UNITED STATES COURT OF APPEALS
FOR THE EIGHTH CIRCUIT

Case No. 08-2555
CIVIL

DONNA SCROGGIN,

Plaintiff/Appellant

v.

WYETH, WYETH PHARMACEUTICALS, INC.
AND PHARMACIA & UPJOHN COMPANY, LLC,

Defendants/Appellees

On Appeal from the United States District Court
for the Eastern District of Arkansas,Western Division
Judge William R. Wilson, Jr., Presiding

BRIEF OF APPELLANT DONNA SCROGGIN

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ORAL ARGUMENT REQUESTED

SUMMARY OF THE CASE

This is an appeal after jury trial of a case in the hormone therapy MDL proceedings. Plaintiff, Donna Scroggin sued defendants, Wyeth and Upjohn for failing to warn adequately about the risks of combination hormone therapy, causing her to lose both her breasts to cancer. Ms. Scroggin alleged that defendants failed to warn her of discoverable harm they would have known had they engaged in any meaningful study of the perceived breast cancer risk. Wyeth actively sought to discredit studies and distract attention from evidence of breast cancer risk. Upjohn did nothing. The trial was bifurcated. In Phase One, the jury found both defendants liable and awarded Ms. Scroggin $2,750,000 in compensatory damages. In Phase Two, the jury found both defendants liable for punitive damages and ordered Wyeth to pay $16,360,000 and Upjohn to pay $6,760,000. The court denied defendants' motions for judgment as a matter of law and for new trial on liability and compensatory damages but granted those motions with respect to punitive damages. The court entered judgment on the compensatory award, with costs and interest.

Oral argument would assist the Court, given the complexity of the record and issues. The facts in the punitive damages issue are many and varied. Ms. Scroggin anticipates defendants will raise multiple liability issues. Ms. Scroggin therefore requests 30 minutes of oral argument, including rebuttal.

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JURISDICTIONAL STATEMENT

The district court had subject matter jurisdiction based on diversity of citizenship. *See* 28 U.S.C. § 1332. Plaintiff, Donna Scroggin is a resident of Arkansas. Defendant, Wyeth is a Delaware corporation with its principal place of business in New Jersey. Defendant, Wyeth Pharmaceuticals Inc. is a New York corporation with its principal place of business in Pennsylvania. Defendant, Pharmacia & Upjohn Company LLC is a Delaware corporation with its principal place of business in New Jersey. The court had personal jurisdiction because each defendant committed acts in the State of Arkansas that gave rise to Ms. Scroggin's causes of action.

The court of appeals has subject matter jurisdiction because this is an appeal from a final decision of the district court that disposed of all issues regarding all parties. *See* 28 U.S.C. § 1291. After granting judgment on the jury verdict (A-IV-001056-001057, A-IV-001058-001059), the court granted post-trial motions for judgment as a matter of law as to punitive damages on July 8, 2008 (A-V-001353-001404). Plaintiff timely filed her notice of appeal two days later (A-V-001405-001406). *See* Fed. R. App. P. 4(a)(4).

ISSUES PRESENTED FOR REVIEW

1. Did the district court err by striking the testimony of regulatory expert, Dr. Suzanne Parisian, post-trial, and all documents admitted while she was testifying, thereby concluding there was insufficient evidence supporting the punitive damages award, when the documents were admitted independently of Dr. Parisian's testimony, defendants waived any objection to the testimony, the testimony properly focused on FDA regulations and procedures and defendants' witnesses supported the standards upon which Dr. Parisian's opinions were based?

   Marmo v. Tyson Fresh Meats, Inc., 457 F.3d 748 (8th Cir. 2006); *Terrell v. Poland*, 744 F.2d 637 (8th Cir. 1984).

2. Did the district court err by weighing the evidence, assessing witness credibility, adopting inferences from the evidence contrary to the verdict, and relying on evidence the jury was not required to accept, including the testimony of defendants' interested witnesses, in granting judgment as a matter of law against the jury's punitive damages finding?

   Reeves v. Sanderson Plumbing Prods Inc., 530 U.S. 131 (2000); *Boerner v. Brown & Williamson Tobacco Co.*, 394 F.3d 594 (8th Cir. 2005); 9A CHARLES ALAN WRIGHT & ARTHUR R. MILLER, FED. PRAC. & PRO. § 2527 (2d ed. 1995 & Supp. 2004).

