soning in *Mathis*. Thus, the categorical approach applies. Categorically, the Louisiana statute is broader than the generic definition of burglary because it includes vehicles, watercraft, and cemeteries. *See United States v. Cutley*, 476 Fed.Appx. 429, 430 (5th Cir. 2012). The Louisiana burglary also cannot count as the third predicate conviction.

IX. Conclusion

Defendant's *pro se* Motion to Vacate, Set Aside, or Correct Sentence pursuant to 28 U.S.C. § 2255 (Doc. 45) is GRANTED. Defendant has shown that the Court committed *Johnson* error in applying the residual clause to his burglary convictions. The Court further concludes that the error was "substantial and injurious" because the burglary convictions do not alternatively qualify as predicate convictions under the enumerated offense clause.

Defendant has served approximately 113 months. Without application of the ACCA enhancement, Defendant's new guidelines range will likely be 30 to 37 months. Thus, it appears Defendant is entitled to immediate release. The United States Probation Office is ordered to prepare a revised PSR based on the Court's rulings herein on an expedited basis and submit the PSR to the Court and the United States. After review of the PSR, the United States shall file a Notice stating whether it objects to resentencing at the high end of the guideline range on any basis other than those already raised. The Notice shall be filed no less than three days after receipt of the PSR.

SO ORDERED this 25th day of January, 2017.

Ernesteen JONES, Plaintiff,

v.

NOVARTIS PHARMACEUTICALS CORPORATION,Defendant.

Case No.: 2:13–CV–624–VEH

United States District Court,
N.D. Alabama, Southern Division.

Signed 01/26/2017

Background: Consumer brought action in state court against pharmaceutical manufacturer for alleged injuries sustained from consuming one of manufacturer's products. Following removal, manufacturer moved to strike expert testimony.

Holdings: The District Court, Virginia Emerson Hopkins, J., held that:

(1) doctor was not qualified as expert on causation or causal association;

(2) doctor was qualified to testify as an expert on label compliance and adequacy of labeling;

(3) doctor was qualified to testify as an expert on whether manufacturer complied with advertising and marketing regulations;

(4) expert's methodology to reach conclusion that drug could cause the type of injury suffered by consumer was not reliable,

(5) statistics expert's methodology was not reliable;

(6) surgeon was not qualified to offer expert opinion on cause of consumer's injury; and

(7) consumer's doctor was not qualified to offer expert opinion on cause of consumer's injury.

Motion granted in part and denied in part.

1. Evidence ⚿470

For expert evidence to be admissible, a district court must find by a preponderance of the evidence that: (1) the expert is qualified to testify competently regarding the matters he intends to address; (2) the methodology by which the expert reaches his conclusions is sufficiently reliable as determined by the sort of inquiry mandated in *Daubert*; and (3) the testimony will assist the trier of fact, through the application of scientific, technical, or specialized expertise, to understand the evidence or to determine a fact in issue. Fed. R. Evid. 702.

2. Evidence ⚿536

To show that an expert is qualified to testify competently regarding the matters he intends to address, a party must show that the expert has sufficient knowledge, skill, experience, training, or education to form a reliable opinion about the relevant issue. Fed. R. Evid. 702.

3. Evidence ⚿536

Experience in a particular field is not enough to qualify an expert; the expert must have experience with the issue before the court. Fed. R. Evid. 702.

4. Evidence ⚿555.2

A district court has substantial discretion in deciding how to test the reliability of an expert's testimony; this deferential abuse of discretion standard is applied stringently, even if a decision on expert testimony is outcome determinative. Fed. R. Evid. 702.

5. Evidence ⚿555.2

Pursuant to the second *Daubert* prong, a court should consider the following non-exhaustive factors in determining whether an expert's methodology is reliable: (1) whether the expert's methodology can be tested; (2) whether the expert's scientific technique has been subjected to peer review and publication; (3) whether the method has a known rate of error; and (4) whether the technique is generally accepted by the scientific community. Fed. R. Evid. 702.

6. Evidence ⚿555.5

Reliable expert testimony must establish both general and specific causation of an alleged toxic substance. Fed. R. Evid. 702.

7. Products Liability ⚿147, 217

General causation for a toxic substance products liability claim refers to the general issue of whether a substance has the potential to cause the plaintiff's injury.

8. Products Liability ⚿147, 217

Specific causation for a toxic substance products liability claim refers to the issue of whether a plaintiff has demonstrated that the substance actually caused injury in her particular case.

9. Evidence ⚿555.2

Whether a *Daubert* hearing is necessary is a decision within the sound discretion of a district court. Fed. R. Evid. 702.

10. Federal Courts ⚿3600

The abuse of discretion standard applies as much to a trial court's decisions about how to determine reliability of an expert's opinion as to its ultimate conclusion. Fed. R. Evid. 702.

11. Evidence ⚿546

There is no requirement that a *Daubert* hearing always be held. Fed. R. Evid. 702.

12. Evidence ⚿555.2

Experts are permitted to draw conclusions from a set of observations that are based on their extensive and specialized experience. Fed. R. Evid. 702.

13. Evidence ⚿544

Doctor, who formerly worked at Food and Drug Administration (FDA), was not qualified as expert on causation or causal association, and therefore, such testimony was excluded from consumer's action against pharmaceutical manufacturer for alleged injuries sustained from consuming one of manufacturer's products; doctor was regulatory expert, rather than medical expert, "causal association" was a term in FDA regulations, but doctor was not able to distinguish her opinions on the term from medical causation, and doctor did not have expertise to review medical literature on issues in consumer's case. Fed. R. Evid. 702.

14. Evidence ⚿538, 544

Doctor, who formerly worked at Food and Drug Administration (FDA), was qualified to testify as an expert on FDA label compliance and adequacy of labeling but not about potential impact of label change on prescribing physicians, as required for testimony to be admissible in consumer's action against pharmaceutical manufacturer for alleged injuries sustained from consuming one of manufacturer's products; doctor had extensive experience reviewing proposed labeling and providing comments for patient brochures, and doctor designed study that discussed label changes and risks to the public. Fed. R. Evid. 702.

15. Evidence ⚿536

Doctor, who formerly worked at Food and Drug Administration (FDA), was not qualified to testify as an expert in consumer's products liability action that certain studies allegedly put pharmaceutical manufacturer on notice that one product could cause harm, where doctor was a regulatory expert, but she was not an expert on bisphosphonate medications, a toxicologist, or a pharmacologist. Fed. R. Evid. 702.

16. Evidence ⚿538

Doctor, who formerly worked at Food and Drug Administration (FDA), was qualified to testify as an expert on whether pharmaceutical manufacturer complied with FDA advertising and marketing regulations in consumer's action against manufacturer for alleged injuries sustained from consuming one of manufacturer's products; doctor helped draft FDA guidance documents, she trained FDA reviewers, and she reviewed marketing applications. Fed. R. Evid. 702.

17. Evidence ⚿538

Doctor, who formerly worked at Food and Drug Administration (FDA), was permitted to testify regarding adequacy of pharmaceutical manufacturer's reports to FDA in consumer's action against manufacturer for alleged injuries sustained from consuming one of manufacturer's products; doctor was a regulatory expert, she cited applicable regulations, and doctor applied those regulations to manufacturer's conduct. Fed. R. Evid. 702.

18. Evidence ⚿536

Doctor, who formerly worked at Food and Drug Administration (FDA), could not testify as an expert in consumer's products liability action against pharmaceutical manufacturer as to manufacturer's intent or state of mind but could testify as to information that was or should have been in manufacturer's possession pursuant to FDA regulations. Fed. R. Evid. 702.

19. Evidence ⚿536

Doctor, who formerly worked at Food and Drug Administration (FDA), was not permitted to testify as an expert as to injuries associated with drug in consumer's action against pharmaceutical manufacturer for alleged injuries sustained from consuming a different drug; doctor was a regulatory expert. Fed. R. Evid. 702.

20. Evidence ⚿544

Doctor, who was a bioorganic chemist and practicing gynecologist, was qualified as expert on causation in consumer's action against pharmaceutical manufacturer for alleged injuries sustained from consuming one of manufacturer's products; doctor had multiple degrees in chemistry, he had performed extensive research on related topics, and he had published multiple peer-reviewed articles. Fed. R. Evid. 702.

21. Evidence ⚿555.10

Expert's methodology to reach conclusion that drug could cause the type of injury suffered by consumer was not reliable, and therefore, excluded from consumer's action against drug manufacturer, where expert did not identify a single study that established a causal association between drug and the injury suffered, expert relied on association of consumer's injury with class of drugs to which drug at issue belonged, and expert did not substantiate claim that such an association could be extrapolated to drug at issue. Fed. R. Evid. 702.

22. Evidence ⚿555.10

Expert's methodology to reach conclusion that drug caused injury suffered by consumer was not reliable, and therefore, excluded from consumer's action against drug manufacturer, where expert used a general causation method to form specific causation opinion. Fed. R. Evid. 702.

23. Federal Civil Procedure ⚿1278

In consumer's product liability action against pharmaceutical manufacturer, expert's deposition testimony that he used differential diagnosis to conclude that drug caused injury suffered by consumer violated Federal Rule of Civil Procedure requiring disclosure of all opinions expert would express and basis for them; expert did not discuss reliance of differential diagnosis in expert report or supplemental report. Fed. R. Civ. P. 26(a)(2)(B)(i).

24. Federal Civil Procedure ⚿1274

Expert reports must include both "how" and "why" the expert reached a certain result, not just conclusory opinions. Fed. R. Civ. P. 26(a)(2)(B)(i).

25. Evidence ⚿555.5

If no expert has been offered who can provide an admissible general causation opinion, then an expert may not rely on a differential diagnosis to prove specific causation. Fed. R. Evid. 702.

26. Evidence ⚿538

Doctor, who was a bioorganic chemist and practicing gynecologist, was not qualified to testify as an expert on pharmaceutical manufacturer's compliance with Food and Drug Administration (FDA) regulations in consumer's products liability action; doctor had no experience with FDA labeling and marketing regulations. Fed. R. Evid. 702.

27. Evidence ⚿544

Proposed expert was not qualified to offer testimony on causation in consumer's products liability action against pharmaceutical manufacturer, where expert had bachelor of science in mathematics and developed software to provide consulting and training on statistics, but did not have medical degree and had not served as principal designer of protocol for a clinical trial. Fed. R. Evid. 702.

28. Evidence ⚿555.10

Statistics expert's methodology was not reliable in offering general causation opinion regarding drug consumer took and consumer's injury, warranting exclusion in consumer's products liability action against pharmaceutical manufacturer; expert relied on background rate from a certain medical paper but that rate conflicted with

other reports, expert did not explain why he used chosen rate, expert conducted improper re-analysis of data published in an article, expert was unfamiliar with need to separate injuries different from that suffered by consumer that were identified in article data, his opinion relied upon different injury type, expert did not explain his use of lower bound of confidence interval rather than full confidence interval, and expert's test to calculate confidence interval was not explained. Fed. R. Evid. 702.

29. Evidence ⚿555.7

Statistics expert's methodology was not reliable in offering opinion that pharmaceutical manufacturer's clinical trials did not demonstrate safety of drug consumer took, warranting exclusion in consumer's products liability action, where expert did not indicate ways in which trial failed to meet safety standards, and expert admitted that trials might never be adequately powered to find rare adverse events. Fed. R. Evid. 702.

30. Evidence ⚿555.7

Statistics expert's methodology was not reliable in offering opinion that pharmaceutical manufacturer provided Food and Drug Administration (FDA) with incomplete statistical data, warranting exclusion in products liability action, where expert did not review protocol of manufacturer's clinical trial. Fed. R. Evid. 702.

31. Evidence ⚿544

Surgeon was not qualified to offer expert opinion on cause of consumer's injury, warranting exclusion in consumer's products liability action against pharmaceutical manufacturer, where surgeon had not conducted research or given presentations on consumer's type of injury, and he had not published or submitted academic publications on the drug class at issue. Fed. R. Evid. 702.

32. Evidence ⚿555.10

Surgeon's differential diagnosis methodology was not reliable in concluding that consumer's injury was caused by drug, warranting exclusion of proposed expert testimony in consumer's products liability action against manufacturer, where surgeon failed to rule out other causes since he did not have access to consumer's full medical records. Fed. R. Evid. 702.

33. Evidence ⚿544

Consumer's doctor was not qualified to offer expert opinion on cause of consumer's injury, warranting exclusion in consumer's products liability action against pharmaceutical manufacturer, where doctor did not treat consumer's symptoms and took an absence while she was treated for injuries at issue, and he did not have access to certain of her medical records. Fed. R. Evid. 702.

34. Evidence ⚿555.10

Consumer's doctor's differential diagnosis methodology was not reliable in concluding that consumer's injury was caused by drug, warranting exclusion of proposed expert testimony in consumer's products liability action against manufacturer, where doctor relied on opinions of another physician, and he did not diagnose consumer. Fed. R. Evid. 702.

Leah O. Taylor, Tammy M. Smith, Taylor & Taylor, Birmingham, AL, for Plaintiff.

Catherine Stolar, Andrew L. Reissaus, Robert E. Johnston, Stephen A. Klein, Hollingsworth LLP, Washington, DC, Frederick G. Helmsing, Jr., Edward S. Sledge, III, McDowell Knight Roedder & Sledge LLC, Mobile, AL, for Defendant.

MEMORANDUM OPINION AND ORDER

VIRGINIA EMERSON HOPKINS, United States District Judge

I. INTRODUCTION

This case comes before the court on Defendant Novartis Pharmaceutical Corporation ("Novartis" or "NPC")'s Motions To Strike Expert Testimony. Novartis has moved to exclude the testimony of the following experts:

- Dr. Suzanne Parisian ("Dr. Parisian"), the "Parisian Motion" (doc. 108); [1]
- Dr. William B. Hinshaw ("Dr. Hinshaw"), the "Hinshaw Motion" (doc. 112);
- Dr. Wayne A. Taylor ("Dr. Taylor"), the "Taylor Motion" (doc. 116);
- Dr. James Worthen ("Dr. Worthen") and Dr. Timothy Mark Ricketts ("Dr. Ricketts"), collectively in the "Non–Retained Experts Motion" (doc. 118).

II. PROCEDURAL HISTORY

Plaintiff Ernesteen Jones ("Jones") initiated this lawsuit against Novartis on April 4, 2013 (doc. 1), alleging that she developed atypical femur fractures ("AFF") [2] as a result of taking Novartis' medication Reclast, which is a type of bisphosphonate ("BP") drug. Jones was prescribed Reclast by Dr. Thomas Traylor, her treating physician for her osteoporosis. (Doc. 54) at 2, ¶ 9.[3] She was administered an annual five milligram Reclast injection, as prescribed, on February 10, 2009, March 16, 2010, and March 17, 2011. *Id.* at 2, ¶ 8.

On October 26, 2011, Jones's right femur fractured, requiring surgery. *Id.* at 3, ¶¶ 13–14. In early 2012, Jones began experiencing pain in her left thigh. *Id.* at 3, ¶ 16. After a bone scan revealed a stress fraction on her left femur, she had surgery on her left femur to prevent a complete fracture. *Id.* at 3, ¶¶ 17–18.

Jones has asserted the following claims against Novartis: violations of the Alabama Extended Manufacturer's Liability Doctrine ("AEMLD") (Count 1, *id.* at 6–9); failure to warn (Count II, *id.* at 10); negligence and wantonness (Count III, *id.* at 10–12); and breach of warranty of merchantability. (Count IV, *id.* at 13).

III. STANDARD FOR THE ADMISSIBILITY OF EXPERT TESTIMONY

A. General Requirements—Judge as Gatekeeper

Regarding expert testimony, the Federal Rules of Evidence provide:

> 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;

1. All page references to (Doc. ___) correspond with the court's CM/ECF numbering system.

2. An atypical femur fracture is an ''atraumatic or low-trauma fracture[ ] located in the subtrochanteric region or femoral shaft'' that presents with specific ''major'' and ''minor'' clinical features. (Doc. 125–19) at 3 n. 1(citing Shane E. et al., Atypical Subtrochanteric and Diaphyseal Femoral Fractures: Second Report of a Task Force of the American Society for Bone and Mineral Research, J. Bone Miner Res. 2, 13 (2013)(doc. 117–1)).

3. Jones filed a Third Amended Complaint on February 6, 2015. (Doc. 54). This statement of alleged facts and background derives from that Amended Complaint.

> (b) the testimony is based on sufficient facts or data;
>
> (c) the testimony is the product of reliable principles and methods; and
>
> (d) the expert has reliably applied the principles and methods to the facts of the case.

FED. R. EVID. 702 (2011). Rule 702 must be read in conjunction with three seminal decisions by the Supreme Court related to expert testimony: *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993);*Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 118 S.Ct. 512, 139 L.Ed.2d 508 (1997); and *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 119 S.Ct. 1167, 143 L.Ed.2d 238 (1999).

All rulings on *Daubert* motions are reviewed under an abuse of discretion standard. *See, e.g., Joiner*, 522 U.S. at 141, 118 S.Ct. at 517 ("All evidentiary decisions are reviewed under an abuse-of-discretion standard."). "An abuse of discretion can occur where the district court applies the wrong law, follows the wrong procedure, bases its decision on clearly erroneous facts, or commits a clear error in judgment." *United States v. Estelan*, 156 Fed. Appx. 185, 196 (11th Cir. 2005) (citing *United States v. Brown*, 415 F.3d 1257, 1266 (11th Cir. 2005)).

In *Daubert*, the Supreme Court established that district judges act as "gatekeepers" for expert testimony. 509 U.S. at 592–93, 113 S.Ct. at 2796. The district court judge must assess the proffered testimony and make a preliminary determination about the scientific validity of the expert's reasoning and methodology. *Id.*

As another district court in this Circuit has stated,

> Federal Rule of Evidence 702, read together with the trilogy of Supreme Court opinions that led to the Rule's revision in 2011, compels the district courts to perform a "gatekeeping" function when determining the admissibility of expert scientific and technical evidence. *See, e.g.*, *United States v. Abreu*, 406 F.3d 1304, 1306 (11th Cir. 2005) (quoting *United States v. Frazier*, 387 F.3d 1244, 1260 (11th Cir. 2004)). "This function inherently requires the trial court to conduct an exacting analysis of the foundations of expert opinions to ensure they meet the standards for admissibility under Rule 702." *Id.* (internal quotation omitted).

Broussard–Wadkins v. Maples, 895 F.Supp.2d 1159, 1165 (N.D. Ala. 2012), *aff'd sub nom.Broussard v. Maples*, 535 Fed.Appx. 825 (11th Cir. 2013).

The burden under Rule 702 rests squarely with the proponent of the expert witness:

> The proponent of the expert testimony carries a substantial burden under Rule 702. "The burden of laying the proper foundation for the admission of the expert testimony is on the party offering the expert, and admissibility must be shown by a preponderance of the evidence." *Allison v. McGhan Med. Corp.*, 184 F.3d 1300, 1306 (11th Cir. 1999) (citing *Daubert*, 509 U.S. at 592 n. 10, 113 S.Ct. 2786). Thus, the proponent must demonstrate that the witness is qualified to testify competently, that his opinions are based on sound methodology, and that his testimony will be helpful to the trier of fact. *See, e.g., Frazier*, 387 F.3d at 1260 ("The burden of establishing qualification, reliability, and helpfulness rests on the proponent of the expert opinion. . . ."); *McCorvey v. Baxter Healthcare Corp.*, 298 F.3d 1253, 1257 (11th Cir. 2002); *Maiz[v. Virani]*, 253 F.3d [641,]at 664 [(11th Cir. 2001)].

See Cook ex rel. Estate of Tessier v. Sheriff of Monroe Cty., Fla., 402 F.3d 1092, 1107 (11th Cir. 2005).

B. The Eleventh Circuit Test for Admissibility

[1] The Eleventh Circuit has established a three-part inquiry for district courts to follow in performing their gatekeeper role. For evidence to be admissible under Rule 702, the district court must find that:

> (1) the expert is qualified to testify competently regarding the matters he intends to address;
>
> (2) the methodology by which the expert reaches his conclusions is sufficiently reliable as determined by the sort of inquiry mandated in *Daubert*; and
>
> (3) the testimony [will] assist[ ] the trier of fact, through the application of scientific, technical, or specialized expertise, to understand the evidence or to determine a fact in issue.

Hendrix ex rel. G.P. v. Evenflo Co., Inc., 609 F.3d 1183, 1194 (11th Cir. 2010) (citing *United States v. Frazier*, 387 F.3d 1244, 1260 (11th Cir. 2004)). The party offering the testimony must meet each prong by a preponderance of the evidence. *Id.*

1. Prong One: The Expert Must Be Qualified To Testify to the Relevant Issue

[2, 3] To meet Prong One, a party must show that the expert has sufficient "knowledge, skill, experience, training, or education" to form a reliable opinion about the relevant issue. *Hendrix*, 609 F.3d at 1193. Experience in a particular field is not enough to qualify an expert; the expert must have experience with the issue before the court. *See id.* at 1201.

