the nonclinical studies relating to PPIs to support FDA approval;

4) ORDERED, as to all six Bellwether Trial Cases, that Plaintiffs' Omnibus *Daubert* Motion to Exclude Defense Experts be and hereby is DENIED as to the testimony of Dr. Robert Gibbons;

5) ORDERED, as to the *Rieder* and *Bales* cases, that Plaintiffs' Omnibus *Daubert* Motion to Exclude Defense Experts be and hereby is DENIED as to the testimony of Dr. Rajat Deo and that, to avoid any jury confusion, the

juries in the *Rieder* and *Bales* trials will be instructed in connection with Dr. Deo's testimony that he was not asked to and did not consider or form any opinions as to whether Plaintiff Rieder's or Plaintiff Bales's use of PPIs was a cause of either of their CKD;

6) ORDERED, as to the *Rieder* case, that Plaintiffs' Omnibus *Daubert* Motion to Exclude Defense Experts be and hereby is GRANTED as to the testimony of Dr. Caren Palese;

7) ORDERED, as to all six Bellwether Trial Cases, that Defendant AstraZeneca's Motion to Exclude Opinion Testimony from Dr. David Ross Under Federal Rule of Evidence 702 and, as to the *Bales* case, Defendant Takeda's Motion to Exclude Testimony of Dr. David Ross, be and they hereby are DENIED, except as follows;

   a. The motion is GRANTED in part to the extent that Dr. Ross shall be precluded from testifying as to FDA's level of understanding of the difference between ATIN and CTIN, except that if AstraZeneca, which elicited such testimony in Dr. Ross's deposition, opens the door by seeking to use his deposition testimony on this topic on cross-examination or to elicit it again at trial, such testimony shall be permitted;

b. The motion is GRANTED in part to the extent that any testimony by Dr. Ross about FDA staffing and resources in periods after the conclusion of his service at FDA shall not be permitted and any such testimony shall be limited to his personal experience during his tenure at FDA or upon objective evidence of such issues;

8) ORDERED, as to all six Bellwether Trial Cases, that Defendants AstraZeneca's and Takeda's Motions to Exclude Opinion Testimony from Dr. Martin Wells Under Federal Rule of Evidence 702 be and hereby are GRANTED to the extent they seek to exclude Dr. Wells from offering an opinion on general causation that PPIs cause CKD or are harmful to the kidneys (per stipulation by the Parties) and are DENIED if evidence of data provided to PRAC or PRAC's analysis or conclusions is introduced at trial.

9) ORDERED that, as to all six Bellwether Trial Cases, Defendant AstraZeneca's Motions to Exclude Opinion Testimony from Plaintiffs' General Causation Experts Under Federal Rule of Evidence 702 be and hereby are DENIED as to the testimony of Dr. David Charytan.

10) ORDERED that, as to the *Bales, Lee, Nelson, Foster,* and *Rieder* cases, Defendant AstraZeneca's Motions to Exclude Opinion Testimony from Plaintiffs' General Causation Experts Under Federal Rule of Evidence 702

be and hereby are GRANTED IN PART and DENIED IN PART as to the testimony of Dr. Wajahat Mehal, as follows:

a. The motions are GRANTED to the extent that they seek to exclude Dr. Mehal from offering the following opinions:

i. The adequacy of labeling of PPIs (per stipulation by the Parties);

ii. Medical marketing and its impact on sales of PPIs; and

iii. The impact of the Montreal definition of GERD in any case where the plaintiff underwent medical testing that specifically confirmed a GERD diagnosis;

b. The motions are otherwise DENIED, including but not limited to, with respect to Dr. Mehal's general causation opinions.

11) ORDERED that, as to the *Rieder* case, Defendant AstraZeneca's Motion to Exclude Opinion Testimony from Plaintiffs' Specific Causation Experts Under Federal Rule of Evidence 702 be and hereby is DENIED as to the testimony of Dr. Derek Fine;

12) ORDERED, as to all six Bellwether Trial Cases, that Defendant AstraZeneca's Motions to Disqualify Dr. Gilbert Moeckel be and hereby are DENIED;

13) ORDERED that, as to all six Bellwether Trial Cases, Defendant AstraZeneca's Motions to Exclude Opinion Testimony from Dr. Gilbert Moeckel Under Federal Rule of Evidence 702 and, as to the *Bales* case, Defendant Takeda's Motion to Exclude Expert Testimony of Dr. Gilbert Moeckel be and they hereby are DENIED;

14) ORDERED that, as to all six Bellwether Trial Cases, to the extent the Parties have raised any arguments in their motions that are not specifically addressed in Special Master Reisman's R&R, such arguments be and hereby are rejected and the corresponding motions are DENIED to the extent that they rely on those rejected arguments.

_____

Claire C. Checchi
United States District Judge