STATEMENT OF THE CASE

This is an appeal in a case tried to a jury in the hormone therapy multidistrict litigation proceedings. On October 8, 2004, Plaintiff Donna Scroggin filed suit against defendants, Wyeth, Wyeth Pharmaceuticals Inc. (hereafter collectively "Wyeth") and Pharmacia & Upjohn Company L.L.C. (hereafter "Upjohn"). Ms. Scroggin alleges the defendants failed to warn adequately of the risk of breast cancer from using combination hormone therapy, meaning estrogen combined with progestin ("E+P") (A-III-000879-000932).[1] In particular, Ms. Scroggin contends that both defendants were on notice of the risk of breast cancer but deliberately failed to study that risk because they did want the world to know their profitable drugs were dangerous. As a result, Ms. Scroggin lost both her breasts and suffered through painful treatment.

The case was tried to a jury beginning February 5, 2008. Two phases of the trial occurred. The first phase involved entitlement to compensatory damages, whereas the second phase involved entitlement to punitive damages. After

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[1] This lawsuit is the product of a severance of a separate lawsuit, hence the date on the original complaint is October 8, 2004 even though the lawsuit was filed on April 7, 2004.

For ease of reference, all trial transcript entries are designated with a capital "T" followed by the volume numbers (in roman numerals) of the transcripts and the page-line designations. All trial exhibits and court docket entries are part of the appendix and are designated with a capital "A" followed by the relevant page numbers of the appendix.

listening to approximately four weeks of testimony and reviewing extensive documents, the jury returned verdicts favoring Ms. Scroggin after both phases. On February 25, 2008, the jury returned a verdict in Phase One, finding both defendants liable for failing to warn adequately of the risks of their products and awarding compensatory damages of $2,750,000 (Addendum 1). On March 6, 2008, the jury returned a verdict in Phase Two, finding that both defendants engaged in conduct warranting punitive damages and imposing awards of $16,360,000 against Wyeth and $6,760,000 against Upjohn (Addendum 2).

Judge William R. Wilson of the Eastern District of Arkansas, Western Division, presided over the trial. The district court entered judgment pursuant to the verdict (A-IV-001056-001057; A-IV-001058-001059). On April 10, 2008, the court denied the defense motions for judgment as a matter of law and for new trial, insofar as they related to compensatory damages (A-V-001350). But on July 8, 2008, the court granted the motions with respect to punitive damages (A-V-001353-001404). Ms. Scroggin filed her notice of appeal two days later (A-V-001405-001406). The court ultimately issued an amended judgment with the punitive damage award removed (A-V-001407).

STATEMENT OF FACTS

Donna Scroggin lost both her breasts to cancer because Wyeth and Upjohn deliberately refused to conduct studies that would have established the breast cancer risk from ingestion of menopausal combination hormone therapy. Wyeth reacted to mounting evidence of the risk with a comprehensive campaign to dismiss the data while distracting the public and media. Upjohn did nothing.

Menopausal combination hormone therapy is a prescription pharmaceutical regimen consisting of estrogen (E) with progestin (P) (collectively "E+P"). For years, Ms. Scroggin used Premarin (Wyeth's estrogen product) with Provera (Upjohn's progestin product) (T-V-757:21-758:1; T-V-777:14-17). She eventually switched to Prempro (Wyeth's combination E+P pill) (T-V-776:7-13). She used E+P for approximately 11 years before her breast cancer diagnosis in 2000. (T-V-752:14-17; T-V-865:9-17;T-VI-1094:4-1095:1).

I. WYETH'S STRATEGY: DISMISS-AND-DISTRACT

Wyeth and Upjohn were on notice that E+P could cause breast cancer. Yet neither company did any studies. Wyeth went one step further: Wyeth deliberately downplayed the breast cancer risk while taking active steps to convince doctors and women that the combination was safe.