The Sixth Circuit, in a similar case, concluded that a district court did not abuse its discretion in excluding the testimony of the plaintiff's expert. *See Thomas v. Novartis Pharms. Corp.*, 443 Fed.Appx. 58, 63 (6th Cir. 2011). The expert in *Thomas* was "an experienced maxillofacial surgeon who ha[d] treated several patients suffering from osteonecrosis of the jaw." *Id.* However, the expert had not established his credentials to "diagnose the cause of [the plaintiff's] osteonecrosis ... which [was] the salient issue his opinion was offered to establish." *Id.*

2. Prong Two: The Expert's Opinion Must Be Sufficiently Reliable

[4] To meet Prong Two, the party proffering the expert's testimony must show that the expert's opinion is sufficiently reliable. A district court has substantial discretion in deciding how to test the reliability of an expert's testimony. *Rink v. Cheminova, Inc.*, 400 F.3d 1286, 1292 (11th Cir. 2005). "This deferential abuse of discretion standard is applied stringently, even if a decision on expert testimony is 'outcome determinative.' " *Chapman v. Procter & Gamble Distrib., LLC*, 766 F.3d 1296 (11th Cir. 2014) (citing*Joiner*, 522 U.S. at 142–43, 118 S.Ct. at 517).

[5] Pursuant to the second *Daubert* prong, the court should consider the following factors: "(1) whether the expert's methodology can be tested; (2) whether the expert's scientific technique has been subjected to peer review and publication; (3) whether the method has a known rate of error; and (4) whether the technique is generally accepted by the scientific community." *Rink*, 400 F.3d at 1292 (citing *Quiet Tech. DC–8, Inc. v. Hurel–Dubois UK Ltd.*, 326 F.3d 1333, 1341 (11th Cir. 2003)). However, these factors are not exhaustive and a court "should consider any additional factors that may advance its Rule 702 analysis." *Quiet Tech.*, 326 F.3d at 1341.

C. Legal Standard for Causation Experts

[6] In the Eleventh Circuit, other than in a small number of cases where the

medically community generally recognizes and agrees upon the toxicity of the substance at issue to the injury alleged, both general and specific causation must be established through expert testimony if the Plaintiff's claims require proof of causation:

> For analyzing cases involving alleged toxic substances, we have delineated two categories. *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1239 (11th Cir. 2005). The first category consists of "cases in which the medical community generally recognizes the toxicity of the [substance] at issue" to "caus[e] the injury plaintiff alleges." *Id.*; *Hendrix ex rel. G.P. v. Evenflo Co.*, 609 F.3d 1183, 1196 (11th Cir. 2010). In this category are "toxins like asbestos, which causes asbestosis and mesothelioma; silica, which causes silicosis; and cigarette smoke, which causes cancer." *McClain*, 401 F.3d at 1239 ... [i]n cases where the cause and effect or resulting diagnosis has been proved and accepted by the medical community, federal judges "need not undertake an extensive *Daubert* analysis on the general toxicity question." *Id.* at 1239.
>
> In contrast, the second category contains cases, where the medical community generally does not recognize the substance in question as being toxic and having caused plaintiff's alleged injury. *Id.* These cases require a two-part *Daubert* analysis, comprised of (1) general causation, "whether the [substance] *can* cause the harm plaintiff alleges," *id.*, and (2) specific causation, whether experts' methodology determines the substance "caused the plaintiff's *specific* injury," *Hendrix*, 609 F.3d at 1196 (citing *McClain*, 401 F.3d at 1239). For cases in category two, a district judge "must assess the reliability of the expert's opinion on general, as well as specific, causation." *Id.* (first emphasis added).

Chapman, 766 F.3d at 1303–04. This case clearly falls into the latter category. Accordingly, reliable expert testimony must establish both general and specific causation.

1. General Causation Standard

[7] General causation refers to the "general issue of whether a substance has the potential to cause the plaintiff's injury." *Chapman*, 766 F.3d at 1307 (citing *Guinn v. AstraZeneca Pharm. LP*, 602 F.3d 1245, 1248 n.1 (11th Cir. 2010) (per curiam)); *see also McClain v. Metabolife Intern., Inc.*, 401 F.3d 1233, 1239 (11th Cir. 2005) (emphasis in original) ("In the second category of toxic tort cases, the *Daubert* analysis covers not only the expert's methodology for the plaintiff-specific questions about individual causation but also the general question of whether the drug or chemical *can* cause the harm plaintiff alleges. This is called general causation."). General causation exists "when a substance is capable of causing a given disease." *Restatement (Third) of Torts: Liability for Physical and Emotional Harm* § 28 cmt. c(3) (2010) ("Restatement").

2. Specific Causation Standard

[8] Specific causation refers to "the issue of whether the plaintiff has demonstrated that the substance actually caused injury in her particular case. Specific causation is often distinguished from general causation, which refers to the more general issue of whether a substance has the potential to cause the plaintiff's injury." *Guinn*, 602 F.3d at 1248 n. 1; *Chapman*, 766 F.3d at 1308; *see also* Restatement § 28 cmt. c(3) ("Scientists who conduct group studies do not examine specific causation in their research. No scientific methodology exists for assessing specific causation for an individual based on group studies. Nevertheless, courts have

reasoned from the preponderance-of-the-evidence standard to determine the sufficiency of scientific evidence on specific causation when group-based studies are involved.").

The Eleventh Circuit in *McClain* laid out four criteria, based on an article published by the Federal Judiciary Center, for proving causation between exposure to a chemical and a particular illness in an individual:

> 1. "[T]he toxic substance in question must have been demonstrated to cause the type of illness or disease in question . . . this focuses on the issue of general causation;"
> 2. "[T]he individual must have been exposed to a sufficient amount of the substance in question to elicit the health effect in question . . . this focuses on the issue of individual causation;"
> 3. "[T]he chronological relationship between exposure and effect must be biologically plausible . . . this also focuses on individual causation;"
> 4. "[T]he likelihood that the chemical caused the disease or illness in an individual should be considered in the context of other known causes . . . this refers to the background risk of a specific disease."

401 F.3d at 1242–43 (citing David Eaton, *Scientific Judgment and Toxic Torts—A Primer in Toxicology for Judges and Lawyers*, 12 J.L. & POL'Y 1, 38–40 (2003)).

D. Lack of Necessity of a Daubert Hearing

[9–11] Whether a *Daubert* hearing is necessary is a decision within the sound discretion of a district court. *Cook*, 402 F.3d at 1113. The abuse of discretion standard "applies as much to the trial court's decisions about how to determine reliability as to its ultimate conclusion . . . [i]ndeed, the Rules seek to avoid unjustifiable expense and delay as part of their search for truth and the just determination of proceedings." *Kumho*, 526 U.S. at 139, 152–53, 119 S.Ct. 1167 (internal citations omitted). There is no requirement that a *Daubert* hearing always be held. *See United States v. Hansen*, 262 F.3d 1217, 1234 (11th Cir. 2001); *Frazier*, 387 F.3d at 1264.

In this case, after extensively reviewing the parties' briefings and exhibits, the court determined that a *Daubert* hearing was not necessary. Furthermore, the parties agreed to submit their *Daubert*-related Motions on their respective briefs. (*See* Doc. 194). Accordingly, the court made a determination as to the admissibility of testimony by Dr. Parisian, Dr. Hinshaw, Dr. Taylor, Dr. Worthen, and Dr. Ricketts based on the briefing submitted by the parties.

IV. ANALYSIS

A. Dr. Suzanne Parisian

Jones offers the opinions of Dr. Parisian into evidence in this case. Dr. Parisian has offered an expert report, dated August 31, 2015. (Doc. 125–22, the "Parisian Report"). Dr. Parisian also offered a supplemental expert report, dated May 2, 2016. (Doc. 125–23, the "Parisian Supplemental Report"). Dr. Parisian was deposed on June 14, 2016, and the deposition transcript was filed into the record. (Doc. 125–13, the "Parisian Deposition").

On August 15, 2016, Novartis filed a Motion To Strike Dr. Parisian's expert testimony (Doc. 108). A day later, Novartis filed a brief in support of its Motion (doc. 125–15, the "Parisian Brief"). On September 23, 2016, Jones filed a Response opposing Novartis' Motion To Strike. (Doc. 166–39, the "Parisian Response"). On October 14, 2016, Novartis filed a reply brief in

support of its Motion To Strike. (Doc. 175, the "Parisian Reply").

1. Dr. Parisian's Qualifications

Dr. Parisian has been offered by Jones to address "regulatory requirements applicable to pharmaceutical manufacturers and drug labeling." Parisian Response, (Doc. 166–39) at 4. She formerly served as a Medical Officer at the Food and Drug Administration ("FDA"). Parisian Curriculum Vitae, (Doc. 109–5) at 1. She is board-certified in anatomic and clinical pathology and holds a masters degree in biology. *Id.* at 16; Parisian Report, (Doc. 125–22) at 2, ¶ 2. From 1991 to 1995, Dr. Parisian served as Lieutenant Commander in the United States Public Health Service and was assigned to the FDA. *Id.* at 2, ¶ 4. From 1991 to 1995, she was also employed by the FDA in several roles, including as Medical Officer in the Office of Health Affairs, Chief Medical Officer in the Office of Device Evaluation, and as an instructor in the FDA's staff college. *Id.* at 2, ¶ 5.

While at the FDA, her responsibilities included assessing the health hazard and health risk of products; assessing safety alerts, reviewing adverse event reports; drafting and review of product labeling; promotions, advertising, and corporate records; pre-market evaluation of new product applications and clinical trials; review of marketing applications for safety and efficacy; and training of FDA reviewers regarding the design and evaluation of clinical data for proposed products. *Id.* at 2–3, ¶ 5.

As a Medical Officer in the Office of Device Evaluation ("ODE"), Dr. Parisian participated in the review of proposed clinical trials and pre-marketing applications. *Id.* at 4, ¶ 9. She also trained new medical officers and scientific reviewers in application, clinical trial, and labeling evaluations as well as methods for health risk assessments, health hazard evaluations, annual report requirements, adverse event reporting, and labeling review. *Id.* As an instructor in the FDA's staff college, she had primary responsibility for review of marketing applications and labeling and instruction on evaluation and review of product marketing. *Id.* at 5, ¶ 11. She also presided over 162 health risk assessments convened to advise the FDA on health risk issues for the public. *Id.* at 3, ¶ 6. Dr. Parisian advised and trained other FDA employees regarding FDA requirements and how to make a determination regarding the clinical impact of FDA actions on the public. *Id.* at 5–6, ¶ 14.

Since leaving the FDA in 1995, Dr. Parisian has served as a consultant on issues related to the FDA and is the owner and founder of MD Assist, Inc. ("MD Assist"), a firm specializing in FDA regulation of products. *Id.* at 1, ¶ 1. She is also the author of FDA Inside and Out, a textbook on the history, rules, and regulations of the FDA. *Id.* at 2, ¶ 3. At MD Assist, she designs and markets new medical products; presents marketing applications to the FDA; designs, conducts, and reviews clinical studies, creates and evaluates marketing applications; drafts product labeling; investigates potential adverse events; and instructs about the requirements of the FDA. She has provided litigation support since 1997. *Id.* at 7, ¶ 20.

Dr. Parisian claims that she reached her opinions in this case using the methodology that she was first trained to use at the FDA for clinical review and health risk assessment, as well as her own education, training, and experience. *Id.* at 8, ¶ 21. Jones's response brief states that her primary role is threefold: she will explain the responsibilities of a pharmaceutical drug manufacturer in the context of the FDA's regulatory scheme both before and after a drug is placed on the market; she will provide opinions on the failure of Novartis

to act as a reasonable pharmaceutical manufacturer by failing to comply with FDA regulations; and she will explain the meaning of specialized terminology. Parisian Response, (Doc. 166–39) at 5.

2. Dr. Parisian's Opinions

In her report, Dr. Parisian offers the following opinions:

(1)There is a trend in the United States for increasing numbers of non-healing atypical femur fractures in women. This trend is a national public health safety issue, (doc. 125–22) at 9–10;

(2) Novartis failed to adequately design, study, test, research, or investigate whether Reclast could safely be used by post-menopausal patients, *id.* at 10–33;

(3) Novartis failed to effectively use pharmacovigilance surveillance tools to identify a signal with zoledronic acid/Reclast, *id.* at 33–41;

(4) Novartis is required to submit truthful and accurate information to the FDA. Novartis failed to adequately and timely update the FDA with relevant safety information regarding the risk of femur fracture, *id.* at 41–50;

(5) It is not the responsibility of the FDA to ensure the adequacy of a drug label; that responsibility lies with the drug sponsor, *id.* at 50–51;

(6) Novartis did not adequately warn patients of the risks of Reclast in its patient brochure, *id.* at 52;

(7) As the Reclast sponsor, Novartis was required to provide physicians with adequate warnings about its drugs. Novartis did not adequately warn prescribing physicians regarding the risk of femur fracture associated with Reclast, *id.* at 52–58;

(8) Novartis, through its sales force, including Kelly Pyron, helped delay providing health care providers with adequate and truthful information about the long-term risks of Reclast. Novartis' drug advertising and communications with health care providers were not fair and balanced, *id.* at 58–66;

(9) Novartis' conduct regarding acknowledging a risk of femur fractures is similar to its conduct regarding bisphosphonate-related osteonecrosis of the jaw, *id.* at 66–71;

(10) Ernesteen Jones fit the profile for Novartis' marketing strategy, *id.* at 71–74;

(11) The report on Ms. Jones's adverse events is indicative of Novartis' failure to conduct meaningful pharmacovigilance, *id.* at 74–75;

(12) Novartis' actions regarding Reclast do not support that patient safety was its highest priority. Its actions were misleading and directly impacted the quality of life of patients, including Ernesteen Jones, *id.* at 75.

Dr. Parisians's supplemental report offers the following opinions:

(1) Novartis submitted a 2008 report to the FDA that was inaccurate and misleading and downplayed the risk of AFF with Reclast, (doc. 125–23) at 6–8;

(2) Novartis in 2015 submitted inaccurate and misleading information to the FDA in its Errata Document regarding AFF, *id.* at 8–25;

(3) Opinions on the Expert Report of Dr. David Feigal, *id.* at 26–43.

3. Novartis' Motion To Exclude Dr. Parisian's Testimony Is Granted in Part and Otherwise Is Denied

Novartis first argues that all of Dr. Parisian's testimony should be fully excluded because she lacks adequate expertise, she does not employ a reliable methodology, and her opinions would not assist the jury.

The court finds that Dr. Parisian is qualified, based on her experience at the FDA

as a Medical Officer, to offer testimony about regulatory requirements for the testing, marketing, and development of prescription drugs. Even though her time at the FDA was primarily spent on medical devices, Dr. Parisian has extensive experience with the regulation of drugs. Her report further demonstrates that she has particularized knowledge of the FDA standards that apply to drug manufacturers.

[12] She has also followed an appropriate methodology. Experts are permitted to draw conclusions from a set of observations that are based on their extensive and specialized experience. *Kumho Tire*, 526 U.S. at 156, 119 S.Ct. at 1178. Dr. Parisian is a regulatory expert who has drawn conclusions based on her review of regulatory filings and company documents in light of FDA regulations and her experience at the FDA. She claims she used the methodology she was trained to use at the FDA "for clinical review and health risk assessment, as well as her scientific and medical education, professional training, and experience." Parisian Report, (Doc. 125–22) at 7–8, ¶¶ 20–21. However, the court's general acceptance of her methodology does not mean that all aspects of her testimony will be admitted.

Further, to the extent that her opinions are admissible, her assessment would be helpful to the jury to understand the complex, technical topic of FDA regulations. *See In re Mirena IUD Products Liability Litigation*, 169 F.Supp.3d 396, 474 (E.D.N.Y. 2016) ("Expert testimony from a regulatory expert on complicated schemes like the FDA's statutory framework, as well as opinions on the adequacy of a drug's label and the reasonableness of a pharmaceutical company's conduct, are useful in assisting the trier of fact.").[4]

Novartis relies on *Hogan v. Novartis Pharms. Corp.*, No. 06–CV–260, 2011 WL 1533467 (E.D.N.Y. Apr. 24, 2011), which is one of the few cases where the court fully excluded all testimony by Dr. Parisian.[5] However, *Hogan* differs from the current litigation because, in that case, the plaintiff brought common law claims that were unrelated to FDA regulations, so testimony from a regulatory expert was not needed. *Id.* at *2. Here, Jones argues that FDA regulations impact her claims, so Dr. Parisian's testimony and her expertise would be helpful to a jury. Parisian Response, (Doc. 166–39) at 15.

Novartis also relies on *In re Prempro Prod. Liab. Litig.*, 554 F.Supp.2d 871 (E.D. Ark. 2008), *aff'd in part, rev'd in part*, 586 F.3d 547 (8th Cir. 2009), to demonstrate that Dr. Parisian's testimony should be excluded. The district court in

4. The court in *In re Mirena* also found that the methodology used by Dr. Parisian and other regulatory experts does not have to strictly conform to the four-factor model found in *Daubert* because those factors apply to scientific expert opinions, not non-scientific regulatory reports. 169 F.Supp.3d at 480.

5. Dr. Parisian has served as a plaintiff's regulatory expert in almost 100 cases against Novartis. Of those cases, only a handful have excluded her testimony completely, and Novartis cites repeatedly to those cases in its briefing. *See In re Trasylol Prods. Liab. Litig.*, 709 F.Supp.2d 1323, 1345 (S.D. Fla. 2010); *Kaufman v. Pfizer Pharmaceuticals*, No. 02–CV–22692, 2011 WL 7659333 (S.D. Fla. Aug. 4, 2011) (finding Dr. Parisian failed to provide reliable bases for her testing opinion); *Lopez v. I–Flow Inc.*, 2011 WL 1897548 (D. Ariz. Jan. 26, 2011) (excluding Dr. Parisian's testimony because she gave narrative testimony and formed improper legal conclusions). However, the overwhelming number of courts who have analyzed Dr. Parisians qualifications and methodology have allowed her to testify, at least in part. In any event, each court addressing a *Daubert* challenge to an expert, such as this court, must decide the challenge based on its application of relevant law to the facts before it.

In re Prempro initially allowed her to testify in both the compensatory and punitive damages phases of the trial. However, the district court struck her punitive damages testimony post-trial because Dr. Parisian had mainly read from documents and provided unhelpful narrative testimony. 586 F.3d at 570. The Eighth Circuit held that the district court's error in admitting Dr. Parisian's testimony in the punitive damages phase was prejudicial error that warranted a new trial on punitive damages.*Id.* at 573. While *In re Prempro* guides the court to scrutinize Dr. Parisian's testimony closely for narrative testimony or other impermissible statements, it does not suggest that Dr. Parisian's testimony should be excluded in full.

To support her claim that Dr. Parisian's testimony is credible, Jones cites to several cases where Dr. Parisian's testimony was permitted in part and excluded in part. *See, e.g., Kruszka v. Novartis Pharms. Corp.*, 28 F.Supp.3d 920, 934 (D. Minn. 2014) (denying motion to fully exclude Dr. Parisian's testimony); *Lemons v. Novartis Pharms. Corp.*, 849 F.Supp.2d 608, 613 (W.D.N.C. 2012) ("Exclusion of [Dr. Parisian's] testimony in the entirety would be inappropriate.").

As explained below, Dr. Parisian is qualified and will be permitted to testify about the FDA regulatory process. However, her testimony will be limited and excluded in part. Jones agrees that Dr. Parisian will not testify as to Novartis' intent or state of mind, so any testimony on these issues is not admissible. Parisian Report, (Doc. 125–22) at 9, ¶ 23. Additionally, Dr. Parisian is not qualified and will not be permitted to testify regarding causation or "causal association"; whether and when Novartis was put on "notice"; whether any advertising or marketing changes might have impacted the opinion of a physician; studies conducted on other BP drugs; pharmaceutical industry standards; correlations between AFF and osteonecrosis of the jaw; and other improper legal conclusions.

a. *Causation and "Causal Association"*

[13] Novartis argues that Dr. Parisian lacks the expertise to testify on either causation or "causal association." In her deposition, Dr. Parisian agreed that she is not a causation expert and does not intend to offer a medical opinion about causation. Parisian Deposition, (Doc. 125–13) at 13(46:9–47:2) ("For Mrs. Jones—in terms of one patient, I'm not the causation person. It has to be the surgeon who's taking care of her."). As a regulatory expert rather than a medical expert, Dr. Parisian does not have the expertise or qualifications to testify as to general or specific causation.

Jones argues, however, that Dr. Parisian should be able to testify relating to "causal association," as the term is used in FDA regulations. *See* 21 C.F.R. 201.57(c)(6)(i) (providing that a drug's "labeling must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitively established."). In her Response brief, Jones attempts to distinguish Dr. Parisian's use of causal association terminology from medical causation. Parisian Response, (Doc. 166–39) at 27–31; *see* Parisian Deposition, (Doc. 125–13) at 78–79(309:13–310:1)("[I]n terms of the way the FDA is talking about causal association, it's not that high of a bar. It's not causation."). Novartis counters that Dr. Parisian is engaging in "verbal semantics" and is attempting to create a back-door method of testifying to medical causation without violating her stipulation. Parisian Reply Brief, (Doc. 175) at 7.

Dr. Parisian's attempts to distinguish her opinion as a "causal association" opinion rather than a causation opinion fall

short of the mark. First, Dr. Parisian has failed to sufficiently define causal association, as found in 21 C.F.R. 201.57(c)(6)(i), or distinguish it from medical causation.[6] She states in her deposition that in order to make a label change pursuant to FDA regulations, you must have "reasonable evidence of a causal association." Parisian Deposition, (Doc. 125–13) at 78(309:22–310:1). Dr. Parisian will be permitted to tell the jury what FDA regulations require in terms of label changes, including what action is required if a drug manufacturer has "reasonable evidence" of a causal association between a drug and an injury. However, she will not be permitted to testify whether Novartis had reasonable evidence or whether Novartis should have changed its label for Reclast.

