

**UNITED STATES DISTRICT COURT  
EASTERN DISTRICT OF ARKANSAS**

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**IN RE:  
PREMPRO PRODUCTS LIABILITY  
LITIGATION**

**MDL DOCKET NO. 4:03-CV-1507-WRW**

**JOINT MEMORANDUM ORDER**

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**UNITED STATES DISTRICT COURT  
DISTRICT OF MINNESOTA**

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**Natalie Beylin, et al.,**

**Civil No. 06-3112 (ADM/JJG)**

Plaintiffs,

v.

**JOINT MEMORANDUM ORDER**

**Wyeth, et al.,**

Defendants.

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**Jeanne Yobs, et al.,**

**Civil No. 06-3120 (ADM/JJG)**

Plaintiffs,

v.

**Wyeth, et al.,**

Defendants.

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**Pamela Dawn Thorne, et al.,**

**Civil No. 06-3123 (ADM/JJG)**

Plaintiffs,

v.

**Wyeth, et al.,**

Defendants.

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W. Stewart Calwell and Alex McLaughlin, The Calwell Practice, PLLC, Charleston, WV; and Robert A. Schwartz, Law Office of Robert A. Schwartz, Houston, TX, on behalf of plaintiffs.

Loren H. Brown, DLA Piper LLP, New York, NY; and F. Lane Heard, III, Williams & Connolly LLP, Washington, DC, on behalf of Wyeth Inc. and associated defendants (the defendants).

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**A. Introduction**

The primary question in this litigation is whether the plaintiffs developed breast cancer from hormone replacement therapy (HRT) medications. Most plaintiffs received Prempro, a combined hormone replacement therapy (CHRT) consisting of estrogen and progesterone. The parties have already litigated the admissibility of expert testimony on whether CHRT causes breast cancer.

Some plaintiffs received Premarin, which generally is described as an estrogen-only form of hormone replacement therapy (EHRT). We have yet to consider the admissibility of expert testimony on whether EHRT causes breast cancer, and trials involving this issue are anticipated in both the multidistrict litigation in Arkansas and in the satellite litigation in Minnesota. The plaintiffs accordingly seek admission of expert testimony on this issue, and the defendants move to exclude this testimony.

The admissibility of expert testimony is governed by Rule 702, which provides:

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

When considering scientific evidence, this rule requires us to perform as gatekeepers, separating legitimate scientific inquiry from subjective speculation. *Presley v. Lakewood Eng'g & Mfg.*

Co., 553 F.3d 638, 643 (8th Cir. 2009) (quoting *Glastetter v. Novartis Pharm. Corp.*, 252 F.3d 986, 989 (8th Cir. 2001)).

To perform this gatekeeping function, we examine whether expert testimony is reliable and whether it is relevant. See, e.g., *Barrett v. Rhodia, Inc.*, 606 F.3d 975, 980 (8th Cir. 2010) (quoting *Marmo v. Tyson Fresh Meats, Inc.*, 457 F.3d 748, 757 (8th Cir. 2006)); *In re Prempro Products Liability Litig.*, 586 F.3d 547, 565 (8th Cir. 2009) (quoting *Unrein v. Timesavers, Inc.*, 394 F.3d 1008, 1011 (8th Cir. 2005)). Although the admissibility of expert testimony is favored unless fundamentally flawed, the testimony should be excluded where these standards are not met. See, e.g., *Polski v. Quigley Corp.*, 538 F.3d 836, 839-841 (8th Cir. 2008). The objective is to ensure that scientific evidence will assist the jury in resolving disputed fact issues. *Miller v. Baker Implement Co.*, 439 F.3d 407, 412 (8th Cir. 2006).

To determine reliability, we focus on an expert's methodology, considering whether the expert was using scientifically valid reasoning to assess the facts. *In re Prempro Products Liability Litig.*, 586 F.3d at 565; *Synergetics, Inc. v. Hurst*, 477 F.3d 949, 955 (8th Cir. 2007) (quotation omitted). As the U.S. Supreme Court explained in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, many factors inform this analysis, including but not limited to (1) whether the methodology is tested; (2) whether it is subject to peer review or publication; (3) whether it has a known rate of error; and (4) whether the theory is generally accepted by the scientific community. 509 U.S. 579, 593-94 (1993).