Hormone therapy (HT) relieves menopausal symptoms, such as hot flashes and vaginal atrophy (E.g., A-III-000839; A-III-000837). Wyeth began selling the

first HT product, Premarin, in 1942 (T-III-418:24-419:2). Premarin mimics a woman's natural estrogen, though it consists of conjugated equine estrogen, meaning estrogen derived from the urine of pregnant mares (T-III-273:6-13). Premarin eventually became Wyeth's biggest selling product and one of the most prescribed drugs in the country (A-II-000525).

A. The Endometrial Cancer Crisis: The Origin of "Dismiss/Distract"

As Premarin sales rose in the late 1960s, so did endometrial (uterine) cancer rates (T-VII-1269:17-24). By the end of 1975, medical studies confirmed that Premarin had caused an endometrial cancer crisis (T-II-189:16-191:14; T-III-433:3-7; T-XI-2130:20-2131:2; T-XV-2754:22-24). Instead of immediately disseminating this information to physicians, Wyeth started a "dismiss-and-distract" strategy that was employed for the next two decades whenever adverse cancer information about hormone therapy was uncovered.

The FDA rebuked Wyeth for this inappropriate policy as early as 1975. Despite an FDA advisory committee confirming that menopausal estrogen use was strongly linked to endometrial cancer (A-I-000170; T-II-181:2-9) (A-I-000174; T-XV-2682:4-23), Wyeth disseminated a "Dear Doctor" letter,[2] disputing that its drug was linked to the epidemic (A-I-000171). The FDA was outraged, scolding

[2] A "Dear Doctor" letter is sent by a drug company to inform physicians of recent findings about a drug (T-II-232:5-17).

Wyeth that the letter had "insensed [sic] the FDA at all levels, including the Commissioner of Food and Drugs" (A-I-000173). The FDA expected Wyeth to formulate "a sound medical and scientific response to this new information" (A-I-000174), not to issue a letter that "misrepresents the scientific findings as published in the literature."[3]

Wyeth was squarely on notice of the need to study adverse HT findings. The FDA criticized Wyeth's "passive" response (A-I-000174, A-I-000176), urged Wyeth to study the cancer risk and propose new warnings (A-I-000176), and advised the company to remain vigilant for future developments (A-I-000176). Wyeth ignored these admonitions.

B. The Lack of Adequate E+P Study

Shortly after the 1975 FDA meeting, the concept of using progestin (P)[4] to counterbalance the effects of estrogen (E) on the endometrium was born. Physicians began prescribing E+P to their patients who had not had a hysterectomy (T-III-275:23-25; T-III-276:15-22). Using E+P quickly became standard medical practice (A-II-000426; T-IV-564:20-23). But this use was "off-label" because

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[3] The memo references "Ayerst." Wyeth and Ayerst are the same company (T-XV-2683:16-18).

[4] "Progestin" refers to synthetic progesterone known as medroxyprogesterone acetate ("MPA"), the active ingredient in Upjohn's Provera.

combination E+P was not FDA-approved for treating menopausal symptoms. FDA approval would require actual safety and efficacy studies.

Simultaneously, Wyeth's researchers discovered that E+P may promote breast cancer. A 1976 internal memorandum noted that estrogen drugs stimulate the growth of hormone positive cancers (cancers that test positive for the presence of estrogen and progesterone receptors). The memo further noted that the role of progesterone in the etiology of breast cancer "is another area that needs clarification" (A-I-000185-000186; T-IV-503:23-504:2). Justin Victoria, Wyeth's associate director of regulatory affairs (T-III-417:24-418:23), confirmed that Wyeth knew of the potential breast cancer link to E+P by 1976 (T-III-434:1-20; T-IV-505:16-19).

In 1977, Wyeth knew that, for E+P use, "the number of published, well-designed studies [was] small or practically non existent" (A-II-000426). Yet Wyeth did nothing, preferring to profit from this lack of knowledge rather than conducting the needed studies. That situation remained unchanged in 1990, when the FDA's advisory committee meeting unanimously concluded that no well-designed studies on E+P and breast cancer existed (T-VII-1292:23-1293:4; T-VII-1304:5-10; T-VII-1375:2-5; A-I-000212). Wyeth admitted, in both 1990 and 1993, that the breast cancer risk from E+P remained unknown (T-III-450:13-19; T-III-451:22-452:8; T-III-459:7-10).