Despite her assertions to the contrary, Dr. Parisian has implicitly provided her own causation opinion in both her report and her deposition. *See* Parisian Supplemental Report, (Doc. 125–23) at 38–39, ¶ 93 ("[bisphosphonates] may not be the only cause of AFF, but it is one drug class that has been linked to AFF."); *Id.* at 38, ¶ 92 ("it is my opinion that . . . there is '*reasonable evidence of a causal association*' sufficient to trigger Novartis' duty to update its Reclast label to provide adequate risk information.") (emphasis in original).

In her Supplemental Expert Report, Dr. Parisian states that she has based her causation association opinion on "the evidence of [bisphosphonates] and zoledronic acid"; the "occurrence of femur fractures in Study 2301"; the "lack of adequate pharmacovigilance practices to work up femoral fractures"; and the "literature." Parisian Supplemental Report, (Doc. 125–23) at 38, ¶ 92. However, Dr. Parisian cites to no specific medical literature establishing a causal association, and she neither specifies why Study 2301 demonstrated a causal association nor explains why Novartis should be responsible for the lack of adequate pharmacovigilance practices. *Id.* Dr. Parisian is not an endocrinologist and does not otherwise have the expertise to review medical literature on femoral fractures and opine on whether a correlation between a disease and an alleged injury amounts to a causal association.

As another district court recently determined, Dr. Parisian is not qualified to opine "either that the risk was clinically significant or that there was reasonable evidence of causal association"; she could "testify as to what Defendants should have done in terms of investigation based on the post-marketing information available to them, but may not opine that information amounted to evidence of causal association sufficient to warrant a label change." *In re Mirena*, 169 F.Supp.3d at 476 n.76.

Jones cites to *Hill v. Novartis Pharms. Corp.*, No. 06–CV–939, 2012 WL 5451809 (E.D. Cal. Nov. 7, 2012) to support her argument that Dr. Parisian is qualified to opine as to whether a pharmaceutical company should be responsible for failing to warn of a causal association. However, the court in *Hill* merely denied the defendant's motion to exclude Dr. Parisian's testimony on causal association as a "causation opinion in disguise" without providing any explanation to help guide this court's analysis. Therefore, this court will not rely on *Hill* as persuasive authority.

6. *See Dopson–Troutt v. Novartis Pharms. Corp.*, No. 06–CV–1708, 2013 WL 1344755 at *3 (M.D. Fla. April 2, 2013) (finding Dr. Parisian failed to meaningfully distinguish causal association from causation, so her regulatory causation discussion would not assist the jury's decision-making process); *Rowland v. Novartis Pharms. Corp.*, 9 F.Supp.3d 553, 562 (W.D. Pa. 2014) (excluding Dr. Parisian from offering "causation testimony of any kind").

Dr. Parisian's expertise lies in FDA regulations and in corporate compliance with FDA regulations. Her expertise does not lie in reviewing medical literature or determining whether causal associations exist between products and clinically significant hazards. Therefore, she has the expertise to explain the technical terminology of 21 C.F.R. 201.57(c)(6)(i) to a jury, but she does not have the expertise to assess whether a causal association existed that would impact Novartis' alleged failure to warn. Therefore, none of Dr. Parisian's testimony as to the existence of either causation or causal association will be permitted in front of a trier of fact in this case.

b. *Labeling*

[14] Novartis also argues that Dr. Parisian does not have sufficient experience to discuss labeling and product warnings. However, this argument overlooks Dr. Parisian's extensive experience with reviewing proposed labeling and providing comments for patient brochures. For example, Dr. Parisian's report states that while she was at the FDA's Office for Device Evaluation, she trained medical officers on labeling review, among other types of assessments. Parisian Report, (Doc. 125–22) at 4, ¶ 9. Further, during her time at the FDA, she helped design an FDA epidemiologic study that was created to capture risk to the public and "trigger the appropriate label changes for both the involved drugs and devices in order to protect the public." *Id.* at 4, ¶ 8.

Several other courts that have scrutinized Dr. Parisian's qualifications and only allowed her testimony in part have allowed Dr. Parisian to testify about communications between the FDA and Novartis regarding Novartis' labeling. *See Lemons v. Novartis Pharms. Corp.*, 849 F.Supp.2d 608, 614 (W.D.N.C. 2012) ("Dr. Parisian's experience and expertise with the FDA and its regulatory scheme does render her fit to offer testimony on the issue of Novartis' interactions with the FDA on the subject of labeling."); *Rowland v. Novartis Pharms. Corp.*, 9 F.Supp.3d 553, 561 (W.D. Pa. 2014) (allowing Dr. Parisian to testify about the FDA's requirements for labeling and the adequacy of the product warnings and labels due to her FDA experience and expertise). The court in *Rowland*, however, found Dr. Parisian's testimony regarding alternative actions physicians *might* have taken had they received different warnings required an "impermissible degree of speculation from Dr. Parisian, as she is not an oncologist." *Id.* at 562; *see also Stambolian v. Novartis Pharms. Corp.*, No. 12–CV–4378, 2013 WL 6345566 at *11, 2013 LEXIS 173016 at *29 (C.D. Cal. Dec. 6, 2013) ("Dr. Parisian is not qualified to offer testimony as to what decisions prescribing doctors would have made had they been given different labeling information ... Dr. Parisian is not an oncologist. Therefore, such testimony would be outside the scope of her expert knowledge.").

Novartis cites to this court's decision in *Thomas v. Evenflo Co.*, No. 2:02–CV–2001, 2005 WL 6133409, at *14 (N.D. Ala. August 11, 2005), *aff'd* 205 Fed.Appx. 768 (11th Cir. 2006), where the plaintiff was not permitted to testify on labeling because he did not follow accepted methodology in determining warnings were defective and did not provide alternative warning language. However, unlike the expert in *Thomas*, this court finds that Dr. Parisian has the expertise to discuss the adequacy of warnings and labels based on her contributions to the FDA study that discussed label changes and

the associated risks to the public.[7] Dr. Parisian substantiates her methodology by stating that she employed the same approach while at the FDA, and her opinion on Novartis' label cites frequently to applicable FDA regulations. Parisian Report, (Doc. 125–22) at 50–51.

This court finds persuasive the distinction other courts have drawn between allowing Dr. Parisian to discuss FDA label compliance and adequacy of labeling versus allowing her to speculate about the potential impact of a label change on prescribing physicians. Therefore, Dr. Parisian will be permitted to testify to communications between Novartis and the FDA regarding Reclast label changes and the adequacy of the Reclast label, but she will not be permitted to testify to the potential impact a Reclast label change would have had on treating physicians if the labeling change had occurred.

c. *"Notice" to Novartis, including Study 2202*

[15] Novartis seeks to prevent Dr. Parisian from testifying that certain events should have put Novartis on notice that Reclast could cause harm. First, for the purposes of this litigation, Dr. Parisian will not be permitted to testify to any studies, reports, or trials that were published after September 2011, when Jones alleges that she first developed symptoms of thigh pain, as they could not have put Novartis—or Jones's treating physicians—on notice.

Second, Dr. Parisian was involved in clinical trials as a medical officer in the FDA's Office of Device Evaluation. *See* Parisian Report, (Doc. 125–22) at 4, ¶ 9 ("I participated in the review of proposed clinical trials, the review of pre-marketing applications . . . and training new medical officers" in clinical trial evaluation). Therefore, she is qualified to testify about the operations of clinical trials and the FDA review process for proposed clinical trials.

However, Dr. Parisian will not be permitted to testify to "notice" as a method of circumventing the court's ruling preventing her from discussing causation, and Jones's assertion that Dr. Parisian should be permitted to testify about *all* notice to Novartis is overbroad. *See* Parisian Response, (Doc. 166–39) at 32. Dr. Parisian is a regulatory expert, yet in her report she opines that certain drug potencies, a study on match factory workers in the 19th century, and causal associations between *other* BP drugs and femur fractures should all have put Novartis on "notice." *See* Parisian Report, (Doc. 125–22) at 10–13, ¶¶ 30–36. Dr. Parisian is not an expert on bisphosphonate medications, a toxicologist, or a pharmacologist, and she will not be permitted to opine that Novartis should have conducted safety evaluations more quickly or should have noticed a link between bisphosphonates and femur fractures earlier. *See Kruszka v. Novartis Pharms. Corp.*, 28 F.Supp.3d 920, 934 (D. Minn. 2014)(finding that Dr. Parisian is not an expert on bisphosphonate medications and may not offer testimony on that issue).

In particular, Novartis objects to Dr. Parisian's reliance on Study 2202 to demonstrate that Novartis was put on notice. Study 2202 was a clinical trial where children with a severe genetic disorder called osteogenesis imperfecta ("OI") were inject-

7. Plaintiff cites to *In re Ethicon,* MDL No. 2327, 2016 LEXIS 119460 at *18 (S.D.W. Va. Sept. 2, 2016), to support her claim that Dr. Parisian is qualified to testify to the *accuracy* of product warnings and labels. However, the court in *In re Ethicon* construed plaintiff's counsel's position as a concession that Dr. Parisian would not testify about the *adequacy* of the labels, so it did not reach the question of whether Dr. Parisian was qualified to testify on label adequacy, rather than accuracy.

ed with zoledronic acid either once or twice a year. Parisian Report, (Doc. 125–22) at 19, ¶ 58. While Study 2202 was conducted on pediatric patients with OI, Reclast is a drug designed for postmenopausal women with osteoporosis. *See* Parisian Reply Brief, (Doc. 175) at 14. As the Eleventh Circuit has stated, "even minor deviations in chemical structure can radically change a particular substance's properties and propensities." *Rider v. Sandoz Pharm. Corp.*, 295 F.3d 1194, 1201 (11th Cir. 2002) (internal quotation and citation omitted).

Though Dr. Parisian is qualified to testify generally to the review process for Study 2202, as well as the results, she does not have the expertise to opine that Study 2202 put Novartis on "notice" or to compare the chemical structures of the drug used in Study 2202 with Reclast.

d. *Advertising and Marketing*

[16] Novartis argues that Dr. Parisian is not qualified to discuss a pharmaceutical company's marketing or advertising to physicians. It also argues that her opinion is not reliable because she has formed improper conclusions about the extent to which Reclast advertising and marketing was communicated to one of Jones's prescribing physicians. (Doc. 125–15) at 22. Jones counters that her experience at the FDA fully qualifies her to render her opinion on advertising and marketing. (Doc. 166–39) at 33.

Dr. Parisian is qualified to give her opinion on whether Novartis' marketing and advertising complied with FDA regulations. While at the FDA, Dr. Parisian helped draft FDA guidance documents that outlined "the requirements for obtaining FDA's marketing approval and the FDA Safety Alerts directed to healthcare providers and their patients." Parisian Report, (Doc. 125–22) at 5, ¶ 13. Further, while serving as an instructor in the FDA's Staff College for training FDA reviewers, she was responsible for reviewing marketing applications and "teach[ing] medical officers the process for evaluation and review required by FDCA directed to product marketing." *Id.* at 4–5, ¶ 10. Therefore, Dr. Parisian has the expertise to opine on whether Novartis' marketing complied with FDA regulations.

Dr. Parisian's report cites to 21 C.F.R. § 202.1, which sets out the requirements for prescription drug advertisements, as well as 21 C.F.R. §§ 201, 202, 314, and 352. *See id.* at 61, ¶200; 66, ¶ 213. Her report also cites to 21 C.F.R. § 314.80, which outlines the requirements of post-marketing reporting of adverse drug experiences. *Id.* at 61, ¶200 ("It is also required as part of pharmacovigilance (21 C.F.R. 314.80) to have investigated and obtained accurate post-market safety information about the risks of Reclast."). In some areas of her report, she properly ties her analysis of Novartis' marketing and sales practices to pertinent FDA regulations. *See id.* (concluding that a directive to the Novartis sales team was "not permitted by the FD & C Act or implementing regulations").

However, other areas of her report impermissibly extend beyond compliance with FDA advertising and marketing and into the "intent" or "state of mind" of Novartis. *See id.* at 58, ¶190 ("Novartis chose not to accurately update its sales force or prescribers about the growing risk of association."). Her report also speculates about whether Jones's prescribing physician, Dr. Traylor, was actually provided with certain sales and marketing information before prescribing Reclast. *Id.* at 58–59, ¶191. Allowing Dr. Parisian to testify as to the actions prescribing doctors *would have taken* with adequate labeling amounts to impermissible speculation by her. In these speculative statements, Dr. Parisian does not outline a sufficiently sound methodology for assessing the ade-

quacy of advertising or marketing and does not apply the language of any FDA regulation to an allegedly improper marketing mechanism.

Novartis' briefing cites to other courts which have found that Dr. Parisian does not possess the qualifications to assess whether Novartis' communication of risks to health care providers, through drug sponsors or members of the sales team, was appropriate. *See Lemons v. Novartis Pharms. Corp.*, 849 F.Supp.2d 608, 615 (W.D.N.C. 2012) ("Dr. Parisian does not possess the requisite experience or expertise, as an employee or insider of a pharmaceutical drug sponsor, to opine on the conduct of Novartis."); *Kruszka v. Novartis Pharms. Corp.*, 28 F.Supp.3d 920, 935 (D. Minn. 2014) ("Dr. Parisian may testify as to whether Novartis's marketing complied with FDA regulations, as that is within her area of expertise, but she will not be permitted to expand the discussion beyond those as she has in the past."); *see also Deutsch v. Novartis Pharms. Corp.*, 768 F.Supp.2d 420, 468 (E.D.N.Y. 2011) ("Dr. Parisian is not qualified to opine on the ethical standards in the pharmaceutical industry, not is she qualified to testify as to any obligations Novartis may have had to the medical community in addition to the FDA requirements.") (emphasis added).

Jones cites to *Earp v. Novartis Pharms. Corp.*, No. 5:11–CV–680, 2013 WL 4854488 (E.D.N.C. Sept. 11, 2013) for the proposition that Dr. Parisian should be allowed to provide all of the advertising and marketing opinions in her report and deposition. However, the court in *Earp* merely summarily states that her expertise at the FDA qualified her to testify to the approval, advertising, and marketing of drugs without any further specificity or helpful parameters. *Id.* at *4. Jones also cites to *Stambolian*, 2013 WL 6345566 at *10, 2013 LEXIS 173016 at *29, where the court found that Dr. Parisian was qualified to speak to the FDA's requirements for labeling and marketing. However, the court in *Stambolian* also excluded Dr. Parisian's testimony on the actions physicians might have taken with adequate labeling or marketing and other matters outside the scope of her knowledge. *Id.* at *10, 2013 LEXIS 173016 at *28.

Therefore, like with the court's "labeling" analysis, the court finds that Dr. Parisian is qualified to opine whether Novartis complied with FDA advertising and marketing regulations. However, Dr. Parisian will not be permitted to extend her testimony beyond that scope.

e. *Novartis' 2008 and 2015 Reports to the FDA*

[17] Novartis argues that Dr. Parisian should not be permitted to testify regarding the adequacy of Novartis' 2008 and 2015 reports to the FDA because her opinions do not properly cite to FDA regulations and her opinion would be both unreliable and unhelpful to a jury. Parisian Brief, (Doc. 122–15) at 24–25. Jones counters that Dr. Parisian has the expertise to testify that Novartis' communications in its 2008 and 2015 reports to the FDA were misleading and inaccurate. Parisian Response, (Doc. 166–39) at 33–36. Novartis also argues that any omission it may have made in its reports was a product of "inadvertent human error," so Dr. Parisian's opinions on the adequacy of Novartis' reporting are irrelevant. Parisian Reply, (Doc. 175) at 13.

Generally speaking, an assessment of the reasonableness of a pharmaceutical company's conduct in conforming with FDA regulations and in communicating with the FDA would be helpful to a jury. Further, it is well within Dr. Parisian's area of expertise to discuss a company's compliance with FDA regulations.

Jones cites to *In re Mirena*, 169 F.Supp.3d at 481, where the court allowed Dr. Parisian to testify as to the reasonableness of another pharmaceutical company's conduct so long as Dr. Parisian did not attempt to offer narrative testimony or merely regurgitate statements from company documents with little analysis. Jones also cites to *Deutsch v. Novartis Pharms. Corp.*, 768 F.Supp.2d 420 (E.D.N.Y. 2011), where the court found that Dr. Parisian had the expertise to discuss the "reasonableness of Novartis' conduct in its interactions with the FDA." *Id.* at 468 (emphasis added).

Novartis argues that Dr. Parisian should not be allowed to opine on communications between the FDA and Novartis regarding the 2008 and 2015 reports because she does not cite to specific FDA standards that were purportedly violated. To support its claim, Novartis cites to *In re Trasylol Prods. Liab. Litig.*, where the court barred Dr. Parisian's testimony in full because she did not back up her opinions that the company behaved inappropriately with a citation to any FDA standard that was violated. 709 F.Supp.2d 1323, 1350 (S.D. Fla. 2010). Novartis also cites to this court's opinion in *Thomas*, 2005 WL 6133409 at *15, where this court excluded the expert's opinion as nothing more than a "bare assertion" without any citations to the record to support his opinions.

However, Novartis does not dispute that Dr. Parisian is qualified to testify to the communications between the FDA and a pharmaceutical company, particularly regarding requests made by the FDA. Further, Dr. Parisian's Supplemental Report, which criticizes Novartis' 2008 and 2015 reports as inaccurate and misleading, specifically references FDA regulations and applies those regulations to Novartis' conduct. *See* Supplemental Report, (Doc. 125–23) at ¶¶ 65, 75, 83, 94. She also discusses in detail FDA terminology and processes, including the process of conducting a safety labeling change notification. *Id.* at 35, ¶ 83.

Therefore, Dr. Parisian has demonstrated that she applied appropriate methodology in formulating her opinions on Novartis' 2008 and 2015 reports to the FDA. She will be permitted to testify regarding the adequacy of these communications, and Novartis will be able to critique her methodology on cross-exam.

f. *Intent and State of Mind*

[18] Jones agrees that Dr. Parisian will not testify as to Novartis' intent or state of mind. Parisian Brief, (Doc. 125–15) at 22; *see also* Parisian Report, (Doc. 125–22) at 9, ¶ 23 ("There are no unsupported opinions intended to be offered regarding the 'state of mind' or 'intent' of Novartis."). Accordingly, any testimony on these issues will be excluded.

However, Jones argues that Dr. Parisian should still be able to express opinions on what Novartis was "aware" of or "knew" based on the information that was in its possession. She cites to *Block v. Woo Young Med. Co.*, 937 F.Supp.2d 1028, 1045 (D. Minn. 2013), where the court excluded testimony on corporate motive or intent but allowed Dr. Parisian to testify to "the state of the medical literature, the state of FDA approval, and other information about which [the company] should have been aware." Jones also cites to *In re Mirena*, 169 F.Supp.3d at 479, where the court allowed Dr. Parisian to testify to what the company "knew," in the sense of what information was in its possession. The court also allowed Dr. Parisian to testify to what the FDA "would have done in a typical situation when presented with a set of facts" and to what the FDA or the company's intent was, only to the extent that it was clear from public documents. *Id.* at 479–80.

Novartis, in comparison, relies on *Jenkins v. Novartis Pharms. Corp*, 2012 WL 6213494 at *6 (E.D. Tenn. Dec. 13, 2012), where the court allowed Dr. Parisian to testify about when certain materials were submitted to the FDA but excluded testimony on what Novartis "knew" because knowledge is an issue properly reserved for the jury. *See id.* ("Dr. Parisian has no specialized knowledge or scientific/medical expertise that provides her with a superior ability to judge Novartis's knowledge, and there is no basis for finding that the jury needs her assistance in evaluating Novartis's knowledge."); *see also In re Trasylol*, 709 F.Supp.2d at 1338 (excluding Dr. Parisian from addressing Novartis' intent, motive, or bad faith); *Bartoli v. Novartis Pharms. Corp.*, No. 3:13–CV–0724, 2014 WL 1515870 at *5 (M.D. Pa. April 17, 2014) (same); *Lopez v. I–Flow, Inc.*, 2011 WL 1897548 at *1 (D.Ariz. Jan. 9, 2012) (excluding Dr. Parisian from testifying to the knowledge, state of mind, or motivations of either the pharmaceutical company or the FDA itself).

Regardless of Jones's reassurances, any testimony on Novartis' state of mind or intent is excluded as a question for the jury rather than for Dr. Parisian. Dr. Parisian may, however, testify regarding what information was or should have been, *pursuant to specific FDA regulations*, in Novartis' possession.

g. *References to Osteonecrosis of the Jaw ("ONJ")*

[19] Novartis argues that Dr. Parisian should be excluded from opining on bisphosphonate-related osteonecrosis of the jaw ("BRONJ") or osteonecrosis of the jaw generally ("ONJ"), as she does in both her report and supplemental report. Jones counters that because Zometa, another Novartis drug that was associated with BRONJ, and Reclast, the subject of this litigation, are "chemically identical," it is proper for Dr. Parisian to discuss the entire class of drugs. Parisian Response, (Doc. 166–39) at 38. However, arguments of counsel are not evidence. Moreover, even if the two drugs are "chemically identical," even Jones admits the dosages are different, as are the alleged injuries. *Id.*

As the Eleventh Circuit has explained, even "minor deviations in chemical structure can radically change a particular substance's properties and propensities." *Rider v. Sandoz Pharm. Corp.*, 295 F.3d 1194, 1201 (11th Cir. 2002) (internal quotation and citation omitted) (excluding an expert witness from testifying that, because other drugs in the same class cause a certain effect, a drug from that class must cause the same effect as well). Jones has not cited any case law to support her claim that a regulatory expert should be able to opine on a different type of injury, associated with a different drug, than the injury that is the subject of the current litigation. Further, Jones has not established why any discussion of chemical analogies would help, rather than confuse, a jury. Therefore, Dr. Parisian is prohibited from testifying regarding ONJ, BRONJ, and Novartis' drug Zometa.