To determine relevancy, we consider whether an expert's opinion can be applied to facts at issue. See, e.g., *Barrett*, 606 F.3d at 980. This is sometimes described as whether expert testimony "fits" with the issues. *Daubert*, 509 U.S. at 591; see generally Federal Judicial Center, *Reference Manual on Scientific Evidence* 12 (2d ed. 2000) (hereinafter *Reference Manual*). Even

where an expert opinion is reliable, if it cannot be applied to the specific facts of the case, the opinion should be excluded. *Concord Boat Corp. v. Brunswick Corp.*, 207 F.3d 1039, 1056 (8th Cir. 2000).

The proponent of expert testimony has the burden to show both reliability and relevancy. *Barrett*, 606 F.3d at 980 (quoting *Marmo*, 457 F.3d at 757). When deciding whether this burden is met, we are accorded substantial flexibility. See, e.g., *In re Prempro Products Liability Litigation*, 586 F.3d at 565; *Marmo*, 457 F.3d at 757.

Here, the plaintiffs have designated two experts to opine about general causation. This means the experts considered only the broad question of whether EHRT can cause breast cancer in the general population; they have not considered specific causation, meaning whether EHRT caused breast cancer in any particular plaintiff. Dr. Jasenka Demirovic, an epidemiologist, evaluated the statistical relationship between use of EHRT and the risk of breast cancer, and Dr. Marcelo Aldaz, a cell biologist, assessed the biological plausibility of EHRT causing breast cancer. After considering the *Daubert* standard, we conclude that their proposed testimony is not sufficiently reliable and relevant, and must be excluded.

**B. Dr. Demirovic**

Although the defendants have challenged the underlying qualifications of Dr. Demirovic, we have concluded that other concerns have greater weight. These concerns are informed by a decade-long clinical study conducted by the Women's Health Initiative (the WHI), a subdivision of the U.S. Department of Health and Human Services. (Exhs. 1, 2.)<sup>1</sup>

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<sup>1</sup> Exhibits are cited in an appendix that follows this order.

## 1. The WHI Study

In one branch of this study, the WHI tracked women receiving CHRT; the other tracked women receiving EHRT, specifically Premarin. Both branches were controlled and blind studies, meaning that neither treating physicians nor the participants were informed about which participants received EHRT. (Exhs. 1, 2.)

When the recipients of CHRT started displaying increased risk of breast cancer, the WHI terminated that branch of the study in 2002. (Exh. 1 at 1647-48.) The EHRT branch, however, continued until 2004. After that branch terminated, WHI scientists found there was no increased risk of breast cancer from Premarin.<sup>2</sup> (Exh. 2 at 3243-44.)

The only countervailing evidence to the WHI studies is from observational studies. Unlike clinical studies, which are blinded and controlled, observational studies select patients from existing populations, based on whether or not they have or will be receiving treatment. Because this procedure lacks controls, observational studies are more susceptible to bias and other confounding factors, and so are less reliable than clinical studies, which are often referred to as the “gold standard.” See *Reference Manual* 338-39. Neither Dr. Demirovic nor the parties contest these general principles. (See Exh. 3 at 76-77, 304-05.)

As the sole clinical study to examine the relationship between EHRT and breast cancer, the WHI study has substantially influenced scientific thinking on this question. Prior to the WHI study, several observational studies suggested a link between EHRT and increased risk of breast

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<sup>2</sup> In statistical terms, this outcome was expressed as a relative risk of 0.82, meaning users of Premarin were 82% as likely to develop breast cancer as those not receiving EHRT. This finding had a confidence interval from 0.65 to 1.04. (Exh. 2 at 1650.) Because this interval included 1.00, the reduction in risk was not deemed statistically significant, consistent with standard epidemiological practice. See generally, *Reference Manual* 360-61.

cancer. (See, e.g., Exh. 4.) When the WHI study showed contrary results, those observational studies were called into serious doubt.