4. Conclusion as to the Admissibility of Dr. Parisian's Testimony

Based on the foregoing, Novartis' Motion To Strike Dr. Parisian's testimony (doc. 108) is **due to be DENIED** to the extent that it seeks to exclude Dr. Parisian's testimony in its entirety. However, Novartis' Motion is **due to be GRANTED IN PART** and **DENIED IN PART** as to the particular areas of Dr. Parisian's testimony that it seeks to exclude.

Dr. Parisian may testify on the following issues: (1) Novartis' interactions with the FDA on the subject of labeling; (2) compliance and/or noncompliance with FDA regulations on advertising and marketing; (3) Novartis' conduct in communicating with

the FDA, including the 2008 and 2015 reports; and (4) what information Novartis should have had, *based on specific FDA regulations.*

Dr. Parisian may not testify on the following issues: (1) causation, including "causal association"; (2) how a change in labeling might have impacted the decision of a prescribing physician; (3) whether or not Novartis was put on "notice," including by Study 2202; (4) how a change in advertising and marketing might have impacted the decision of a prescribing physician; (5) Novartis' state of mind, intent, or motive, including what Novartis "knew"; and (6) comparisons between ONJ, BRONJ, or the drug Zometa.

B. Dr. William B. Hinshaw

Jones also offers the opinions of Dr. Hinshaw into evidence. Dr. Hinshaw has offered both an expert report (doc. 125–26, the "Hinshaw Report") and a supplemental expert report (doc. 125–25, the "Hinshaw Supplemental Report"). Dr. Hinshaw was deposed on June 1, 2016, and the deposition transcript was filed into the record (doc. 125–21, the "Hinshaw Deposition").

On August 15, 2016, Novartis filed a Motion To Strike Dr. Hinshaw's expert testimony (Doc. 112) and a brief in support of its Motion (doc. 125–20, the "Hinshaw Brief"). On September 19, 2016, Jones filed a Response opposing Novartis' Motion To Strike. (Doc. 166–41, the "Hinshaw Response"). On October 14, 2016, Novartis filed a reply brief in support of its Motion To Strike. (Doc. 180, the "Hinshaw Reply").

1. Dr. Hinshaw's Qualifications

Dr. Hinshaw is Jones's designated scientific expert and offers opinions on both general and specific causation. Hinshaw Response, (Doc. 166–41) at 4. Dr. Hinshaw is a bioorganic chemist and a practicing gynecologist, specializing in menopause and clinical management of bone fragility. Hinshaw Report, (Doc. 125–26) at 2. He received a B.S. degree in Chemistry in 1963 from Duke University and a Ph.D. in Biomimetic Organic Chemistry in 1967 from Stanford University. *Id.* He received a medical degree from Albany Medical College in 1978. *Id.* Subsequently, he completed a four-year residency in Obstetrics and Gynecology at Albany Medical Center Hospital, serving as the chief senior resident. *Id.*

Since 1983, Dr. Hinshaw has worked as a board-certified gynecologist. Hinshaw Curriculum Vitae, (Doc. 125–26) at 21–23. Approximately ninety percent of his current gynecological practice is devoted to "hormonal aberrations of menopause which are associated with problems of bone fragility." Hinshaw Response, (Doc. 166–41) at 7. Dr. Hinshaw served as an assistant investigator during a clinical trial involving a non-Reclast BP drug around 1997. Hinshaw Deposition, (Doc. 125–21) at 7 (18:14–19:23).

In 2012, Dr. Hinshaw authored a peer-reviewed article titled "Using Medical Chemistry to Solve an Old Medical Mystery" that discussed unusual femur fractures suffered by match factory workers in the nineteenth century. Hinshaw CV, (Doc. 125–26) at 24. In total, Dr. Hinshaw has published twenty-one peer-reviewed articles, five of which pertained to phosphorous chemistry, bone fragility, and fractures. *See id.* In 2012, he co-authored an article titled "Atypical Femur Fractures: 81 Individual Personal Histories," that was published in the Journal of Clinical Endocrinology and Metabolism. *Id.* In fall 2016, Dr. Hinshaw co-authored an article, titled *An Evaluative History of Bisphosphonate Drugs: Dual Physiologic Effects of Pyrophosphate as Inspiration for a Novel Pharmaceutical Class*, that was accepted

by the Journal of Osteoporosis for publication. *See* (Doc. 169).

Jones claims that Dr. Hinshaw has reviewed scientific literature on the chemistry and kinetics of BPs on bone and has studied early scientific literature of the effect of pyrophosphates on bone. Hinshaw Response, (Doc. 166–41) at 9. Jones states that Dr. Hinshaw has primarily been offered "to explain to the jury the science of bone self-repair and Reclast's deleterious effect on the bone's natural abilities to grow, repair, model, and re model." *Id.* at 4.

2. Dr. Hinshaw's Opinions

In Dr. Hinshaw's Expert Report,[8] he offers the following opinions:

(1) The history of bisphosphonates for the prevention and treatment of osteoporosis and osteopenia is one of conflicting values, perspectives, and interests that has contributed to the present confusion on the meaning of those terms, (doc. 125–26) at 4–5;

(2) At the time of its distribution to Dr. Traylor, Reclast was defective. Reclast was not reasonably safe as intended to be used. Reclast was defective in design. The design was unreasonably dangerous, *id.* at 5;

(3) Novartis breached its promise or warranty to Ernesteen Jones that Reclast was suitable or fit to treat postmenopausal osteoporosis in the general population, a population to which Ms. Jones belonged, by seeking indications granted from data produced in trials employing very restricted and non-representative populations, *id.* at 5–6;

(4) Novartis and its predecessor companies, including Sandoz Pharmaceuticals and its consultants, had ample notice of the propensity of the bisphosphonates such as zoledronic acid to occasion fractures of the femur and general embrittlement of bone to permit avoidance of its introduction or early warning of this propensity, *id.* at 6–8;

(5) Novartis breached its duty to the clinical population candidates for the treatment by Reclast by making effectiveness representations based upon unrepresentative and manipulated clinical trials, *id.* at 9;

(6) There was a safer and practical alternative design that Novartis could have used at the time the Reclast was manufactured. The safer alternative design would have reduced or eliminated the harm to Ernesteen Jones, *id.* at 9;

(7) Novartis breached its duty to act as a reasonably prudent pharmaceuticals manufacturer in its design, research and testing of Reclast. Novartis failed to conduct appropriate clinical studies to determine the safety of long-term use of bisphosphonate drugs. Furthermore, Novartis failed to recognize, acknowledge or evaluate the increased hazard ratio of atypical femoral fractures in the pivotal clinical trials, although the existence of the risk was well-known at or near the beginning of that trial, *id.* at 10–11;

(8) Novartis breached its duty to act as a reasonably prudent pharmaceuticals manufacturer in its advertising, marketing, distribution, promotion and sale of Reclast, *id.* at 11–12;

(9) Novartis breached its duty to act as a reasonably prudent pharmaceuticals manufacturer in its labeling of Reclast, *id.* at 12;

(10) Novartis did not give Ernesteen Jones an adequate warning about the

8. Dr. Hinshaw offers the same 13 opinions in his supplemental expert report as well. *See* Hinshaw Supplemental Report, (Doc. 125–25).

danger of femur fracture associated with the use of Reclast, *id.* at 12;

(11) Novartis knew or should have known that Reclast could create danger when used as intended in its customary manner, *id.* at 13;

(12) The defective design of Reclast causes atypical femur fractures, *id.* at 13–17;

(13) The defective design of Reclast caused the injuries to Ernesteen Jones, *id.* at 17–19.

3. Dr. Hinshaw Is Qualified To Testify in This Case

[20] Novartis mischaracterizes Dr. Hinshaw's statements on causation as "eccentric" and describes him as a "some-time chemist." Hinshaw Brief, (Doc. 125–20) at 4. Dr. Hinshaw has multiple degrees in chemistry and has done extensive research on biometric pathways, gynecology, postmenopausal medicine, and bone fragility. He has also published a number of peer-reviewed articles, several of which pertain to bone fragility and fractures. Given that Dr. Hinshaw does have extensive training, experience, and expertise in these fields, he will not be excluded from testifying based on his qualifications. However, as discussed below, Dr. Hinshaw's testimony and opinions will be excluded because the methodology he relied upon in forming his opinions has not been shown to be reliable.

4. Dr. Hinshaw's Methodology Is Not Reliable

Dr. Hinshaw's opinion has been offered by Jones to establish both general and specific causation. General causation refers to the "general issue of whether a substance has the potential to cause the plaintiff's injury." *Chapman*, 766 F.3d at 1307 (citing *Guinn*, 602 F.3d at 1248 n.1). Specific causation refers to "the issue of whether the plaintiff has demonstrated that the substance actually caused injury in her particular case." *Guinn*, 602 F.3d at 1248 n. 1.

a. General Causation Opinion

i. *Bradford Hill Methodology*

[21] Dr. Hinshaw primarily relies on the Bradford Hill methodology to reach his conclusion that Reclast generally causes atypical femoral fractures. Hinshaw Response, (Doc. 166–41) at 6. Novartis disputes his use of Bradford Hill as both inapplicable and unreliable.

Sir Bradford Hill was a world-renowned epidemiologist who articulated a nine-factor set of guidelines in his seminal methodological article on causality inferences. *Milward v. Acuity Specialty Products Group, Inc.*, 639 F.3d 11, 17 (1st Cir. 2011) (citing Arthur Bradford Hill, *The Environment and Disease: Association or Causation?*, 58 Proc. Royal Soc'y Med. 295 (1965)). The Bradford Hill criteria are nine factors "widely used in the scientific community to assess general causation." *In re Stand 'N Seal Products Liab. Litig.*, 623 F.Supp.2d 1355, 1372 (N.D. Ga. 2009)(citing *Gannon v. United States*, 292 Fed. Appx. 170, 173 (3d Cir. 2008)).

Sir Bradford Hill's article explains that "one should not conclude that an observed association between a disease and a feature of the environment (e.g., a chemical) is causal without first considering a variety of 'viewpoints' on the issue." *Milward*, 639 F.3d at 17. The nine viewpoints look to:

(1) the strength of the association;

(2) the consistency of the association;

(3) the specificity of the association;

(4) the temporal relationship of the association;

(5) whether there is a dose-response relationship;

(6) whether causation is biologically plausible;

(7) the coherence of the association;

(8) the presence of experimental evidence; and

(9) evidence by analogy." [9]

In re Stand 'N Seal, 623 F.Supp.2d at 1372.

While the Eleventh Circuit has not yet directly commented on the Bradford Hill criteria, the reliability of the methodology is strengthened by the number of other circuit courts and district courts within this Circuit who have approved of an expert's use of the criteria. Furthermore, the Third Restatement of Torts states that if an association is found between a substance and a disease, "epidemiologists use a number of factors (commonly known as the 'Hill guidelines') for evaluating whether that association is causal or spurious." *Restatement*, § 28 cmt. c(3). As the Bradford Hill methodology has received wide acceptance and approval in the scientific community, Novartis' claims that the methodology is totally unreliable and unacceptable misrepresent the position of the scientific and legal communities and are not well taken by this court.

In his expert report and supplemental report, Dr. Hinshaw applied all nine Bradford Hill factors to reach his conclusion that Reclast causes AFF. Hinshaw Report, (Doc. 125–26). This was wise, as another circuit recently excluded an expert as unreliable whose testimony relied on the Bradford Hill methodology but only discussed three of the nine factors in a limited and sparse manner. *See In re Nexium Esomeprazole*, 662 Fed.Appx. 528, 530–31, 2016 WL 6298741, at *2 (9th Cir. October 28, 2016) (unpublished).

However, Dr. Hinshaw's reliance on the Bradford Hill methodology suffers from a fatal flaw: he cannot point to a study that establishes a causal association between Novartis' drug Reclast and AFFs. Both parties cite to the 2011 Reference Guide on Epidemiology,[10] which is published by the Federal Judiciary Center, and the Restatement to support their respective Bradford Hill claims. These resources explain that the Bradford Hill factors cannot be applied without first establishing a causal association. The 2011 Reference Guide on Epidemiology states,

> In assessing causation, researchers first look for alternative explanations for the association, such as bias or confounding factors ... [o]nce this process is completed, researchers consider how guidelines for inferring causation from an association apply to the available evidence. We emphasize that these [Bradford Hill] guidelines are employed only *after* a study finds an association to determine whether that association reflects a true causal relationship.

2011 Reference Guide on Epidemiology at 598–99 (emphasis added). A supplementary note further explains that "in a number of cases, experts attempted to use these guidelines to support the existence of causation in the absence of any epidemiologic studies finding an association ... [t]here may be some logic to that effort, but it

9. The Reference Manual on Scientific Evidence lists slightly different Bradford Hill factors than Sir Bradford Hill's original factors. However, the factors are ''largely the same'' *In re Lipitor (Atorvastatin Calcium) Mktg., Sales Practices & Prod. Liab. Litig.*, 174 F.Supp.3d 911, 916 n.3 (D.S.C. 2016). *Cf.* Michael D. Green, D. Michael Freedman & Leon Gordis, ''Reference Guide on Epidemiology,'' Reference Manual on Scientific Evidence, p. 600 (3d ed. 2011) (''2011 Reference Guide on Epidemiology'') *with* Sir Austin Bradford Hill, The Environment and Disease: Association or Causation?, 58 Proc. Royal Soc'y Med. 295, 295–300 (1965).

10. 2011 Reference Guide on Epidemiology at 597–606.

does not reflect accepted epidemiologic methodology." *Id.* at 599 n. 141.

The Restatement similarly describes the use of the Bradford Hill methodology as a two-step process. The first step requires that reliable medical studies establish an association between a substance and a disease. Restatement, § 28 cmt. c(3). Then, "if an association is found, epidemiologists use a number of factors (commonly known as the 'Hill guidelines') for evaluating whether that association is causal or spurious." *Id.* (emphasis added); *see also id.* "[h]owever, even when epidemiology finds an association, the observational (rather than experimental) nature of these studies requires an examination [using the Bradford Hill factors] of whether the association is truly causal or spurious." The Bradford Hill factors help determine whether an association is causal, not whether there is an association at all.

Novartis cites to several courts who have required that an expert who intends to rely on Bradford Hill methodology must first cite to an epidemiologic study finding an association. These courts allege that any other type of study establishing causal association would not be sufficient to apply the Bradford Hill factors. *See, e.g.*, *Dunn v. Sandoz Pharms. Corp.*, 275 F.Supp.2d 672, 678–79 (M.D.N.C. 2003) ("[T]he Bradford Hill criteria is a method for determining whether the results of an epidemiological study can be said to demonstrate causation and not a method for testing an unproven hypothesis.") In *Dunn*, the expert's testimony was excluded as unreliable because he developed a hypothesis and attempted to use the Bradford Hill criteria to prove that assertion, rather than using the factors to evaluate whether an association already shown by a reliable study demonstrates causation. *Id.* at 680; *see also In re Lipitor*, 174 F.Supp.3d at 925 ("Courts exclude expert testimony that attempts to start at step two, applying the Bradford Hill criteria without adequate evidence of an association.").

However, the Eleventh Circuit and a substantial number of other Circuit courts have rejected the epidemiologic study threshold for sufficient proof of general causation. *See Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194, 1198 (11th Cir. 2002)("It is well-settled that while epidemiological studies may be powerful evidence of causation, the lack thereof is not fatal to a plaintiff's case."); *see also In re Lipitor*, 174 F.Supp.3d at 916 ("While a causation opinion need not be based on epidemiological studies ... it is well established that the Bradford Hill method used by epidemiologists ***does*** require that an association be established through studies with statistically significant results.") (internal citation omitted) (emphasis in original).

In accordance with the Eleventh Circuit's holding in *Rider*, Dr. Hinshaw was not required to rely on an *epidemiological* study showing a causal association between the drug and the injury alleged. However, he did need to establish that the causal association existed based on existing medical literature.

ii. *Hinshaw Relies on a Class–Wide Association Between BPs and AFFs Rather Than an Association Between Reclast and AFFs*

First, Dr. Hinshaw admits in his deposition that he is not able to point to "any study in the peer-reviewed literature that defines a statistically-significant AFF association for Reclast specifically." Hinshaw Deposition, (Doc. 125–21) at 47(181:11–15). The reliability of his Bradford Hill methodology is called into question by this concession that there is no statistically significant causal association between *Reclast* and AFFs.

To overcome this hurdle, Dr. Hinshaw bases his general causation opinion on a causal association found between the entire class of BP drugs, of which Reclast is one type, and femoral fractures. His report claims that the association requirement is met because bisphosphonate use, not Reclast use, is "associated with a detectable increase in the incidence of non-hip femoral fractures. The ASBMR Task Force has recognized this association and called it 'robust.'" Hinshaw Report, (Doc. 125–26) at 13, ¶ 12.

The 2013 American Society for Bone and Mineral Research ("ASBMR") [11]Task Force Report (the "2013 ASBMR Report") included the following update on the class-wide association: "[a]lthough the Task Force still holds the opinion that a causal relationship between BPs and AFFs has not been established, evidence for an association has continued to accumulate in the 2 years since the first report was published and is quite robust." (Doc. 117–1) at 11 (emphasis added). Dr. Hinshaw agreed at deposition that the Task Force's viewpoint was a "fair characterization." Hinshaw Deposition, (Doc. 125–21) at 38(143:19–21).

This report, however, did not look or pertain specifically to any causal association between Reclast (only one drug in the class of BPs) and AFFs, and neither Dr. Hinshaw's report and deposition nor Ms. Jones's briefing cites to any authority stating that the association between a specific drug and an alleged injury may be extrapolated from a class-wide association. In fact, a number of courts have criticized the use of extrapolation from a class-wide study to an individual drug, as explained below.

iii. ***Dr. Hinshaw Improperly Extrapolates From Studies on the Class of BP Drugs To Form his Causal Association Opinion***

Dr. Hinshaw has not substantiated his claim that a causal association between Reclast and AFFs may be extrapolated from a class-wide association between BPs and femoral fractures. In *Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194 (11th Cir. 2002), the Eleventh Circuit affirmed the decision of a district court that "drew a careful distinction between clinical process, in which conclusions must be extrapolated from incomplete data, and the scientific method, in which conclusions must be drawn from an accepted process, and concluded that the plaintiffs' experts were relying on the former." *Id.* at 1196.

One of the reasons the Eleventh Circuit upheld the district court's decision was based on the plaintiffs' failure to explain why their presumption that a specific drug had the same effects as other drugs in that class was valid:

> [P]laintiffs suggest that because bromocriptine is an ergot alkaloid, it causes vasoconstriction. Although some other ergot alkaloids do cause vasoconstriction, plaintiffs offered insufficient evidence for the district court to find that bromocriptine does so as well. This is not a case where the Court finds the evidence offered to be unreliable. In this case the record contains no evidence at all of this hypothesis. Instead, it contains principally speculation and conjecture. Because the ergot alkaloid class of drugs has a wide range of effects, it is not obvious that bromocriptine should have the same effects as other drugs in that class.

11. The ASBMR is a "professional, scientific, and medical society established to bring together clinical and experimental scientists who are involved in the study of bone and mineral metabolism." *See* ABOUT ASBMR, http://www.asbmr.org/About/Overview.aspx (last visited Jan. 24, 2017).

Id. at 1201 (emphasis added). The court concluded that "scientific evidence must 'fit' the plaintiff's theory of causation," and in this case, the court would have been required to "make several scientifically unsupported 'leaps of faith' in the causal chain" in order to admit the plaintiff's evidence. *Id.* at 1202 (citing *Joiner*, 522 U.S. at 152, 118 S.Ct. at 522).

Some extrapolation is permitted and sometimes even necessary. *See Joiner*, 522 U.S. at 146, 118, 118 S.Ct. 512 S. Ct. At 519 ("[C]onclusions and methodology are not entirely distinct from one another. Trained experts commonly extrapolate from existing data."). However, the Supreme Court in *Joiner* also made clear that "nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert." *Id.*

The Tenth Circuit in *Hollander v. Sandoz Pharms. Corp.*, 289 F.3d 1193 (10th Cir. 2002), for example, held that the district court did not abuse its discretion in concluding that the methodology of an expert who relied on the Bradford Hill criteria was unreliable because there was "simply too great an analytical gap" between studies comparing the class of drugs and the disease and the experts' conclusion that the *specific* drug in question caused the alleged injury. *Id.* at 1208 (citing *Joiner*, 522 U.S. at 146, 118 S.Ct. at 512). The court elaborated that "the studies in question [did] not directly address the relationship between [the specific drug] and [the alleged injury]" and critiqued the plaintiff for presenting "no expert analysis as to how one might extrapolate" from the drug's effect on a group with one syndrome to another group who took the drug for a different purpose. *Id.*

Novartis cites to several examples in Dr. Hinshaw's deposition where he distinguished certain BP drugs from others in the class. Dr. Hinshaw admitted that one could not reliably extrapolate results from studies of oral BPs administered either weekly or monthly to non-oral BPs infused once a year, like Reclast:

Q. [referring to one of the BP studies] (By Mr. Klein) But they did find a statistical difference—but they did find a safety signal for some of the other bisphosphonates; is that correct?

A. That's correct. They were comparing a drug which is given on a regular periodic basis to a drug that was given on a once-a-year basis. And this is a completely invalid comparison from the beginning because the presence of a drug in the environment in which the healing of the bone is occurring is paramount to the rate at which it heals.

Q. So you believe—so, just to clarify, Alendronate and the other oral bisphosphonates are given either on a weekly or monthly—

A. Periodically, in one way or another.

Q. And Zoledronic acid is a once-a-year annual infusion; correct?

A. Yes.

Q. If I understand what you just said, its not valid to extrapolate results from studies looking at oral bisphosphonates (inaudible); is that correct?

A. It's not valid because of that fact and because of the fact that under the best of circumstances it's problematic whether the parameter being examined has anything to do with the problem that we're interested in, not healing.

Hinshaw Deposition, (Doc. 125–21) at 47(178:3–179:14) (emphasis added); *see also id.* at 73(282:22–283:16):

Q: Doctor, do you agree different bisphosphonates can have different impacts on the material properties of bone?

A. Probably so. It's—one problem is that, in measuring impact of bisphosphonates on the material properties of bone, the oral bisphosphonates are usually given orally and intravenous bisphosphonates are usually given intravenously and it really produces a set of circumstances that are only assumed to be parallel. They're not likely to be parallel. So—but I do agree there's considerable differences in the bisphosphonates. There's less difference if they're all compared intravenously, which can be done and has been done in some circumstances.

(Emphasis added). Novartis also cites to a study, which Dr. Hinshaw discussed in his deposition, that found a statistically significant loss in bone fatigue life in orally-administered BPs but not in zoledronic BPs like Reclast. *Id.* at 74(286:13–21). Dr. Hinshaw also agreed that different BPs have different "affinities" for bone and that zoledronic acid BPs have the "highest affinity for bone amongst the drugs in the United States." *Id.* at 74(289:5–16).

Dr. Hinshaw concedes that, at least on some level, a comparison between BP drugs administered once a year and oral BPs administered more frequently is invalid. As stated above, Dr. Hinshaw also admitted in his deposition that there is no study in peer-reviewed literature that found a statistically-significant association between Reclast and AFFs. *Id.* at 47(181:11–15).

In her response, Jones relies on the decision of another district court in this Circuit to support her claim that "it is not a requirement in the Eleventh Circuit to prove the exact mechanism of injury." Hinshaw Response, (Doc. 166–41) at 15 (citing *McBride v. Houston Cty. Health Care Auth.*, 2015 WL 3648995 (M.D. Ala. 2015)). Though that may be true, an association must first be established between the drug and the alleged injury in order for an expert to rely on the Bradford Hill methodology to form a general causation opinion. Because Dr. Hinshaw has not first established that there is an association between Reclast and AFFs, his general causation opinion will be excluded.[12]

iv. *Weight of the Evidence Methodology*

Jones also briefly argues that Dr. Hinshaw properly used a "weight of the evidence" methodology in addition to the Bradford Hill criteria. Hinshaw Response, (Doc. 166–41) at 25. Novartis counters in its reply brief that Dr. Hinshaw did not disclose his use of a weight of the evidence methodology in either his initial expert report or his supplemental report and also did not apply the methodology reliably. Hinshaw Reply, (Doc. 180) at 13–14.

Generally speaking, weight of the evidence methodology can be considered reliable. *See Milward*, 639 F.3d at 17 ("This 'weight of the evidence' approach to mak-

12. Novartis also argues that Dr. Hinshaw has conceded that even the class-wide epidemiology studies are conflicting. Hinshaw Brief, (Doc. 125–20) at 11, n. 9; *see* Hinshaw Deposition, (Doc. 125–21) at 55(212:8–13) (agreeing "that the epidemiology that exists in the literature is conflicting"). However, Dr. Hinshaw goes on to clarify that Novartis' attempt to group all the epidemiological studies on BPs together and call them conflicting is like "comparing apples and oranges" because "we are comparing reports that use totally different techniques for evaluating the problem"). *Id.* at 55(212:18–19 and 211:20–25). Therefore, Dr. Hinshaw was actually referring to Novartis' grouping of certain studies when he used the term "conflicting," " not necessarily the studies themselves.

ing causal determinations involves a mode of logical reasoning often described as 'inference to the best explanation,' in which the conclusion is not guaranteed by the premises."). The methodology involves

> six general steps, some of which may be implicit. The scientist must (1) identify an association between an exposure and a disease, (2) consider a range of plausible explanations for the association, (3) rank the rival explanations according to their plausibility, (4) seek additional evidence to separate the more plausible from the less plausible explanations, (5) consider all of the relevant available evidence, and (6) integrate the evidence using professional judgment to come to a conclusion about the best explanation.

Id. at 17–18.

Jones claims that Dr. Hinshaw applied the methodology when he "considered the communication between the FDA and NPC regarding AFFs, documentation regarding clinical trials, postmarket reports and voluminous scientific studies." Hinshaw Response, (Doc. 166–41) at 25. However, Dr. Hinshaw has not described the process he used or the steps he took in applying this methodology, including whether he ranked plausible rival explanations, and Jones's briefing provides no clarity either. Dr. Hinshaw's testimony on his purported weight of the evidence methodology is therefore unreliable and would not assist a trier of fact. As both Dr. Hinshaw's "weight of the evidence" and Bradford Hill methods were applied unreliably, his general causation opinion is due to be excluded.

b. Specific Causation Opinion

[22] Dr. Hinshaw also opines in his Expert Report (doc. 125–26) and Supplemental Report (doc. 125–25) that Reclast caused the injuries to Jones. *See* Doc. 125–26 at 17–19. Like his general causation opinion, his specific causation opinion must meet the Eleventh Circuit's standard for admissibility. For the following reasons, the court finds that Dr. Hinshaw applied an unreliable methodology in forming his specific causation opinion, so his specific causation opinion is also due to be excluded.

i. *Dr. Hinshaw Has not Conceded That He Is Unqualified To Offer Specific Causation Testimony*

Novartis first claims that Dr. Hinshaw admitted in his deposition that he is unqualified to opine on specific causation. Dr. Hinshaw was previously offered as an expert witness in *Barnes v. Merck Sharp & Dohme Corporation*, CV–2011–900393.00, in the Circuit Court of Montgomery County, Alabama. (Doc. 125–26) at 3. A portion of his deposition from *Barnes* was read to Dr. Hinshaw by defense counsel during his deposition. Novartis claims that (1) Dr. Hinshaw admitted in his previous testimony in the *Barnes* case that he was not qualified to offer a specific causation opinion; and (2) Dr. Hinshaw, in his deposition in this case, re-affirmed his testimony in *Barnes.* (Doc. 125–20) at 16–17.

However, Dr. Hinshaw's *Barnes* deposition testimony is not the slam-dunk that Novartis considers it to be. Dr. Hinshaw was asked, "[h]ow would you go about determining whether a particular medicine a patient was taking may have contributed to the development of a fracture?" Hinshaw Deposition, (Doc. 125–21) at 90(350:12–16). In response, he stated that "I don't think, as an individual practitioner, that I could determine that a particular medicine that a particular patient was taking was associated with the cause of the fractures . . . I don't feel that I'm qualified to do that." *Id.* at 90(350:16–23) (emphasis added). Though Dr. Hinshaw agreed that he "still feel[s] that way" in this case, *id.* at 90(350:24–25), he appears to be referring

to his opinion as a treating physician or prescribing practitioner, not as an epidemiologist. Novartis has misconstrued Dr. Hinshaw's agreement with his statement in his prior deposition testimony as a full concession that he is *never* qualified to offer specific causation testimony.

Moreover, because the court has not been provided with Dr. Hinshaw's full deposition in the *Barnes* case, it will not base its decision whether to exclude Dr. Hinshaw on a discussion of an incomplete portion of that prior deposition.

ii. *Dr. Hinshaw Improperly Used Bradford Hill, a General Causation Methodology, To Form his Specific Causation Analysis*

Dr. Hinshaw has stated that he relied on the Bradford Hill criteria to form his specific causation opinion as well as his general causation opinion. While Bradford Hill may be used to reliably establish *general causation*, Jones has not demonstrated that Bradford Hill is an accepted criteria for determining *specific causation.*

Numerous courts have referred to the Bradford Hill criteria as a useful tool to analyze general, rather than specific, causation. *See, e.g., Gannon*, 292 Fed.Appx. at 173 ("Specifically, the Court found that [the expert's] testimony failed to satisfy the 'Bradford Hill' criteria, which are nine factors widely used in the scientific community to assess general causation.") (emphasis added); *In re Stand 'N Seal*, 623 F.Supp.2d at 1372 (same); *see also* 2011 Reference Guide on Epidemiology at 598–600 (listing application of Bradford Hill criteria only as a method of determining general causation).

Jones does not cite to any authority approving of the use of the Bradford Hill criteria alone to support a specific causation opinion. Instead, she argues that because Dr. Hinshaw utilized both the Bradford Hill methodology and a differential diagnosis, his specific causation opinion is reliable. In his deposition, Dr. Hinshaw stated:

> Q. In your report, you say that you arrive at your specific causation opinion based on Bradford–Hill; is that correct?
>
> A. Yes.
>
> Q. Can you cite me any paper—any peer-reviewed literature in which Bradford–Hill was used to arrive at specific causation in a particular patient?
>
> A. A bisphosphonate patient or any patient?
>
> Q. Any patient.
>
> A. Any patient.
>
> Q. Specific Causation.
>
> A. No, I can't.
>
> Q. Do any of the Bradford–Hill criteria involve ruling out other potential causes in a particular patient?
>
> A. No.
>
> Q. Did you perform a differential diagnosis on Ms. Jones?
>
> A. To a limited extent. To the extent of which I was offered the medical record.

Hinshaw deposition, (Doc. 125–21) at 91(355:14–356:14).

Jones cites to *Estate of Tobin v. Smith-Kline Beacham Pharms.*, No. 00–CV–25, 2001 WL 36102161, 2001 LEXIS 26397 (D. Wyo. May 8, 2001) to support her claim that Dr. Hinshaw's specific causation opinion is reliable because it was based both on Bradford Hill criteria and on a differential diagnosis. However, the court in *Estate of Tobin* provided little analysis as to why it allowed an expert's specific causation opinion, other than stating that while the expert relied to some extent "on differential diagnosis in reaching his opinions regard-

ing general and specific causation," he also "relie[d] upon the Bradford Hill Factors ... in reaching his opinion." *Id.* at *15, 2001 LEXIS 26397 at *46. It is not clear whether the Bradford Hill criteria were used to form both the expert's specific and general causation opinions in this case, and Jones did not direct the court to any other authority where the combination of Bradford Hill and differential diagnosis methodologies was sufficient to allow in an expert's specific causation testimony.

Moreover, Dr. Hinshaw's alleged reliance on a differential diagnosis is itself questionable because he concedes that his differential diagnosis analysis was "limited," and he did not discuss the methodology in his expert report.

iii. *Differential Diagnosis Methodology Has Generally Been Accepted by the Eleventh Circuit*

Differential diagnosis is "a medical process of elimination whereby the possible causes of a condition are considered and ruled out one-by-one, leaving only one cause remaining." *Hendrix*, 609 F.3d at 1195.[13] The differential diagnosis method, when applied under circumstances that "ensure reliability," can "provide a valid basis for medical causation opinions." *Id.* To ensure reliability, the court must consider the reasonableness of applying the differential diagnosis approach "to the facts of this case and the validity of the experts' particular method of analyzing the data and drawing conclusions therefrom." *Id.* On several occasions, the Eleventh Circuit has referred to differential diagnosis as a "scientifically accepted methodology." *Chapman*, 766 F.3d at 1307 (citing *Guinn*, 602 F.3d at 1248 n.1).

> As the Eleventh Circuit has explained,
>
> Differential diagnosis includes three steps: (1) the patient's condition is diagnosed, (2) all potential causes of the ailment are considered, and (3) differential etiology[14] is determined by systematically eliminating the possible causes. *McClain*, 401 F.3d at 1252. A reliable differential analysis "need not rule out all possible alternative causes," but "it must at least consider other factors that could have been the sole cause of the plaintiff's injury." *Guinn*, 602 F.3d at 1253. Differential diagnosis, "however, will not usually overcome the fundamental failure of laying a scientific groundwork for the general toxicity of the drug and that it can cause the harm a plaintiff suffered." *McClain*, 401 F.3d at 1252.

Chapman, 766 F.3d at 1308–09 (concluding that the expert did not properly follow the necessary steps for a differential diagnosis because she relied on temporal proximity and failed to fully explore other potential causes of the plaintiff's alleged injury). A differential diagnosis is flawed if it presumes the existence of general causation or if it is improperly based solely on a temporal relationship between the drug and the plaintiff's injuries. *Kilpatrick v. Breg*, 613 F.3d 1329, 1334 (11th Cir. 2010).

13. The Restatement similarly states that differential diagnosis involves identifying a cause "by eliminating the possibility that other known and alternative causes were responsible for the outcome." *Restatement* § 28 cmt. c(3).

14. As the Eleventh Circuit has explained, "[t]echnically, differential diagnosis refers to a method of determining which of two diseases a patient suffers from, whereas differential etiology is a term used to describe the process by which the cause of an injury is determined. Following the trend among federal courts, however, we will use the term differential diagnosis to refer to both concepts." *Guinn*, 602 F.3d at 1253 n.6. As both parties in this case use the term "differential diagnosis" to describe the latter process, this court will do the same.

iv. *Dr. Hinshaw's Testimony at Deposition That He Relied on a Differential Diagnosis Violates Rule 26*

[23] Novartis critiques Dr. Hinshaw's use of the differential diagnosis methodology on both a substantive and procedural level. Novartis claims that because Dr. Hinshaw did not discuss his reliance on a differential diagnosis in either his expert report or the supplemental report, he cannot discuss the methodology for the first time during his deposition. (Doc. 125–20) at 18. Novartis believes that Dr. Hinshaw's specific causation testimony should be excluded on that basis alone, in reliance on *Hamlett v. Carroll Fulmer Logistics Corporation*, 176 F.Supp.3d 1360 (S.D. Ga. 2016). In *Hamlett*, the magistrate judge excluded the expert's newly-presented opinions, which he supplied for the first time at deposition, because "Rule 26(a)(2) deters procrastination and sandbagging," and the expert "did both." 176 F.Supp.3d at 1365.

[24] Rule 26 requires that the disclosure of the identity of expert witnesses shall be accompanied by a written report that contains a "complete statement of *all* opinions the witness will express and the basis and reasons for them," as well as "the facts or data considered by the witness" in forming his or her opinion. FED. R. CIV. P. 26(a)(2)(B)(i) (emphasis added).[15] Expert reports must include both "how" and "why" the expert reached a certain result, not just conclusory opinions. *Hamlett*, 176 F.Supp.3d at 1365. The court in *Hamlett* concluded that it was "unacceptable to make a party wait, and thus be surprised, at a deposition ... the defendants were prejudiced because they were denied, prior to the deposition, the full opportunity to digest [the expert's] information and formulate their deposition questions based on the same." *Id.*

Jones counters [16] that, although he does not explicitly describe it as a differential diagnosis, Dr. Hinshaw "reference[d] other conditions he ruled out as being the sole cause of her fractures" on page 13 of his Supplemental Report. (Doc. 166–41) at 27 n.10. However, page 13 of Dr. Hinshaw's Supplemental Report merely discusses one condition associated with fragility fractures, hyperparathyroidism ("HPP"), and rules out HPP based on a lack of causal association in the medical literature. Hinshaw Supplemental Report, (Doc. 125–25) at 14. Despite directing the court's attention to this specific page, Jones fails to demonstrate that Dr. Hinshaw sufficiently considered, and then eliminated, other risk factors associated with femoral fractures in

15. The Advisory Committee Notes further clarify that Rule 26(a)(2) ''imposes an additional duty to disclose information regarding expert testimony sufficiently in advance of trial that opposing parties have a reasonable opportunity to prepare for effective cross-examination.'' FED. R. CIV. P. 26(a)(2), Advisory Committee Notes, 1993 Amendment, 146 F.R.D. 633.

16. In a footnote, Jones also argues that because Dr. Hinshaw was cross-examined by defense counsel at deposition, Novartis will ''not be surprised at trial.'' (Doc. 166–41) at 27 n. 10. She cites to one of this court's previous opinions, *Diasource, Inc. v. Gamble*, 2005 WL 6000494 (N.D. Ala. August 18, 2005), for this proposition. However, the plaintiff in *Diasource*, unlike in the current case, submitted a supplemental affidavit that ''at least minimally complied with Rule 26(a)(2)(B),'' so this court concluded that the defendants had enough information from the affidavit to select their own expert, depose plaintiff's expert, and avoid surprise at trial. *Id.* at *2. Jones does not cite to any authority for the proposition that an expert who first reveals the ''basis and reasons'' for his opinion for the first time at deposition, and has not included those bases and reasons in his expert report or any supplemental filing, has not violated Rule 26's disclosure requirements.

preparing his expert report.[17] In fact, all of Jones's citations in her Response brief, where she alleges that Dr. Hinshaw utilized a differential diagnosis, derive from his deposition testimony, not from his expert report or supplemental report. *See* Hinshaw Response Brief, (Doc. 166–41) at 27–28.

Therefore, Dr. Hinshaw violated Rule 26, and did not put Novartis on notice, by failing to sufficiently provide the methods and bases that he alleges he used in opining on specific causation in his expert reports.

v. *The Lack of Reliable General Causation Opinion Makes a Specific Causation Opinion Using a Differential Diagnosis Methodology Unreliable*

[25] Finally, Dr. Hinshaw's opinion is unreliable because general causation has not been established between Reclast and AFFs. The Eleventh Circuit has explained that if no expert has been offered who can provide an admissible general causation opinion, then an expert may not rely on a differential diagnosis to prove specific causation. *See McClain*, 401 F.3d at 1253 ("A valid differential diagnosis, however, only satisfies a *Daubert* analysis if the expert can show the general toxicity of the drug by reliable methods."). In *McClain*, the medical articles and analogies the experts relied on were not sufficient to establish general causation, and "[i]n the absence of such a foundation for a differential diagnosis analysis, a differential diagnosis generally may not serve as a reliable basis for an expert opinion on causation in a toxic tort case." *Id.; see also id.* ("[A]n expert does not establish the reliability of his techniques or the validity of his conclusions simply by claiming that he performed a differential diagnosis on a patient.")

The court has already ruled that Dr. Hinshaw's general causation opinion is based on unreliable methodology. Therefore, based on the lack of reliable general causation opinion, Dr. Hinshaw's differential diagnosis is unreliable, and his specific causation opinion will be excluded.

c. Dr. Hinshaw Is not Qualified To Opine on Novartis' Compliance with FDA Regulations

[26] Dr. Hinshaw will not be permitted to testify as to whether Novartis' clinical trials and warnings were adequate and in compliance with FDA regulations. Though Jones claims that Dr. Hinshaw "certainly intends to defer to Dr. Parisian as to specific FDA regulations," the brief also argues that his opinion is relevant to whether Novartis had "reasonable evidence of a causal association with a drug" such that a warning regarding femur fractures was warranted. Hinshaw Response, (Doc. 166–41) at 29 (citing 21 C.F.R. § 201.57(c)(6)(i)). His eighth and ninth opinions also conclude that Novartis did not act as a "reasonably prudent pharmaceutical manufacturer" in its advertising, marketing, promotion, distribution, sale, and labeling of Reclast. (Doc. 125–26) at 11–12.

Dr. Hinshaw has experience reviewing clinical trial documents and, according to his deposition, was an assistant investiga-

17. These other factors, as Novartis points out, include age and steroid use. Dr. Hinshaw does discuss how Ms. Jones's age and corticosteriod use are "associated with an increasing risk of fracture," in his deposition, but he does not identify, and subsequently eliminate, these factors in any differential diagnosis analysis in his reports. Hinshaw Deposition, (Doc. 125–21) at 91(356:16–25). In fact, Dr. Hinshaw admitted during deposition that at least some studies show an increased or significant association between glucocorticoid steroids and AFFs, which undermines his opinion that Reclast causes AFFs. *Id.* at 96(376:20–377:25).

tor in a trial involving another bisphosphonate drug. Hinshaw Response, (Doc. 166–41) at 32 (citing Hinshaw Deposition, (Doc. 125–21) at 7(19:5–23)). However, Dr. Hinshaw's qualifications do not extend to FDA labeling and marketing regulations. He is qualified to discuss the scientific components of studies that were the subject of communications between Novartis and the FDA, but he may not opine on the adequacy of those communications themselves or on whether Novartis acted as a reasonably prudent manufacturer should.

Dr. Hinshaw will also not be permitted to testify to whether Novartis complied with FDA regulations, including whether Novartis failed to report fractures to the FDA in July 2008. *See* Hinshaw Response, (Doc. 166–41) at 32. Fortunately for Jones, Dr. Parisian does have the expertise to discuss the adequacy of Novartis' communications with and disclosures to the FDA, and she will be permitted to do so, with certain limitations.

5. Conclusion as to the Admissibility of Dr. Hinshaw's Testimony

Although Dr. Hinshaw is qualified to testify in this case, other than to Novartis' compliance with FDA regulations, he did not employ a reliable methodology in forming either his general or specific causation opinions. Therefore, Dr. Hinshaw's testimony is due to be **EXCLUDED** in full, and the Motion to strike his testimony (doc. 112) is due to be **GRANTED**.