Several major authorities, such as the National Cancer Institute, the American Cancer Society, and the National Institutes of Health, have since cited the WHI study for the proposition that Premarin does not increase the risk of breast cancer. We believe these authorities represent the generally accepted scientific view of the issue. (Exhs. 5, 6, 7.)

Dr. Demirovic contends that the WHI study has numerous deficiencies, and that when other observational studies are considered, there is reason to conclude that EHRT increases the risk of breast cancer. Because some of these observational studies were published after the WHI study, they arguably could rebut the WHI findings. We, accordingly, examine whether Dr. Demirovic can, consistent with reliable scientific methodology, disregard a generally accepted clinical study and instead rely on contrary observational studies.

## **2. Observational Studies**

The defendants assert that, in her efforts to distinguish the WHI study, Dr. Demirovic has misconstrued other observational studies. According to Dr. Demirovic, the WHI study failed to account for various confounding factors. (Exh. 8 at 20-21.)

The record does not include all the observational studies that Dr. Demirovic cited in her report. Nor is there any practical means to review the relevant literature and determine whether Dr. Demirovic reliably has presented the range of scientific opinion in this area. To the contrary, the record suggests there may be dozens of germane studies, and so Dr. Demirovic necessarily had to select some studies to form the basis for her opinion.

**a. Data Selection**

Dr. Demirovic selected studies that purportedly explain why the WHI study was deficient. Brinton (2008) and Rosenberg (2006), for example, found increased risk of breast cancer in certain lean women who received EHRT for more than ten years. But when reviewing these studies, Dr. Demirovic focused on those subgroups with the greatest risk, while discounting subgroups where EHRT had no statistically significant effect. (Exh. 8 at 14-15, 17-18.)

This concern can be illustrated by Rosenberg. The Rosenberg study found no statistically significant evidence, overall among women taking EHRT more than 10 years, of an increased risk of breast cancer. (Exh. 9 at 762.) Yet Dr. Demirovic focused on one statistically significant finding, in a subgroup of leaner women, that there was increased risk. (See Exh. 8 at 15.)

Dr. Demirovic offered a similar analysis of Brinton. Although the study found only “weak associations” between EHRT and breast cancer, Dr. Demirovic focused on subgroups involving leaner women or certain types of cancer. This sort of selective presentation raises substantial doubt about whether Dr. Demirovic used reliable methods when evaluating scientific literature. (See Exh. 8 at 17-18; Exh. 10 at 3151.)

At the hearing, the plaintiffs devoted considerable discussion to Prentice (2007), an observational study that the WHI conducted parallel to its clinical study. Although the observational study suggested the possibility of a higher risk of breast cancer, the study found that none of this data was statistically significant. (Exh. 11 at 1410-12.)

Prentice further suggested that, where the clinical study contradicted the observational study, it could be explained by the fact that participants in the clinical study did not commence EHRT immediately after menopause. But contrary to what the plaintiffs suggest, the authors did not find that the lag between menopause and EHRT could conceal a heightened risk of breast

cancer. Instead, the authors found their results to be consistent with the clinical study, concluding that there was no increased risk of breast cancer from EHRT. (Exh. 11 at 1413-14.) And in her report, Dr. Demirovic did not contest this proposition. (Exh. 8 at 19.)

**b. Statistical Significance**

As the preceding discussion illustrates, Dr. Demirovic sometimes cited studies, such as Rosenberg or Prentice, where the relative risk of breast cancer was not found to be statistically significant. The plaintiffs thus argue that, even where relative risk is not statistically significant, it still is sufficiently reliable to prove general causation. In support of this position, the plaintiffs cite a case from the District of Minnesota, *In re Viagra Products Liability Litigation*, 572 F. Supp. 2d 1071 (D. Minn. 2008), *vacated in part*, 658 F. Supp. 2d 936 (D. Minn. 2009).

There, the court ruled that “lack of statistical significance under some circumstances does not detract from the reliability of [a] study.” *Id.* at 1081 (quoting *In re Phenylpropanolamine Prods. Liability Litig.*, 289 F. Supp. 2d 1230, 1241 (W.D. Wash. 2003)) (quotation marks omitted). We agree that statistical significance, by itself, should not mechanically control whether an epidemiological analysis is sufficiently reliable to be admissible. But as many federal courts observe, if an expert places undue emphasis on statistically insignificant evidence, it may indicate that the expert’s methods are unreliable. See, e.g., *Wells v. SmithKline Beecham Corp.*, 601 F.3d 375, 380 & n. 23 (5th Cir. 2010); *Pritchard v. Dow Agro Sciences*, — F. Supp. 2d —, 2010 WL 936767, at \*16 (W.D. Pa. 2010); *cf. General Elec. Co. v. Joiner*, 522 U.S. 136, 145-47 (1997) (ruling that, where expert opinion was founded on statistically insignificant data and other doubtful evidence, the district court did not abuse its discretion by excluding the opinion).

Considering the record as a whole, it appears that Dr. Demirovic selected study data that best supported her opinion, while downplaying contrary findings or conclusions. Dr. Demirovic

also has partially relied on data that is not statistically significant. These concerns, taken together, significantly undermine the reliability of her proposed testimony.

### **3. Chemical Composition**

The defendants further contend that, although the current issue only involves Premarin, Dr. Demirovic bases her opinion in part upon observational studies that considered other forms of EHRT. To the extent these studies involve other substances, the inquiry becomes whether they reliably predict the effects of Premarin.

Estrogen is not itself a single substance, but rather a class of hormones; its major forms are estriol, estrone, and estradiol. The most potent is estradiol, which is also the most commonly prescribed mode of EHRT in Europe. But the plaintiffs, in the current litigation, were prescribed Premarin, generically referred to as conjugated equine estrogen (CEE). About a third of CEE is estrone and less than 1% is estradiol.

In her report, Dr. Demirovic cited some European studies that attributed an increased risk of breast cancer to estradiol, implying that the studies were equally applicable to Premarin. (See Exhs. 12 at 725; 13 at 449; 14 at 1355.) But she did not distinguish between CEE and estradiol, nor explain how the substances are equivalent. (Exh. 8 at 13, 16.)

At her deposition, Dr. Demirovic could not identify the three forms of estrogen, nor was she able to identify their respective concentrations in CEE. (Exh. 3 at 58-60.) When asked to explain why CEE and estradiol were equivalent, Dr. Demirovic opined that all forms of estrogen had a common “class effect.” (*Id.* at 80.) She testified that “the effect of estrogen . . . is the same regardless of the product used” and that “there were no differences regarding the type of estrogen or the route of administration.” (*Id.* at 200, 284.) She mentioned that certain studies supported her contention, but she did not identify them. (*Id.* at 79-80.)

The Court of Appeals for the Eighth Circuit has stated, “Even minor deviations in molecular structure can radically change a particular substance’s properties and propensities.” *Glastetter v. Novartis Pharms. Corp.*, 252 F.3d 986, 990 (8th Cir. 2001). For this reason, where an expert summarily attributes effects of one substance to another similarly classified substance, federal courts have consistently concluded that such methodology is not reliable. See, e.g., *McClain v. Metabolife Int’l, Inc.*, 401 F.3d 1233, 1244-45 (11th Cir. 2005); *Hollander v. Sandoz Pharms. Corp.*, 289 F.3d 1193, 1207 (10th Cir. 2002).

Because Dr. Demirovic did not acknowledge the differences between CEE and estradiol in her report, this generalization signals a defect in her methodology. This concern is reinforced by the fact that, at her deposition, Dr. Demirovic could not describe the formulation of CEE. Dr. Demirovic did not understand the underlying science, therefore, to reliably analyze the observational studies.