C. Dr. Wayne A. Taylor

Jones also offers the opinions of Dr. Taylor into evidence. Dr. Taylor has offered an expert report, dated August 31, 2015, which includes his Curriculum Vitae. (Doc. 125–17, the "Taylor Report"). Dr. Taylor also offered a supplemental expert report, dated May 2, 2016. (Doc. 125–18, the "Taylor Supplemental Report."). Dr. Taylor was deposed by Novartis on June 3, 2016, and the deposition transcript was filed into the record. (Doc. 125–16, the "Taylor Deposition").

On August 15, 2016, Novartis filed a Motion To Strike Dr. Taylor's expert testimony (Doc. 116). A day later, Novartis filed a brief in support of its Motion (doc. 125–19, the "Taylor Brief"). On September 19, 2016, Jones filed a Response opposing Novartis' Motion To Strike. (Doc. 166–40, the "Taylor Response"). On October 14, 2016, Novartis filed a reply brief in support of its Motion To Strike. (Doc. 177, the "Taylor Reply").

In his report, Dr. Taylor offers the following opinions: (1) Novartis' clinical trials H2301 and L2310 do not demonstrate the safety of Reclast; (2) Novartis' clinical trial H2301 offers "evidence of causality" between Reclast and AFFs; and (3) Novartis provided incomplete and biased information to the FDA.

1. Dr. Taylor's Qualifications

According to his curriculum vitae, Dr. Taylor received a bachelor of science in mathematics from Purdue University in 1976. (Doc. 117–3) at 3, the "Taylor CV." He received an M.S. in Statistics from Purdue University in 1978 and a Ph.D. in Statistics from Purdue University in 1983.- *Id.* at 3. Dr. Taylor worked as a statistician at Baxter Healthcare Corporation for 22 years and at one point was responsible for their Six Sigma program.[18] *Id.* at 2. In 2000, Dr. Taylor retired from his position as the Director of Quality Technologies at Baxter and founded Taylor Enterprises, Inc. ("Taylor Enterprises"). *Id.*

18. Dr. Taylor testified at deposition that he was involved in health hazard review boards that dealt with the safety of drugs manufactured by Baxter. Taylor Deposition, (Doc. 125–16) at 8 (25:21–22).

At Taylor Enterprises, Dr. Taylor develops software packages and provides consulting and training on statistics. *Id.* He is a leading expert on acceptance sampling in the pharmaceutical, medical device, and diagnostics industries, and his articles on selecting statistically valid sampling plans are used by the FDA in their new inspector training. *Id.* He has taught two courses on acceptance sampling to over 5,000 students and 50 companies, including the Center for Devices and Radiological Health. *Id.*

According to his deposition testimony, Dr. Taylor has designed statistical method sections for clinical trials of pharmaceutical products and medical devices. Taylor Deposition, (Doc. 125–16) at 5(13:14–14:17). He also claims to have expertise in contributing information on variables that could affect the outcome of a study to clinical trial design experts. *Id.* at 42(161:14–23).

2. Dr. Taylor Is Qualified To Offer Some, but not All, of his Opinions

a. Dr. Taylor Was not Designated as a Causation Expert

Novartis first briefly argues that Dr. Taylor should not be permitted to offer a causation opinion because he was not designated as a general causation expert in this case. Taylor Brief, (Doc. 125–19) at 7 n.5. Jones's Response brief provides little clarity as to the purpose for which Dr. Taylor's opinion is offered. His opinion certainly does not appear to be offered for specific causation, as Dr. Taylor's expert report does not even reference Ms. Jones. Novartis alleges that Dr. Taylor was not designated as a general causation expert in Jones's Rule 26(a)(2) disclosures. Taylor Brief, (Doc. 125–19) at 7 n.5; *see* Jones's Expert Disclosures, (Doc. 119–1). Yet in his expert report and during his deposition, Dr. Taylor offers causality opinions. Taylor Expert Report, (Doc. 125–17) at 3(claiming Study H2301 "offers evidence of causality").[19]

Jones does not respond to Novartis' expert designation argument or provide any evidence that Dr. Taylor was properly designated as a causation expert. Instead, she counters that Dr. Taylor is not offering a medical causation opinion but rather is offering a causation opinion based on statistical methods. Taylor Response, (Doc. 166–40) at 12.

While Rule 26(a)(2) does require that retained experts provide a written report with a complete statement of all experts' opinions and the facts and data to support those opinions, the Rule does not require that an expert specifically be designated as a *causation* expert. *See* FED. R. CIV. P. 26(a)(2)(B). Novartis has failed to point to any binding authority stating that a retained expert must be specifically referred to as a "causation" expert before that expert can offer causation opinions, and this court has not found any. Novartis does not claim that it was prejudiced in any way by such a technical omission. Accordingly, Dr. Taylor's causation opinions will not be excluded on this basis alone.

b. Dr. Taylor Is not Qualified To Offer a Causation Opinion

[27] Dr. Taylor lacks the expertise to offer a general causation opinion, particularly an opinion based on his improper reanalysis of medical data. He has expertise in designing statistical method sections for clinical trials and in contributing statistical information on variables that could affect the outcome of a study to clinical trial

19. During his deposition, Dr. Taylor was asked, "Are you offering a causation opinion in this case?" Taylor Deposition, (Doc. 125–16) at 37(143:11–12). Dr. Taylor responded, "[r]elative to the analysis I did in this report, yes." *Id.*

design experts. (Doc. 125–16) at 5(13:14–14:17); 42(161:14–23). However, Dr. Taylor has never served as the principal designer of the protocol of a clinical trial. *Id.* at 5(15:23–16:2). He does not have a medical degree and does not have any medical expertise in bisphosphonate use or atypical femur fractures. *Id.* at 3(7:13–20); 31(118:14–20). Dr. Taylor himself admitted that his review of the medical literature was limited to ten journal articles. *Id.* at 60(235:14–16).

Given that Dr. Taylor does have extensive training and expertise in statistics in the pharmaceutical and medical device industries, he will not be excluded from opining on statistical methods or other matters within his expertise. However, as discussed below, he is not qualified to offer his general causation opinion. Additionally, his general causation opinion will be excluded because the methodology Dr. Taylor relied upon in forming it is unreliable and will not assist the trier of fact.

3. Dr. Taylor's Methodology Is Unreliable

a. The Background Risk Methodology Has Been Accepted by the Eleventh Circuit

[28] Jones's briefing states that Dr. Taylor relied on a background risk of the disease methodology in forming his causation opinions. Taylor Response Brief, (Doc. 166–40) at 4. Novartis counters that, while the background risk methodology is widely accepted, Dr. Taylor did not satisfy the criteria of the methodology.

A reliable methodology must take into account the background risk of a specific disease, which is "the risk that everyone faces of suffering the same malady that a plaintiff claims without having exposure to the same toxin." *McClain*, 401 F.3d at 1243. As the Eleventh Circuit has explained,

> The background risk is not the risk posed by the chemical or drug at issue in the case. It is the risk a plaintiff and other members of the general public have of suffering the disease or injury that plaintiff alleges *without* exposure to the drug or chemical in question. The background risks include all those causes of a disease, whether known or unknown, excluding the drug or chemical in question.

Id. (emphasis in original). A failure to assess or identify the background risk of a disease is a "serious methodological deficiency" because, "[w]ithout a baseline, any incidence may be coincidence." *Chapman*, 766 F.3d at 1307–08 (internal citations omitted).

Ignoring available evidence about background risks may be fatal to an expert's general causation opinion. *Kilpatrick*, 613 F.3d at 1342 (finding that the expert impermissibly "ignored such background risks. While recognizing the existence of idiopathic (or unknown) causes of [the disease], he dismissed them by merely stating that the risk of idiopathic [disease] is essentially zero. The failure to take into account the potential for idiopathically occurring [disease] placed the reliability of [the expert's] conclusions into further doubt.").

Jones correctly points out that in *Chapman*, *McClain*, and *Kilpatrick*, unlike with Dr. Taylor's opinion, the experts altogether failed to assess the background risk of the relevant disease in question. Taylor Response, (Doc. 166–40) at 16. However, an *unreliable* application of a background risk methodology leads to the same result as a failure to consider the background risk at all: the expert's opinion will be excluded.

Novartis claims that Dr. Taylor's application of the methodology was flawed for five reasons: (1) Dr. Taylor ignored other estimates of background rates of AFFs;

(2) Dr. Taylor improperly re-categorized fractures described in a paper by Dr. Black; (3) Dr. Taylor improperly compared the lower bound of a Reclast rate confidence interval to a point estimate in another paper; (4) Dr. Taylor improperly used a one-tailed, rather than two-tailed, test to calculate the confidence interval; and (5) Dr. Taylor improperly included a spiral fracture in the Reclast-treated portion of his study.

b. *Dr. Taylor Ignored Other Background Rates*

Dr. Taylor based his opinion on a historical, or background, rate of .6 per 10,000 patient years, as set out in a paper by Dr. Feldstein. Taylor Response, (Doc. 166–40) at 9 (referencing A. Feldstein et al., *Incidence and Demography of Femur Fractures With and Without Atypical Fractures*, 27 J. Bone Miner Res. 997 (2012) (the "Feldstein Paper")). Jones claims that Dr. Taylor relied on this historical rate because the Feldstein Paper "used a large database with hundreds of thousands of patients (millions of patient years)" and "discusses other papers with different background rates." Taylor Response, (Doc. 166–40) at 9–10. Jones claims that Dr. Taylor also considered background rates of AFFs of .17 per 10,000 patient years[20] and .32 per 10,000 patient years,[21] both of which were smaller studies. *Id.* at 10.

However, Dr. Taylor's reliance on the results found in the Feldstein Paper conflicts with the findings of the 2010 and 2013 ASBMR Task Force Reports. The 2010 ASBMR Task Force Report [22] determined that "the incidence of atypical femoral fractures has come to medical attention principally in the setting of BP use and that *the incidence in the general population not exposed to BPs is unknown.*" The 2010 ASBMR Report, (Doc. 117–9) at 4 (emphasis added). The more recent 2013 ASBMR Report noted that every study of AFFs included patients who had not been treated with bisphosphonates, "suggesting that the 'background rate' of AFF in osteoporosis patients is not zero." [23] (Doc. 117–1) at 15.

Further, Jones admits that the more recent ASBMR Report found that "the historical rate was still unknown," yet she fails to explain why Dr. Taylor's use of the Feldstein Paper background rate is reliable when other reports have found that the background rate is still unknown or unclear. Taylor Response, (Doc. 166–40) at 16. Jones conclusorily states that it is "reasonable and reliable" for Dr. Taylor to use

20. This rate is derived from B. Edwards et al., *Bisphosphonates and Nonhealing Femoral Fractures: Analysis of the FDA Adverse Event Reporting System (FAERS) and International Safety Efforts,* J. Bone Joint Surg. Am. 2013 (the ''Edwards article,'' Doc. 139–9).

21. This rate is derived from R. Meier et al., *Increasing Occurrence of Atypical Femoral Fractures Associated with Bisphosphonates Use,* 172 ARCHIVES OF INTERNAL MED. E1, E6 (2012)(the ''Meier article,'' Doc. 139–10).

22. Shane E, et al., Atypical Subtrochanteric and Diaphyseal Femoral Fractures: Report of a Task Force of the American Society for Bone and Mineral Research, J. Bone Miner Res. 2010 (''the 2010 ASBMR Report''). Reports that linked long-term use of BPS with atypical femur fractures led the ASBMR to appoint a task force of 28 multidisciplinary experts to address key questions related to the problem. *Id.* at 2. The task force reviewed relevant articles from January 1990 to April 2010 in forming their analysis. *Id.* at 3.

23. Shane E, et al., Atypical Subtrochanteric and Diaphyseal Femoral Fractures: Second Report of a Task Force of the American Society for Bone and Mineral Research, J. Bone Miner Res. 2013 (''the 2013 ASBMR Report'')(Doc. 117–1) at 15. The 2013 ASBMR Report reviewed studies on AFFs that were published since 2010. *Id.*

the Feldstein Paper rate, but she fails to provide any support for this assertion. *Id.*

Dr. Taylor further conceded in his deposition that he did not come across any papers published prior to the Feldstein Paper that identified a background rate for AFFs, partly because he "did not extensively look for other articles" and apparently relied only on the articles and rates cited in the Feldstein Paper. Taylor Deposition, (Doc. 125–16) at 21(77:25–78:16). He also admitted that he did not conduct a search for any relevant articles published after the Feldstein Paper and provided no explanation as to why he chose not to do so. *Id.* at 21(78:23–25).

If any step in Dr. Taylor's methodology is flawed, it is a fatal defect under *Daubert*, as "*any* step that renders the analysis unreliable under the *Daubert factors renders the expert's testimony inadmissible.*" *McClain*, 401 F.3d at 1245 (emphasis in original, internal citations omitted). Dr. Taylor's failure to substantiate his use of the Feldstein Paper rate, or explain why he did not review other articles to determine that his use of that rate was reliable, draws the admissibility of his background risk methodology into doubt.

c. *Dr. Taylor Conducted an Improper Re–Analysis of Data in Dr. Black's 2010 Analysis*

Novartis also takes issue with several other aspects of Dr. Taylor's methodology. In particular, Novartis critiques Dr. Taylor's re-analysis of data originally published in an article by Dr. Dennis Black in the *New England Journal of Medicine* in 2010. Taylor Brief, (Doc. 125–19) at 15–17. Dr. Black co-authored a report that re-analyzed the results of three large, randomized bisphosphonate trials, including Novartis' trial H2301, for evidence of atypia in hip and femur fractures. *Id.* at 11 (citing Black DM, et al., *Bisphosphonates and Fractures of the Subtrochanteric or Diaphyseal Femur,* N. Engl. J. Med. 362: 1761–71, 1768 (2010)) (the "Black 2010 Analysis", Doc. 117–12). Dr. Taylor's background risk methodology relies on the data and findings of Dr. Black's analysis, so in order for Dr. Taylor's opinions to be considered reliable, his re-analysis of Dr. Black's data and findings must also be reliable.

Jones does not dispute Novartis' description of Dr. Black as a world-renowned statistician and epidemiologist with over twenty years of experience investigating osteoporosis and treatment therapies. Taylor Brief, (Doc. 125–19) at 11. Jones further does not dispute Novartis' summary of Dr. Black's analysis. Novartis states that Dr. Black's report concluded:

> There was no statistically significant difference between the occurrence of subtrochanteric and diaphyseal femur fractures in the Reclast-treated population and the placebo-treated population. Dr. Black was not able to fully assess other indicia of atypia, such as non-comminution, and therefore expressly did not determine whether any of these fractures were, in fact, AFFs.

Id. at 11–12 (emphasis added).

Novartis argues that Dr. Taylor improperly took the six femur fractures that Dr. Black identified in his analysis and reclassified three of those fractures as AFFs, despite lacking the medical background or expertise to do so. Taylor Brief, (Doc. 125–19) at 15–17; Taylor Reply, (Doc. 177) at 11–12.

Dr. Black's analysis states that "in all three studies, atypical fractures could not be fully assessed, since radiographs were not generally available." The Black 2010 Analysis, (Doc. 117–12) at 9. Dr. Black's analysis further explains,

> In the three studies we reviewed, even among women with up to 10 years of

> bisphosphonate exposure, the risk of fracture of the subtrochanteric or diaphyseal femur ranged from one to six cases per 10,000 patient-years. If we had been able to assess atypical characteristics (e.g., cortical thickness and fracture morphology) and limit our consideration to atypical fractures, we probably would have excluded some additional events; this would have further reduced the risk.

Id. (emphasis added). Dr. Black's analysis makes clear that he was not able to, and did not, analyze the prevalence of AFFs.

Dr. Taylor admitted at deposition that he is not a medical doctor and does not have any medical expertise that would allow him to evaluate whether or not a fracture is atypical. Taylor Deposition, (Doc. 125–16) at 31(118:14–20). He further admitted that he took Dr. Black's assessment, added Dr. Black's statements on whether there was a presence of trauma associated with those fractures, and concluded that three of the fractures were in fact atypical femoral fractures. *Id.* at 31–33(120:13–125:19). Upon further questioning, Dr. Taylor admitted,

> Q: Okay, its possible, is it not, that all of those fractures are subtrochanteric or diaphyseal and still don't qualify as atypical femur fractures, isn't it?
>
> A: That I don't know.
>
> Q: You don't know, but you looked at the table on trauma that's in [Dr. Black's] paper and you made the decision that they did, those three did qualify as atypical femoral fractures, but the two in the placebo did not, isn't that correct?
>
> A: That is correct, based on the presence or absence of trauma.

Id. at 125:8–19. Dr. Taylor's deposition testimony reveals that he only compared each of the fractures in Dr. Black's analysis with the presence of trauma associated with each incident. However, trauma is only one of the five major features of an atypical femoral fracture that are required to satisfy the case definition of an AFF.[24] Neither Dr. Taylor's expert report nor his deposition testimony discusses whether he found evidence of the other four necessary major features in forming his conclusion that three of the femur fractures identified by Dr. Black were AFFs.

Novartis argues that, as a statistician, Dr. Taylor is not qualified to make a determination that associations between fractures and trauma means that some fractures do not meet the case definition for AFFs, while other fractures do. Novartis further argues that, even if Dr. Taylor were qualified, his methodology is flawed because he only relied on the presence or absence of trauma, rather than all five major features of an AFF, in forming his conclusions that certain fractures in Dr. Black's analysis were AFFs.

Jones does not respond to this line of criticism. Instead, she merely distinguishes Dr. Black's analysis from Dr. Taylor's by stating that he relied on a different meth-

24. The 2010 ASBMR Report states that evidence of all five major features of an atypical femoral fracture is required to satisfy the AFF case definition. (Doc. 117–9) at 4. The five major features required to find an AFF are (1) location "anywhere along the femur from just distal to the lesser trochanter to just proximal to the supracondylar flare"; (2) association "with no trauma or minimal trauma, as in a fall from a standing height or less"; (3) "transverse or short oblique configuration"; (4) Non-comminution; and (5) "Complete fractures extend through both cortices and may be associated with a medial spike; incomplete fractures involve only the lateral cortex." *Id.* The 2013 ASBMR Report slightly altered these mandatory major features in the AFF case definition by relaxing the "non-comminution" factor to include "minimal comminution" and adding a sixth major requirement that there be a periosteal stress reaction at the fracture site. (Doc. 117–1) at 2.

odology and had a different object of his analysis. Taylor Response, (Doc. 166–40) at 17–18. Her Response also claims that there are approximately fifty published studies showing a statistically significant AFF association with bisphosphonate use, but she does not specifically cite or reference the findings of any of these studies. *Id.* at 18. She merely concludes that Dr. Taylor's re-analysis is sound and any critique of his methodology should be reserved for cross-examination. *Id.*

Dr. Taylor's re-analysis of Dr. Black's analysis meets the same fate as that of the expert in *Perry v. United States*, 755 F.2d 888 (11th Cir. 1985). In *Perry*, the expert re-diagnosed a number of cases in the data collection that other doctors had diagnosed differently in order to present his evidence of a statistical relationship between a disease and a vaccine. *Id.* at 891. The Eleventh Circuit affirmed the district court's exclusion of the expert's testimony because the expert reached a conclusion as to the connection between the disease and the vaccine "before commencing his research . . . a scientist who has a formed opinion as to the answer he is going to find before he even begins his research may be less objective than he needs to be in order to produce reliable scientific results." *Id.* at 892.

In *Jack v. Wellcome, Inc.*, 239 F.Supp.2d 1308 (N.D. Ga. 2002), the court similarly excluded an expert's testimony as unreliable because it was not supported

> by sufficient facts or data. Instead, his conclusion is more properly classified as a theory. This theory he derived from a reclassification and analysis of data from prior studies. His methodology, however, is far too speculative for the court to allow. [The expert] has reclassified data based on his belief that certain events should properly be classified under different categories than those the original researchers chose. He has done so largely without review of any facts specific to any specific patient or event. Rather, he has essentially hypothesized a possible or probable scenario whereby the reclassification is justified. This post hoc approach is certainly not reliable absent a particularized reason for the individual reclassification . . . he did not rely on the raw data from the previous studies.

Id. at 1316 (emphasis added).

Jones does not explain *why* Dr. Taylor is qualified to determine that certain of the fractures in Dr. Black's analysis were AFFs, when Dr. Black's analysis itself expressly denied making such a finding. Jones also does not explain *why* finding an absence of *trauma* in relation to a fracture is sufficient to determine that a fracture meets all five factors in the case definition of an AFF. Additionally, like in *Jack*, Dr. Taylor has not claimed he relied on the raw data from Dr. Black's analysis; instead, he performed a *post hoc* analysis based on the evidence as presented by Dr. Black. Dr. Taylor concluded that Dr. Black's data showed AFFs and worked backwards from that step without sufficiently demonstrating that these fractures met the appropriate case definition, so his re-analysis is unreliable. Because his re-analysis formed the basis of his background risk methodology, *see* Taylor Response, (Doc. 166–40) at 17, his methodology is independently unreliable for this reason.

d. *Dr. Taylor's Inclusion of a Spiral Fracture From Dr. Black's Analysis Was Improper*

Novartis also alleges that Dr. Taylor improperly failed to exclude a spiral fracture from his re-analysis of the Black 2010 Report's findings. Novartis claims that one of the three fractures that Dr. Taylor labeled as an AFF was actually a spiral fracture, which is expressly excluded from

the AFF case definition. Taylor Brief, (Doc. 125–19) at 21. Novartis argues that because these spiral fractures are excluded from the AFF definition, the spiral fracture identified by Dr. Black should not have been considered an AFF by Dr. Taylor in his re-analysis. Taylor Brief, (Doc. 125–19) at 12–13, 21–22.

The 2010 ASBMR Report explicitly excludes "intertrochanteric fractures with spiral subtrochanteric extension" from the case definition of AFFs. *See* 2010 ASBMR Report, (Doc. 117–9) at 4. Dr. Taylor's report re-summarizes the results from the H2301 study that were analyzed and reported in the Black 2010 Analysis. Taylor Report, (Doc. 125–17) at 4. Dr. Taylor states that the Black 2010 Analysis reported six cases of fractures that were the result of 5 events, as one patient broke both hips simultaneously. *Id.* After determining which of these five events was "associated with no or minimal trauma, as in a fall from a standing height or less," [25] Dr. Taylor concluded that the three fractures in the treatment group receiving Zoledronic acid were Atypical Femoral Fractures. *Id.* at 3–4.

However, in his deposition, Dr. Taylor admitted that he did not know whether a spiral fracture was disqualified from being labeled an AFF and conceded that the presence of only two AFFs in the treatment group that received Zoledronic acid, rather than three, would alter his analysis:

> Q: [Reading from Dr. Black's 2010 analysis of the three fractures identified in the treated group] In three women, receiving Zoledronic acid, one had simultaneous fractures of both femoral shaft[s]. One had a transverse fracture but no beaking and no focal or generalized cortical thickening on radiography, and one had a spiral fracture on radiography, although the morphologic features were not described as atypical in case reports.
>
> Do you see that?
>
> A: Uh-huh.
>
> Q: Do you know whether a spiral fracture disqualifies a fracture from being considered atypical under the minor—major feature requiring transverse or short oblique configuration?
>
> A: No, I don't.
>
> Q: So you don't know whether that's actually an—the fact that it's spiral disqualifies it as an atypical femur fracture or not, do you?
>
> A: No, I don't.
>
> Q: We'd have to rely on a doctor to figure that out, wouldn't we?
>
> Ms. Taylor: We object to that.
>
> Mr. Johnston: Q: A medical doctor.
>
> Ms. Taylor: We object.
>
> The Witness: Yes.
>
> Mr. Johnston: Q: Your position is that three AFFs in the Reclast arm of 2301 compared to the single point rate in the Feldstein article results in a statistically significant differen[ce] in AFFs and Reclast treated patients, right?
>
> A: Yes.
>
> Q: What if there were only two patients in the AFF side of the equation, two out of 11,580?
>
> A: That would alter my analysis.
>
> . . . .
>
> A: Certainly if there were only two fractures that qualified as atypical femur fractures in the Reclast treated population, the lower bound of your number would be less than 7.1 per 100,000 patient years, wouldn't it?

25. Association with no trauma or minimal trauma is only one of five major features of an AFF. Evidence of all five major features is required to satisfy the AFF case definition. (Doc. 117–9) at 4.

A. Yes, it would lower the lower bound.

Q: And it may in fact lower the lower bound below Feldstein's rate of 5.9 events per 100,000 patient years, couldn't it?

A. If it lowers it, it may.

Taylor Deposition, (Doc. 125–16) at 34–35(131:8–133:16) (citing Black 2010 Analysis, (Doc. 117–12) at 6–7).

Dr. Taylor's deposition testimony reveals that he failed to determine whether the fractures identified in the 2010 Black Analysis met *all five* of the major features associated with the case definition of an AFF. His testimony also reveals his unfamiliarity with the need to differentiate spiral fractures from AFFs. Dr. Taylor's report shows that he erroneously relied on the spiral fracture in the 2010 Black Analysis in forming his opinion, and his deposition testimony demonstrates that, had the spiral fracture been excluded, his analysis would change. Dr. Taylor's inclusion of a spiral fracture in his analysis, in contravention of the AFF case definition in the 2010 ASBMR Report, renders his methodology unreliable for this independent reason.

e. *Dr. Taylor's Comparison of the Lower Bound of the Confidence Interval to the Feldstein Point Estimate Was Improper*

Novartis also believes that Dr. Taylor improperly compared the *lower bound* of the confidence interval to the point estimate in the Feldstein Paper. Taylor Brief, (Doc. 125–19) at 17–19. Jones counters that Dr. Taylor's comparison of the lower bound of the confidence interval was "reasonable and reliable." Taylor Response, (Doc. 166–40) at 19.

Both parties agree that a point estimate and a confidence interval are both statistical estimates. A point estimate is "an estimate of the value of a quantity expressed as a single number." David H. Kaye & David A. Freedman, "Reference Guide on Statistics," REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 284, 292 (3d ed. 2011) ("2011 Reference Guide on Statistics"). A confidence interval, in comparison, is an

> estimate, expressed as a range, for a parameter. For estimates such as averages or rates computed from large samples, a 95% confidence interval is the range from about two standard errors below to two standard errors above the estimate. Intervals obtained this way cover the true value about 95% of the time, and 95% is the confidence level or the confidence coefficient.

Id. at 284–85; *see also Siharath v. Sandoz Pharms. Corp.*, 131 F.Supp.2d 1347, 1357 (N.D. Ga. 2001), *aff'd sub nom. Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194 (11th Cir. 2002) (citing to an older version of the Reference Guide) (defining a confidence interval as a "range of values calculated from the results of a study, within which the true value is likely to fall; the width of the interval reflects random error."). Novartis also describes the confidence interval as the "full range of values that the true background rate can take." Taylor Brief, (Doc. 125–19) at 17.[26,27]

26. As the 2011 Reference Guide on Statistics further explains, "a confidence interval for the population average is centered at the sample average; the desired confidence level is obtained by adding and subtracting a suitable multiple of the standard error. Statisticians who say that the population average falls within 1 standard error of the average will be correct about 68% of the time. Those who say 'within 2 standard errors' will be correct about 95% of the time, and those who say 'within 3 standard errors' will be correct about 99.7% of the time, and so forth." *Id.* at 244.

27. Additionally, the 2011 Reference Guide on Statistics explains, "[t]he main point is that an estimate based on a sample will differ

In his analysis, Dr. Taylor opined that the lack of overlap between the Feldstein Paper point estimate (0.60) and his calculated rate of the lower confidence interval (0.71) meant that there was a statistically significant difference in the number of AFFs in Reclast-treated patients compared to the background rate. Taylor Brief, (Doc. 125–19) at 17; Taylor Response, (Doc. 166–40) at 13. The upper bound of the Feldstein Paper's confidence interval was 0.74, however, and the Feldstein Paper's confidence interval was 95% (0.46–0.74). (Doc. 125–19) at 17. Dr. Taylor testified as follows at deposition regarding point estimates and confidence intervals:

> Q: Why do statisticians use confidence intervals instead of point estimates? Why do you do that?
>
> A: They often report them both in combination, but its [sic] basically with the point estimate you have no idea how precise it is, and so the confidence interval helps indicate how precise the estimate is.

Taylor Deposition, (Doc. 125–16) at 22(84:4–9). Dr. Taylor further testified,

> Q: And so, given that, with the overlapping confidence intervals, you can't say that the rate of AFFs in the Reclast treated patients is statistically significant different than the background rate as represented by Feldstein if you take into account the confidence interval in Feldstein, can you?
>
> A: Using this approach of the confidence interval in Feldstein and the estimate that I have that falls within the interval so I can't—using this analysis declare that it's statistically different, no.
>
> Q: So you can find that they're statistically different using this difference analysis, its [sic] not the analysis you use, but this different analysis, you would not conclude there's a statistically significant difference, correct?
>
> A: No. I agree.

Id. at 26 (97:21–25 to 98:1–11) (emphasis added). Novartis argues that Dr. Taylor's methodology in his report goes against his own testimony at deposition by unreliably omitting the full confidence interval and relying only on the lower bound of the confidence interval. Taylor Brief, (Doc. 125–19) at 19. Novartis believes that Dr. Taylor should have taken the full confidence interval into consideration and that his failure to do so is in contravention of standard practice for statisticians. *Id.* at 18; Taylor Reply, (Doc. 177) at 13.

Aside from providing the court with definitions for point estimates and confidence intervals, Jones provides the court with no support for her proposition that Dr. Taylor's comparison was reasonable and reliable. *See id* at 19. She does not explain *why* Dr. Taylor's analysis was both reasonable and reliable and cites to no authority, other than Dr. Taylor's own deposition, to support this claim. Jones's summary conclusion that Dr. Taylor has offered reliable evidence is not sufficient to demonstrate his reliability to the court. Yet again, Jones asserts that if Novartis disagrees with the reliability of Dr. Taylor's testimony, its arguments go only to the weight of the

from the exact population value, because of random error. The standard error gives the likely size of the random error. If the standard error is small, random error probably has little effect. If the standard error is large, the estimate may be seriously wrong. Confidence intervals are a technical refinement. . . .'' *Id.* at 246. The Reference Guide also explains that courts have often misinterpreted the confidence level as the chance that repeated estimates will fall into the confidence interval. *Id.* at 247. This interpretation is incorrect; rather, the confidence level ''indicates the percentage of the time that intervals from repeated samples would cover the true value.'' *Id.*

evidence and should be properly argued during cross-examination after Dr. Taylor has been permitted to testify.

Throughout her Response, Jones continually relies on *In re Chantix (Varenicline) Prods. Liab. Litig.*, 889 F.Supp.2d 1272, 1282 (N.D. Ala. 2012) (Johnson, J.), where the district court found that the defendant's arguments to exclude plaintiff's expert went to the weight of his testimony rather than its admissibility. However, in *In re Chantix*, the court also found that "nothing inherent in the defendant's objections to [the expert's] methodology addresse[d] the reliability of his findings." *Id.* Here, Novartis' objections go to the heart of the reliability of Dr. Taylor's testimony. Therefore, Jones's numerous citations to *In re Chantix* are not persuasive. If the expert's testimony is unreliable, it may not be presented to a jury at all.

Jones has failed to adequately demonstrate why Dr. Taylor's use of the lower bound of the confidence interval rather than the full confidence interval was appropriate. Therefore, Dr. Taylor's opinion is independently unreliable for this reason.

f. *Jones Has Failed To Demonstrate That Dr. Taylor's Use of a One–Tailed Rather Than Two–Tailed Test To Calculate the Confidence Interval Was Reliable*

Novartis also claims that Dr. Taylor's use of a one-tailed, rather than two-tailed, test to calculate the lower bound of the confidence interval deviated from both standard statistical practice and FDA guidance. Taylor Brief, (Doc. 125–19) at 19–21. Jones counters that his use of a one-tailed test was appropriate, given that Dr. Taylor's objective was to compare the historical rate of AFF to the rate of AFF in the Reclast-treated group. Taylor Response, (Doc. 166–40) at 20–22.

A one-sided, or one-tailed, hypothesis "[e]xcludes the possibility that a parameter could be, for example, less than the value asserted in the null hypothesis. A one-sided hypothesis leads to a one-sided (or one-tailed) test." 2011 Reference Guide on Statistics at 291. A two-sided, or two-tailed, hypothesis is an "alternative hypothesis asserting that the values of a parameter are different form—either greater than or less than—the value asserted in the null hypothesis. A two-sided alternative hypothesis suggests a two-sided (or two-tailed) test." *Id.* at 300. The terms "one-tailed" and "two-tailed" refer to the "tails or ends of the bell-shape curve, which represents in graph form a random normal distribution." *Palmer v. Shultz*, 815 F.2d 84, 93 (D.C. Cir. 1987) (internal quotations and citations omitted)(discussing whether reliance on a one-tailed or two-tailed test is appropriate in the context of a Title VII discrimination case).

Essentially, the two tests are two different ways of measuring probability. *Palmer*, 815 F.2d at 94; *see also Barrow v. Bristol–Myers Squibb*, No. 96–CV–689, 1998 WL 812318, at *23 n.217 (M.D. Fl. Oct. 29, 1998) ("Whether the study was one-tailed or two-tailed is important because it determines the way relative risk will be spread. In a two-tailed study, the risk is spread between two hypotheses, while in a one-tailed study, all risk is allocated to one hypothesis.").

A two-tailed test is more demanding than a one-tailed test because it

> requires greater departures from the expected numbers for a given level of statistical significance; this implies that a two-tailed test has a larger Type II error rate and less power than a one-tailed test with the same significance level. Since power and statistical significance are both desirable attributes, two-tailed tests should not be used where

> one-tailed tests are appropriate, especially if power is an issue.

Michael O. Finkelstein & Bruce Levin, "Testing Statistical Hypotheses," *Statistics for Lawyers* (2d ed. 2001) at 120–22 (Doc. 117–17) at 6. On the other hand,

> Many scientific researchers recommend two-tailed tests even if there are good reasons for assuming that the result will lie in one direction. The researcher who uses a one-tailed test is in a sense prejudging the results by ignoring the possibility that the experimental observation will not coincide with his prior views. The conservative investigator includes that possibility in reporting the rate of possible error. This routine calculation of significance levels, especially when there are many to report, is most often done with two-tailed tests. Large randomized clinical trials are always tested with two-tails.

Id. at 5. Secondary sources cited by both parties indicate to the court that, depending on the specific circumstances or the objective of the test, either a one-tailed or a two-tailed test may be appropriate.

Novartis argues that Dr. Taylor is not able to point to medical literature where only a one-tailed confidence interval was used. In his deposition, Dr. Taylor was asked,

> Q: And have you ever seen a medical paper that is published in the literature that only addressed a one-tailed confidence interval?
>
> A: I don't recall that I have, but the objective here is different than what generally is [sic] literature reporting estimates of which a two-sided is appropriate for, whereas we're trying to make a determination as to whether the clinical trial data has evidence in it. That's a different objective.

Taylor Deposition, (Doc. 125–16) at 28(107:14–22). He further explained,

> A: So in statistics, the decision to do a one sided or two sided interval is dependent upon the objective of the analysis. If it's a report where you're just estimating rates and reporting information and odds ratio, a two sided approach is best for just an estimate, but when you're trying to compare numbers, specifically a number in one standard whether its higher than it or lower than it, it makes sense to use the one sided that's appropriate for the comparison you are making.

Id. at 28 (108:8–16). Jones argues that a one-tailed test was appropriate in this case because "the test is only interested in the one-tail (i.e. the lower tail). If the historical rate is lower than the confidence interval, then it will necessarily be lower than the higher confidence interval." Taylor Response, (Doc. 116–40) at 21. Novartis believes that the assumptions underlying Dr. Taylor's methodology not only contradict Dr. Taylor's own deposition testimony but also show that Dr. Taylor impermissibly allowed bias into his analysis. Taylor Brief, (Doc. 125–19) at 15.

As the proponent of Dr. Taylor's testimony, Jones bears the burden under Rule 702 of establishing the qualifications, reliability, and helpfulness of testimony. *Frazier*, 387 F.3d at 1260. Jones's briefing does not help clarify why Dr. Taylor's use of a one-tailed test was reliable, and Dr. Taylor may confuse the jury by providing testimony on the subject. Therefore, Dr. Taylor's testimony is independently unreliable because Jones is not able to establish that his use of a one-tailed, rather than two-tailed, test was appropriate.

g. *Dr. Taylor's Opinion on Novartis' Clinical Trials (H2301 and L2310) Should Be Excluded*

[29] In his expert report, Dr. Taylor also opines that Novartis' two clinical tri-

als, H2301 and L2310, do not demonstrate the safety of Reclast relative to AFFs because the studies were "underpowered for definitive conclusions" and Novartis "did not collect all the necessary information to classify many adverse events as Atypical Femur Fractures." Taylor Report, (Doc. 125–17) at 2. Novartis believes that these opinions should be excluded because the trials were approved and deemed appropriate by the FDA. Taylor Brief, (Doc. 125–19) at 17–18. Novartis also argues that Dr. Taylor has limited experience with clinical trials and therefore does not have the expertise to offer this opinion. *Id.* at 5–6.

As above discussed, Dr. Taylor does not have the expertise to offer opinions on compliance with FDA regulatory standards. Additionally, Dr. Taylor does not indicate in what way(s) either trial fails to meet the safety standards established by the FDA. Further, Dr. Taylor admitted during his deposition that clinical trials may never be adequately powered to find some sufficiently rare adverse events, which can only be detected once the medicine is released into the general population after being approved for marketing. Taylor Deposition, (Doc. 125–16) at 9(29:23–30:8). Therefore, Dr. Taylor's opinions on clinical trials H2301 and L2310 are not reliable and will not assist the trier of fact. They will be excluded.

h. *Dr. Taylor's Opinion That Novartis Provided the FDA With Incomplete Data Should Be Excluded*

[30] In his Report, Dr. Taylor claims that Novartis provided incomplete and biased data to the FDA. He opines that in over a third of the adverse event reports given to the FDA in 2008, either no mechanism was reported or the event detail was not provided. Taylor Report, (Doc. 125–17) at 6–7; *see* Taylor Deposition, (Doc. 125–16) at 51(198:20–23) ("I believe [Novartis] should have collected, and at least ask the question as to what were the events that led up to the fracture. It's just a co-variant that should be included in this type of study."). Yet Dr. Taylor admits, conversely, that he is not attempting to offer "an opinion in this case that Novartis used an inadequate methodology to respond to the FDA in 2008." *Id.* at 53(206:8–11).

As stated above, Dr. Taylor is not qualified to and will not be permitted to opine on the adequacy of Novartis' communications with the FDA, including in its 2008 Response to Request for Information. *See* (Doc. 191–5). Even assuming that Dr. Taylor has the expertise to opine on the sufficiency of the statistical data provided by Novartis to the FDA, his deposition testimony reveals that he did not review the protocol of Novartis' clinical trial before determining whether or not the information provided to the FDA was incomplete.

For example, when asked why he thought that information on trauma was not included in the clinical trial, Dr. Taylor resorts to speculation:

> Q: If an investigator fails to report trauma, what is the clinical sponsor supposed to do?
>
> A: I guess it wasn't in the study design. The study—clinical trials study director shouldn't let it get to that point as part of the study design.
>
> Q: Did you look at the efficacy end point evaluation for fractures and what the design there was ?
>
> A: No, I did not.
>
> . . . .
>
> Q: Let me ask you another question. Did you look at the—did you look at the case report forms for the adverse reactions to see what efforts Novartis had made to try to obtain the information on trauma?
>
> A: No, I did not look at those.

Q: Those weren't provided to you?

A: No.

Q: So it's possible that Novartis tried to get that information and that effort is documented, but they never could get it, isn't that correct?

A: That's correct.

Taylor Deposition, (Doc. 125–16) at 51–52(200:16–23 and 204:13–23) (emphasis added).

Dr. Taylor's testimony demonstrates that, having not been provided with all necessary information himself, he is not qualified to form an opinion on Novartis' alleged failure to provide the FDA with complete data. It may in fact be the case that Novartis failed to provide the FDA in 2008 all the information in its possession. However, Dr. Taylor is not qualified to opine on this topic since he failed to review the underlying case reports and is not a regulatory expert. His opinion that Novartis provided incomplete data to the FDA will also be excluded.

4. Conclusion as to the Admissibility of Dr. Taylor's Testimony

Dr. Taylor lacks the expertise to offer the general causation opinion he intends to offer, and he did not employ a reliable methodology in forming his opinion. Therefore, Dr. Taylor's testimony is due to be **EXCLUDED** in full, and the Motion To Strike his testimony (doc. 116) is due to be **GRANTED**.

D. Non–Retained Experts

Jones also offers the opinions of two non-retained experts, Dr. James Worthen and Dr. Timothy Mark Ricketts, into evidence. As neither Dr. Worthen nor Dr. Ricketts was specifically retained by Jones for the purposes of this litigation, neither doctor was required to provide a written report pursuant to Rule 26(a)(2)(B) of the Federal Rules of Civil Procedure.[28] Instead, pursuant to Rule 26(a)(2)(C), Jones was required to disclose (1) the subject matter on which Dr. Worthen and Dr. Rickets were expected to present evidence and (2) a summary of the facts and opinions to which they were expected to testify. FED. R. CIV. P. 26(a)(2)(C). These brief statements may be found in "Plaintiff's Expert Disclosures," which has been admitted into evidence. (Doc. 119–1).

Dr. Worthen was deposed on April 16, 2015 (doc. 119–4, the "Worthen Deposition"), and Dr. Ricketts was deposed on April 14, 2015 (doc. 119–5, the "Ricketts Deposition"). On August 15, 2016, Novartis filed a Motion To Strike the testimony of Dr. Worthen and Dr. Ricketts (doc. 118) and a brief in support of its Motion (doc. 119, the "Non-Retained Experts Brief"). On September 19, 2016, Jones filed a Response opposing Novartis' Motion To Strike. (Doc. 144, the "Non–Retained Experts Response"). On October 14, 2016, Novartis filed a reply brief in support of its Motion To Strike. (Doc. 181, the "Non–Retained Experts Reply").

For the following reasons, Novartis' Motion To Strike the testimony of Dr. Worthen and Dr. Ricketts is due to be **GRANTED** to the extent that either expert intends to offer an opinion on causation.

1. Dr. Worthen

a. Dr. Worthen's Qualifications

Dr. Worthen is a board-certified orthopaedic surgeon who has been continuously practicing orthopaedic surgery since 2005.