To summarize, the record shows that Dr. Demirovic (1) discounted data that undermined her opinion; (2) relied on statistically insignificant data; and (3) did not understand the differences between different forms of EHRT. And although the plaintiffs have the burden to establish that her methods are reliable, they have not been able to muster evidence that does so, assuming such evidence exists. For this reason, Dr. Demirovic’s analysis of the observational studies cannot overcome the reliable and generally accepted findings of the WHI clinical study. We conclude that her opinion must be excluded.<sup>3</sup>

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<sup>3</sup> The defendants further argue that, for Dr. Demirovic’s opinion to be relevant, it must indicate that EHRT causes the relative risk of breast cancer to exceed 2.0. We find this proposition without merit. Of the courts that impose this threshold, most do so when an expert opines on specific causation, whereas the experts in the current litigation are opining on general causation. See, e.g., *Henricksen v. ConocoPhillips Co.*, 605 F. Supp. 2d 1142, 1158 (E.D. Wash. 2009). Many other federal courts, moreover, have rejected this threshold altogether. See, e.g., *In*

**C. Dr. Aldaz**

The defendants have also challenged the underlying qualifications of Dr. Aldaz. But we set aside this issue to consider the defendants' chief argument—they principally contend that Dr. Aldaz's opinion does not sufficiently relate to Premarin, and therefore, his opinion cannot apply.

This argument implicates both reliability and relevancy. In the context of reliability, the issue is whether Dr. Aldaz can extrapolate the effects of Premarin from laboratory studies. In the context of relevancy, the issue is whether Dr. Aldaz's analysis of carcinogenic effects of estrogen has probative value as to Premarin.

**1. Animal and Tissue Studies**

In his report, Dr. Aldaz relies on a significant number of animal and tissue studies. These studies generally show that estrogen can foster the development or growth of breast cancer. The defendants contend that, as the studies only establish the effects of estrogen in highly controlled laboratory settings, they cannot reliably demonstrate the effects of Premarin in living humans.

Federal courts have consistently cautioned against extrapolation of human effects from animal studies. In addition to the biological differences between species, most animal studies involve significantly higher concentrations of a substance than would ever be present in humans. For this reason, where an expert relies on animal studies, the expert must be prepared to explain how such studies can be reliably extrapolated to prove comparable effects in humans. See, e.g., *General Elec. Co. v. Joiner*, 522 U.S. 136, 144 (1997); *Allison v. McGhan Medical Corp.*, 184 F.3d 1300, 1313-14 (11th Cir. 1999); *In re Paoli R.R. Yard PCB Litigation*, 35 F.3d 717, 743 (3d Cir. 1994).

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*re E. & S. Dist. Asbestos Litig.*, 964 F.2d 92, 97 (2d Cir. 1992); *Pritchard v. Dow Agro Sciences*, — F. Supp. 2d —, 2010 WL 936767, at \*13 (W.D. Pa. 2010).

These considerations have equal force for *in vitro* studies. Even where human tissue is studied, an expert must still explain how laboratory results will reliably predict effects in living humans. See *Allen v. Pennsylvania Eng'g Corp.*, 102 F.3d 194, 198 (5th Cir. 1996) (ruling that, where *in vitro* studies showed that certain substances were mutagenic, the studies alone did not reliably prove that the substances caused cancer); see also *In re Rezulin Prods. Liability Litig.*, 369 F. Supp. 2d 398, 406-07 (S.D.N.Y. 2005); *Bourne ex rel. Bourne v. E.I. DuPont de Nemours & Co.*, 189 F. Supp. 2d 482, 496 (S.D. W.Va. 2002), *aff'd*, 85 Fed. Appx. 964 (4th Cir. 2004).

In his report, Dr. Aldaz reviewed studies that involved rats, mice, hamsters, and human tissue. Some studies used ACI rats, a strain that is bred specifically because of its susceptibility to breast cancer. (See Exh. 15 at 10-13.) And in two of the studies, Dr. Aldaz indicated that “physiological” amounts of certain estrogen metabolites were used, permitting an inference that non-physiological amounts were used in the other studies. (*Id.* at 12, 13.)