28. Rule 26(a)(2)(B) states as follows, "Unless otherwise stipulated or ordered by the court, this disclosure must be accompanied by a written report—prepared and signed by the witness—if the witness is one retained or specially employed to provide expert testimony in the case." FED. R. CIV. P. 26(a)(2)(B).

(Doc. 119–1) at 3, ("Plaintiff's Expert Disclosures"). He attended the University of Alabama Birmingham ("UAB") Medical School and completed his residency in orthopedic surgery at UAB. *Id.* Jones claims that Dr. Worthen has treated thousands of patients who suffered from femur fractures and has treated several patients who have been treated for osteoporosis with bisphosphonate drugs. *Id.*

On October 26, 2011, Dr. Worthen was on call at St. Vincent's Hospital when Jones arrived with a femoral fracture. Worthen Deposition, (Doc. 119–4) at 6 (20:1–9). Dr. Worthen performed surgery on both of Jones's femoral fractures. (Doc. 119–1) at 3.[29] Jones plans to offer Dr. Worthen to testify based on personal knowledge gained from his care and treatment of Jones, including his own examinations, diagnoses, and courses of treatment. *Id.* Dr. Worthen intends to opine that (1) the complete femoral fracture of Jones's right femur was an atypical femur fracture; (2) Reclast "probably caused" Jones's AFF in her right femur; (3) the stress fracture of Jones's left femur "was caused by the infused Reclast following a history of bisphosphonate use." *Id.* at 3–4.

b. *Dr. Worthen Is not Qualified To Offer an Expert Opinion on Causation*

[31] Novartis argues that Dr. Worthen is not qualified to offer an expert opinion about the *cause* of Jones's femoral fractures. Novartis claims that this court's previous decision in *Harvey v. Novartis Pharms. Corp.*, 895 F.Supp.2d 1206 (N.D. Ala. 2012) provides very persuasive authority that Dr. Worthen is not qualified and his opinions are not reliable.

In *Harvey*, this court excluded causation testimony by the plaintiff's non-retained expert because he was not qualified to testify to the cause of the plaintiff's injury, and his attempt to rule out alternative competing explanations for plaintiff's injury using a differential diagnosis was not reliable. *Id.* at 1212–1213. Even though the surgeon in *Harvey* was purportedly aware of the relationship between osteonecrosis and BP use and had extensive surgical training, he had no practical experience in identifying the *causes* of that type of injury and testified that he *assumed* that BP use had caused the plaintiff's injury. *Id.* at 1212; *see id.* at 1211 ("[The surgeon] testified that he does not conduct medical or scientific research, has never researched osteonecrosis of the jaw, has never researched bisphosphonates, has never published or submitted a paper on either osteonecrosis of the jaw or bisphosphonates, and has never taught on either subject."). As the court explained, "the issue before the court is not *if* Harvey had osteonecrosis of the jaw, but what *caused* her to have it.") *Id.* at 1212 (emphasis in original).

Jones has understandably attempted to distinguish this court's opinion in *Harvey* from this litigation, but her attempts fall short of the mark. Like in *Harvey*, Dr. Worthen has little expertise in determining the cause of AFF. In his deposition, Dr. Worthen testified that prior to treating Jones, he had never made any presentations or conducted any research on AFFs. Worthen Deposition, (Doc. 119–4) at 26(99:19–100:2). Similar to the expert in *Harvey*, Dr. Worthen has never published or submitted any academic publications on BPs, and he is not an endocrinologist. *Id.* at 25(94:14–95:6). Dr. Worthen further testified that he has never conducted and is

29. The first surgery was performed on October 27, 2011. (Doc. 144) at 4. She subsequently experienced a second femoral fracture, *id.* at 5, and Dr. Worthen operated on that second fracture on February 10, 2012. *Id.*

not even aware of a study that evaluated the rate of AFFs in patients who received Reclast to treat osteoporosis. *Id.* at 25(95:7–12).

Dr. Worthen is not a member of the ASBMR and has not read either the 2010 or the 2013 ASBMR Task Force's reports that discuss whether there is a correlation between BP use and AFFs. *Id.* at 29(110:11–111:23); *see id.* at 29(112:13–21) ("[Y]ou know, I obviously, didn't spend the time doing the—doing the research. And—and—and there are some prominent names on the list that are part of this task force. There—you know, from a causal association, yes, we haven't—I guess, none of the articles that I was—have seen claim that they've claimed a causal association.").

As this court has previously concluded, "[e]xperience in a particular field is not enough to qualify an expert; the expert must have experience with the issue before the court." *Harvey*, 895 F.Supp.2d at 1209. Dr. Worthen's education, training, and experience do not qualify him to testify regarding the causes of Ms. Jones's femoral fractures. Additionally, as explained below, because Dr. Worthen failed to perform a reliable differential diagnosis, his testimony is independently due to be excluded because it is not sufficiently reliable.

c. *Dr. Worthen Does not Employ a Reliable Differential Diagnosis Methodology*

Dr. Worthen asserts that his causation opinion was reliably based on a differential diagnosis methodology. Worthen Deposition, (Doc. 119–4) at 12 (42:10–13). Novartis argues that Dr. Worthen's differential diagnosis is unreliable because he did not rule out other potential causes of Jones's injury; he did not have access to her full medical history and records; and he did not sufficiently establish the existence of general causation required in order to render his differential diagnosis reliable.

A differential diagnosis is "accomplished by determining the possible causes for the patient's symptoms and then eliminating each of these potential causes until reaching one that cannot be ruled out or determining which of those that cannot be excluded is the most likely." *Guinn*, 602 F.3d at 1253 (11th Cir. 2010) (citing *Westberry v. Gislaved Gummi AB*, 178 F.3d 257, 262 (4th Cir. 1999)).

The Eleventh Circuit has specifically addressed the reliability of differential diagnoses. *See Guinn*, 602 F.3d at 1253; *see also Kilpatrick*, 613 F.3d at 1342–43; *McClain*, 401 F.3d at 1252–53. In *Guinn*, the Eleventh Circuit explained that a reliable differential diagnosis has two steps. 602 F.3d at 1253. First, the expert must identify and consider the factors which could be the "sole cause of the plaintiff's injury." *Id.* Second, the expert "must provide a reasonable explanation" for his conclusion that the other potential causes identified in step one are not the sole cause of the plaintiff's injury. *Id.* A court must examine for itself whether the expert properly considered other potential causes for the plaintiff's injury and properly excluded them. *Id.*

i. *Dr. Worthen Failed To Reliably Rule out Jones's Steroid Use and Other Risk Factors as Causes of her Injuries*

[32] Dr. Worthen's differential diagnosis fails the Eleventh Circuit's reliability test. First, Dr. Worthen failed to rule out other conceivable causes of Jones's injury, which is undoubtedly partly due to the fact that he did not have full access to her medical records. He admitted at deposition that he did not have access to Jones's prior medical records, so his diagnosis relied upon Jones's self-reported medical history rather than a full and extensive review of her records. Worthen Deposition, (Doc.

119–4) at 25(96:2–16). He did not know, for example, the duration, extent, or timing of Jones's use of bisphosphonates other than Reclast. *Id.* at 26(97:7–19).

In *Haller v. AstraZeneca Pharms. LP*, 598 F.Supp.2d 1271 (M.D. Fla. 2009), the court excluded an expert's specific causation testimony as impermissibly "hurried, cursory, and incomplete" because he did not properly consider other factors that could have caused the plaintiff's injury. *Id.* at 1295–96. As the district court explained,

> [t]he Court accepts as a general proposition that a physician need not necessarily examine a patient, interview that patient, or speak with the patient's treating physician(s) in order to render opinions regarding diagnosis, prognosis, course of treatment and perhaps even causation. In other words, the Court does not deem it necessarily fatal that an expert medical witness has relied on medical records alone to reach a specific causation opinion. However, [the plaintiff's] particular circumstances expose the failings of applying *to this specific case* what might otherwise be considered a generally acceptable methodology ... [g]iven this background [of a pattern of weight gain and loss and a recent release from prison], simple logic and common sense dictated that [the expert] do more than merely "skim" [the plaintiff's] medical records and summaries to ascertain the cause of [the alleged injury].

Haller, 598 F.Supp.2d 1271, 1294–95 (M.D. Fla. 2009)(emphasis added).

Like in *Haller*, Dr. Worthen did not sufficiently determine whether there were pre-existing factors other than Jones's Reclast injections that could have caused the alleged injury, particularly Jones's previous high-dose steroid use to treat a different condition. When questioned at deposition about whether he considered Jones's steroid use, Dr. Worthen responded as follows:

> Q: Did you consider any other medications other than bisphosphonates?
>
> A: Yeah. So there's other—there's other medications that slow—that make bones weaker. The form of steroid use that she has had before, that's a consideration for fractures. But, usually, with steroid use, they're more associated with the typical osteopenic fractures or osteoporosis fractures, not with atypical femur fractures.
>
> Q: So, what methodology did you use to rule out steroid use, then, as a potential cause?
>
> A: It being an atypical femur fracture.

Worthen Deposition, (Doc. 119–4) at 32(124:1–16). However, he also testified that "you can't rule [steroid use] out" as a possible cause of an atypical fracture. *Id.* at 33(126:14–127:2). Dr. Worthen's deposition testimony on his exclusion of steroid use as a potential cause is circular, self-contradictory, and would likely be confusing to a jury.

Jones had a number of other risk factors, including age and postmenopausal status, and Dr. Worthen's testimony does not demonstrate that he reliably ruled out these other factors, or even if he was aware of their existence. Dr. Traylor, the rheumatologist who first prescribed Reclast to Jones to treat her osteoporosis, stated that she had pre-existing "persistent osteoporotic T-scores" and continued to exhibit "persistent osteoporosis" at the time of her third infusion of Reclast. (Doc. 119–2) at 25(95:10–23). Additionally, Dr. Traylor testified that Jones was diagnosed with dorsal kyphosis as of January 2009, prior to her first Reclast injection, which is a "sign" of " compression fractures that are unrecognized." *Id.* at 29(112:9–20). Regardless of whether Dr. Worthen was aware of these pre-existing conditions

based on the medical history he was provided by Jones, he failed to rule out these alternative causes.

Because Dr. Worthen never sufficiently explained why other potential causes, such as Jones's steroid use, could not have caused her injury, his opinion that Reclast caused Jones's femoral fractures amounts to mere conjecture and speculation. Under *Guinn*, Dr. Worthen's failure to adequately and reasonably explain why other factors could not have contributed to Jones's injury renders his differential diagnosis not sufficiently reliable. 602 F.3d at 1253. Therefore, his specific causation opinion is excluded as unreliable.

ii. *Without a Reliable General Causation Opinion, a Differential Diagnosis Methodology Is Unreliable*

The Eleventh Circuit has previously explained that if no expert can offer a reliable general causation opinion, it would be unreliable for an expert to use a differential diagnosis to prove specific causation. *See McClain*, 401 F.3d at 1253 ("A valid differential diagnosis, however, only satisfies a *Daubert* analysis if the expert can show the general toxicity of the drug by reliable methods."). The Eleventh Circuit concluded that, because the medical articles and analogies the experts relied on were not sufficient to establish general causation, "[i]n the absence of such a foundation for a differential diagnosis analysis, a differential diagnosis generally may not serve as a reliable basis for an expert opinion on causation in a toxic tort case." *Id; see also McClain*, 401 F.3d at 1253 ("[A]n expert does not establish the reliability of his techniques or the validity of his conclusions simply by claiming that he performed a differential diagnosis on a patient.").

Dr. Worthen, who has not conducted research on BPs, does not attempt to provide a general causation opinion himself. In his deposition, Dr. Worthen also admitted he had not read any medical literature where the author claimed to have found a causal association between BP use and AFFs. Worthen Deposition, (Doc. 119–4) at 29(112:18–21). Jones's assertion that Dr. Worthen's specific causation opinion is reliable because it is "based on the information provided by and generally accepted in the scientific community," (doc. 144) at 21, mischaracterizes the scientific consensus and fails to establish the general toxicity of Reclast.

The court has already ruled that Dr. Hinshaw's general causation opinion is based on unreliable methodology, and the general causation opinion of Jones's alternative expert, Dr. Taylor, has also been excluded. Dr. Parisian has also been excluded from opining on causation or causal association. Without the foundation of a general causation opinion, Dr. Worthen's testimony is both unreliable and irrelevant. *See Rink*, 400 F.3d at 1294 (affirming the district court's exclusion of a treating physician as irrelevant because the doctor relied on foundational testimony that the court determined was unreliable); *Allison v. McGhan Med. Corp.*, 184 F.3d 1300, 1320 (11th Cir. 1999) (affirming exclusion of expert witness on relevance grounds because two other experts were excluded that were crucial to the expert's relevance). Therefore, Dr. Worthen's differential diagnosis is unreliable and irrelevant for this independent reason, and his specific causation opinion will be excluded.

2. Dr. Ricketts

a. *Dr. Ricketts's Qualifications*

Dr. Ricketts is an internist and general practitioner who is board certified in internal medicine. Plaintiff's Expert Disclosures, (Doc. 119–1) at 5. He attended UAB Medical School and completed a residency and internship in internal medicine. *Id.* Dr.

Ricketts has provided Ms. Jones with medical care since 2004. (Doc. 119–1) at 5. Dr. Ricketts claims that Jones presented to him with prodromal pain in her legs, which he claims is a sign of impending femur fractures. *Id.* at 6. He also previously treated Jones for polymyalgia rheumatica, which attacks muscles in the upper shoulder or hips. Ricketts Deposition, (Doc. 119–5) at 7(23:19–25).

Jones plans to offer Dr. Ricketts to testify that Jones's Reclast infusions caused her femur fractures, that Jones's medical conditions were of the type described in medical literature caused by BP use, and that there was no other cause of Jones's fractures. (Doc. 119–1) at 5. As Dr. Ricketts is equally as unqualified to testify as Dr. Worthen and offers opinions that are equally as unreliable, he will be excluded from testifying as a causation expert.

b. *Dr. Ricketts Is not Qualified To Offer an Expert Opinion on Causation*

[33] In his deposition, Dr. Ricketts stated that he has seen thousands of patients with osteoporosis, some of whom have had osteoporosis-related fractures. (Doc. 119–5) at 4(10:17–24). However, he testified that he did not directly treat Jones's osteoporosis and took a "long absence" from his practice during the time when Jones was treated for her femoral fractures. *Id.* at 11(37:18–24). Dr. Ricketts also did not review or have copies of any of Jones's femoral x-rays in her chart and merely relied on the orthopedist's evaluation of the fracture because he has "no reason to doubt this guy." *Id.* at 17(62:24–63:–20). Additionally, he stated that Jones "would have been [his] first and only" patient to present with a femoral fracture. *Id.* at 11(37:10–14).

Jones argues that, as her "primary care physician who has managed her overall health for over ten years, Dr. Ricketts is more than qualified to opine to any of her healthcare related questions." Non–Retained Experts Response, (Doc. 144) at 24. While Dr. Ricketts may provide his opinion as to treatment decisions he made, his education, training, and expertise do not qualify him to provide expert testimony as to whether Jones's Reclast injections actually *caused* her femoral fractures. Therefore, his causation opinions are due to be excluded.

c. *Dr. Ricketts Does not Employ a Reliable Differential Diagnosis Methodology*

[34] Additionally, his testimony is independently due to be excluded because it relies substantially on the opinions of another physician and is not itself reliable. In her Response, Jones claims that Dr. Ricketts consulted with Dr. Worthen but also formed his own, independent differential diagnosis. (Doc. 144) at 24. However, Dr. Ricketts does not actually state anywhere in his deposition that he used a differential diagnosis methodology. Further, he admits in his deposition that he is not in a position to reliably testify about the cause of her fracture:

> Q: Okay. So if you were called to testify at trial, you wouldn't be testifying about—you wouldn't have an opinion about the—the cause of her fracture. Is that something that the orthopedist would be in a position to have an opinion on?
>
> Ms. Taylor: Object to the form.
>
> A: Right now I would have the opinion that it did cause it. Not that I diagnosed it, but I trust this surgeon. I saw the pathology reports.[30] And I

30. Novartis also claims that the pathology reports that Dr. Ricketts refers to are non-existent, so there is no way that Dr. Ricketts could rely on them in forming any opinion.

would have to testify that it caused it.

Q. Okay. So the basis for you stating that would be the orthopedist's opinion?

A: Orthopedist's opinion.

Q: Okay.

A: Yeah. Absolutely.

Q: Okay. So you would—you'd be able to relay what your understanding was if the orthopedist—

A: Absolutely.

Ms. Taylor: Object to the form.

A: I can tell exactly what the orthopedist told me.

Q: So you would have had conversations with the orthopedist?

A: Yes.

Ricketts Deposition, (Doc. 119–5) at 9(30:23–31:17). Dr. Ricketts' testimony demonstrates that he did not himself diagnose Jones and would not himself be able to form a specific causation opinion based on his own expertise or methodology.

Lastly, as above explained, a differential diagnosis will only satisfy a *Daubert* inquiry if the expert can show that the general toxicity of the drug has been reliably established. *McClain*, 401 F.3d at 1253. Dr. Ricketts has not reliably established that an association exists between Reclast injections and femoral fractures. Therefore, for the independent reason that Dr. Ricketts cannot show that Reclast has generally been shown to cause AFFs, Dr. Ricketts' specific causation testimony will be excluded.

3. Conclusion as to the Admissibility of Dr. Worthen's and Dr. Ricketts's Testimony

Neither Dr. Worthen nor Dr. Ricketts employed a reliable methodology in forming their respective opinions that Reclast caused Jones' femoral fractures. Therefore, the Motion to Strike the testimony of the Non–Retained Experts (doc. 120) is due to be **GRANTED IN PART**. The Motion is due to be **GRANTED** as to both doctors to the extent that either intends to offer a causation opinion and is otherwise **DENIED**.

V. CONCLUSION

For the above reasons, Novartis' Motion To Strike the expert testimony of Dr. Suzanne Parisian (doc. 108) is **HEREBY DENIED** to the extent that it seeks to exclude Dr. Parisian's testimony in its entirety. However, Novartis' Motion is **due to be GRANTED IN PART** and **DENIED IN PART** as to the particular areas of Dr. Parisian's testimony that it seeks to exclude.

Novartis' Motion To Strike the expert testimony of Dr. Hinshaw (doc. 112) is **HEREBY GRANTED**.

Novartis' Motion To Strike the expert testimony of Dr. Taylor (doc. 116) is **HEREBY GRANTED**.

Novartis' Motion To Strike the expert testimony of the non-retained experts, Dr. Worthen and Dr. Ricketts (doc. 118), is **HEREBY GRANTED** to the extent that either expert intends to offer an opinion on causation and is otherwise **DENIED**.

Novartis' claim is based on Dr. Worthen's testimony at his own deposition that he could not recall any bone pathology being performed on bone fragments from Jones's surgeries. Worthen Deposition, (Doc. 119–4) at 33(127:15–22). Even if Dr. Ricketts was able to review pathology reports that Dr. Worthen did not see or does not remember, Jones has not identified any exhibits offered into evidence as the pathology report in question. Therefore, the pathology report may not form a reliable basis for Dr. Ricketts's differential diagnosis, to the extent that one was conducted.

DONE and **ORDERED** this the 26th day of January.

SHIRE DEVELOPMENT, LLC, Shire Pharmaceutical Development, Inc., Cosmo Technologies Limited and Nogra Pharma Limited, Plaintiffs,

v.

MYLAN PHARMACEUTICALS, INC. and Mylan, Inc., Defendants.

Case No: 8:12–cv–1190–T–36AEP

United States District Court, M.D. Florida.

Signed 01/27/2017

Background: Licensee of patent directed to mesalazine controlled release oral pharmaceutical compositions brought infringement action against competitor that filed Abbreviated New Drug Application (ANDA) seeking approval to manufacture, use, and sell a generic equivalent.

Holdings: Following bench trial, the District Court, Charlene Edwards Honeywell, J., held that:

(1) product described in ANDA would infringe patent;

(2) pharmaceutical company induced infringement of patent; and

(3) company contributed to infringement of patent claims.

Ordered accordingly.

1. Patents ⚿1590, 1828(2)

Within the Hatch–Waxman context, when the specific infringing composition has not yet been made, used, or sold, the relevant inquiry for infringement is whether the patentee has proven by a preponderance of the evidence that the alleged infringer will likely market an infringing product. 35 U.S.C.A. § 271(e)(2).

2. Patents ⚿1555, 1848

Patent infringement is a question of fact, and a patent is infringed if a single claim is infringed. 35 U.S.C.A. § 271(e)(2).

3. Patents ⚿1555

The infringement analysis involves two steps: first, the court determines the scope and meaning of the patent claims asserted, and then the properly construed claims are compared to the allegedly infringing device. 35 U.S.C.A. § 271(e)(2).

4. Patents ⚿1555, 1574(1), 1824

To prevail, the patent infringement plaintiff must establish by a preponderance of the evidence that the accused device infringes one or more claims of the patent either literally or under the doctrine of equivalents. 35 U.S.C.A. § 271.

5. Patents ⚿1555

To prove literal infringement, a plaintiff must show that the accused device contains each and every limitation of the asserted claims. 35 U.S.C.A. § 271.

6. Patents ⚿1574(1)

An accused product that does not literally infringe a claim may still infringe under the doctrine of equivalents if each limitation of the claim is met in the accused product either literally or equivalently.

7. Patents ⚿1574(1)

To find patent infringement under the doctrine of equivalents, there must be a showing that the difference between the claimed invention and the accused product was insubstantial.