Beyond this assertion, Dr. Aldaz has not explained how these studies could be reliably extrapolated to predict the effects of Premarin in humans. And for the most part, he also did not elucidate the relationship between the estrogen metabolites in the studies and those substances actually found in Premarin. In his depositions, furthermore, Dr. Aldaz offered no testimony that might dispel these concerns. So to the extent Dr. Aldaz relies on animal and tissue studies, serious questions arise about both the reliability and relevancy of his opinion.

## **2. Dose-Response Relationship**

The defendants further argue that, even if Dr. Aldaz can show that estrogen can induce breast cancer, he has not indicated what amounts of estrogen present this risk. The underlying principle here, in epidemiological parlance, is the dose-response relationship. It generally stands

for the proposition that exposure to a substance must exceed a certain level before it manifests a risk of adverse health effects. See generally, *Reference Manual* 475.

In accordance with this principle, if an expert's opinion does not specify what level of exposure increases the risk of adverse health effects, the opinion may be deemed unreliable. See, e.g., *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1241-42 (11th Cir. 2005). Moreover, where an expert relies on a study of a high dose to determine adverse effects of a lower dose, without supplying a method to substantiate this inference, courts often rule that such extrapolations are unreliable. See, e.g., *In re Bextra & Celebrex Mktg. Sales Practices & Prod. Liability Litig.*, 524 F. Supp. 2d 1166, 1180 (N.D. Cal. 2007); *Soldo v. Sandoz Pharms. Corp.*, 244 F. Supp. 2d 434, 546-47 (W.D. Pa. 2003).

In his report, Dr. Aldaz consistently opines that estrogen is carcinogenic, but he generally fails to specify what levels of exposure will cause breast cancer in living humans. (Exh. 15 at 9-10, 18-22.) When asked about dose-response relationship at his deposition, Dr. Aldaz acknowledged that the proliferative effects of estrogen follow an "inverted U shape." This means that at very low and very high levels, estrogen is less likely to promote breast cancer. (Exh. 16 at 138-39.) For that matter, Dr. Aldaz admitted that at very high levels, estrogen has been shown to inhibit breast cancer and may be therapeutic. (*Id.* at 137-38.)

We believe that a bald assertion, that estrogen is carcinogenic, is not sufficient. This claim needs to be informed by a tangible threshold at which estrogen measurably increases the risk of breast cancer. Without this information, there is no reliable way to ascertain whether estrogen causes breast cancer, nor it is possible to correlate this risk to the amounts of estrogen prescribed as Premarin.

**3. Relevancy**

We may assume, for the sake of argument, that Dr. Aldaz cited methodologically sound studies in his report. Our concern goes to how Dr. Aldaz interprets the studies and whether this interpretation will be helpful to a jury.

As discussed beforehand, Dr. Aldaz has not explained how allegedly harmful effects of Premarin can be extrapolated reliably from laboratory studies. Nor has he identified a particular dosage of estrogen that results in an increased risk of breast cancer. For that matter, the plaintiffs have not identified any probative scientific evidence that might remedy these deficiencies.

As Dr. Aldaz's opinion does not address these concerns, it is not probative to the question of whether Premarin increases the risk of breast cancer. This opinion is likely to foster confusion, causing the jury to conflate the effects of estrogen in the laboratory with those of Premarin in humans. For these reasons, we conclude that his opinion should be excluded as well.

**D. Conclusion**

Being fully advised of the premises, **IT IS HEREBY ORDERED THAT:**

1. The plaintiffs' motions to admit expert opinion evidence (Doc. No. 2305 in *In re Prempro Products Liability Litigation*; Doc. No. 382 in *Beylin*; Doc. No. 342 in *Yobs*; Doc. No. 747 in *Thorne*) are **DENIED**.
2. The defendants' cross-motions to exclude expert opinion evidence (Doc. No. 2351 in *Prempro Products Liability Litigation*; Doc. No. 384 in *Beylin*; Doc. No. 344 in *Yobs*; Doc. No. 748 in *Thorne*) are **GRANTED**.

Dated this 30th day of August, 2010.

/s Ann D. Montgomery

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ANN D. MONTGOMERY  
United States District Judge

Dated this 30th day of August, 2010.

/s Wm. R. Wilson, Jr.

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WM. R. WILSON, JR.  
United States District Judge

**APPENDIX**

- Exh. 1 Defs.' Mem., Aug. 9, 2010, Exh. 121 (Chlebowski 2005) [Doc. No. 2361 in *Prempro*; Doc. No. 398 in *Beylin*].
- Exh. 2 Defs.' Mem., July 29, 2010, Exh. 25 (Stefanick 2006) [Doc. No. 2352 in *Prempro*; Doc. No. 385 in *Beylin*].
- Exh. 3 Defs.' Mem., July 29, 2010, Exh. 20 (Depo. of J. Demirovic, July 6, 2010) [Doc. No. 2352 in *Prempro*; Doc. No. 385 in *Beylin*].
- Exh. 4 Defs.' Mem., July 29, 2010, Exh. 54 (Collaborative Group 1997) [Doc. No. 2352 in *Prempro*; Doc. No. 387 in *Beylin*].
- Exh. 5 Defs.' Mem., July 29, 2010, Exh. 5 (Nat'l Cancer Institute, "Menopausal Hormone Replacement Therapy (HRT)," at <http://www.cancer.gov/cancertopics/causes/hormonotherapy/menopausal-hormone-use>) [Doc. No. 2352 in *Prempro*; Doc. No. 385 in *Beylin*].
- Exh. 6 Defs.' Mem., July 25, 2010, Exh. 39 (American Cancer Society, "Menopausal Hormone Replacement Therapy and Cancer Risk," at <http://www.cancer.org/Cancer/CancerCauses/OtherCarcinogens/MedicalTreatments/menopausal-hormone-replacement-therapy-and-cancer-risk>) [Doc. No. 2352 in *Prempro*; Doc. No. 385 in *Beylin*].
- Exh. 7 Defs.' Mem., July 25, 2010, Exh. 6 (Press Release of Nat'l Institutes of Health, Apr. 11, 2006, *WHI Updated Analysis: No Increased Risk of Breast Cancer with Estrogen-Alone*, available at <http://www.nhlbi.nih.gov/new/press/06-04-11a.html>) [Doc. No. 2352 in *Prempro*; Doc. No. 385 in *Beylin*].
- Exh. 8 Report of J. Demirovic, June 5, 2010 [Doc. No. 2306 in *Prempro*; Doc. No. 382 in *Beylin*].
- Exh. 9 Defs.' Mem., July 25, 2010, Exh. 59 (Rosenberg 2006) [Doc. No. 2352 in *Prempro*; Doc. No. 387 in *Beylin*].
- Exh. 10 Defs.' Mem., July 25, 2010, Exh. 62 (Brinton 2008) [Doc. No. 2352 in *Prempro*; Doc. No. 387 in *Beylin*].
- Exh. 11 Defs.' Mem., July 25, 2010, Exh. 66 (Prentice 2007) [Doc. No. 2352 in *Prempro*; Doc. No. 387 in *Beylin*].
- Exh. 12 Defs.' Mem., July 25, 2010, Exh. 56 (Stahlberg 2004) [Doc. No. 2352 in *Prempro*; Doc. No. 387 in *Beylin*].

- Exh. 13        Defs.' Mem., July 25, 2010, Exh. 58 (Fornier 2005) [Doc No. 2352 in *Prempro*; Doc. No. 387 in *Beylin*].
- Exh. 14        Defs.' Mem., July 25, 2010, Exh. 61 (Lyytinen 2006) [Doc No. 2352 in *Prempro*; Doc. No. 387 in *Beylin*].
- Exh. 15        Report of C.M. Aldaz, June 2, 2010 [Doc. No. 2306 in *Prempro*; Doc. No. 382 in *Beylin*].
- Exh. 16        Defs.' Mem., July 25, 2010, Exh. 8 (Depo. of C.M. Aldaz, July 23, 2010) [Doc. No. 2352 in *Prempro*; Doc. No. 385 in *Beylin*].