While E alone had been extensively studied, E+P posed more questions than answers. Indeed, the FDA once dubbed HT as the "most studied drug" -- in reference to estrogen-alone therapy -- while the same agency repeatedly told Wyeth that a dearth of information existed on E+P (A-I-000210-000213; T-X-1785:18-24). Dr. Donald Austin, a world-renowned epidemiologist who has published extensively on cancer incidence (T-II-253:4-12; also T-II-172:1-9 & A-II-000579-000581), and one of the principal researchers who exposed the link between postmenopausal estrogen use and the endometrial cancer epidemic (T-II-179:4-180:10), testified that studies on E alone do not provide meaningful information on the breast cancer risk of E+P (T-II-227:24-229:1; T-II-237:15-19).

Upjohn hired The Degge Group, a research company, to review the epidemiological literature on E+P and breast cancer, in preparation for the 1990 FDA meeting (A-III-000718-000719 at 30:21-32:24). The Degge Group concluded that the studies were inadequate to show E+P is safe for the breast and confirmed a serious need to conduct such studies (T-VII-1371:24-1372:1; A-III-000715-000716 at 9:1-13:15; 16:25-17:5; A-III-000719-000721 at 37:16-38:5; 43:8-21; 47:24-48:21).

Wyeth never acted to fill this void. The company chose repeatedly to do nothing. This do-nothing attitude started nearly a decade before. In 1983, Wyeth sought approval of "PremPak," a combination package of E and P pills (A-I-

000193-000194; T-IV-543:3-23). Wyeth feared that the FDA would require actual studies on the combination product and opined that:

> To attempt such demonstration would be very costly, would take many years, and might in the end not prove successful. In fact, the results of the study that would be needed could turn out to be embarrassing.

(A-I-000193-000194). An unsuccessful study meant Wyeth could "kiss the product good-bye" (A-I-000204). Wyeth was so concerned about adverse results, when a PremPak study ultimately began, Wyeth considered "peeking" at the data, an unacceptable practice given the bias it can inject (A-I-000204; T-XV-2687:24-2688:7). Wyeth prematurely abandoned the PremPak study in 1988 (T-IV546:11-16) while continuing to pursue FDA approval of E+P through "paper" applications that cited published studies performed by others. The FDA continually informed Wyeth that these studies were inadequate, even going so far as to detail that "the long-term safety of the combination treatment for human use cannot be assured based on the current submission" (A-I-000342). Wyeth knew that the FDA would not approve E+P "without adequate clinical data to address the benefit/risk ratio of combined estrogen/progestin therapy" (A-I-000214-000215). In 1993, the FDA reiterated that there was insufficient study on the breast cancer risk (A-I-000220).

Wyeth passed up many opportunities to perform or support breast cancer studies on E+P (T-II-241:11-17; T-III-450:13-19; T-III-452:6-8 (past); T-XV-2738:18-24 (present)). For example, in 1993, the Eastern Cooperative Oncology

Group (ECOG) approached Wyeth about support for an E+P breast cancer study. Wyeth refused to provide pills for the study "consistent with company policy" to not fund breast cancer studies (A-I-000224). A Wyeth executive confirmed that the rejection was "customary apparently for studies involving breast cancer" (A-I-000226).

On those rare occasions when Wyeth provided assistance with research, if the study had the potential to generate breast cancer data, Wyeth conditioned its support on the researcher's agreement not to publish anything about the breast cancer risk of E+P. For instance, in 1995, a United Kingdom scientist requested mammograms used in a previous Wyeth study for a study on breast density in E+P users (A-II-000544-000555), because E+P was known to cause breast density. (T-V-751:12-20; T-X-1941:10-1942:1). Wyeth agreed to provide mammograms only if the researcher agreed in writing to (a) not analyze whether E+P increased the risk of breast cancer (A-II-000547) and (b) cede editorial control of the final version of his article to Wyeth (A-II-000548).

C. Adverse Breast Cancer Data: "Dismiss/Distract" Resumes

Wyeth's refusal to study was the product of reckless and deliberate indifference to women's health. Unanswered questions existed about E+P's effect on breast cancer. Wyeth refused to study that risk and went to extraordinary

lengths to suppress, counteract and discount breast cancer findings of legitimate scientists.

1. The Hoover study

In 1976, just months after the endometrial cancer epidemic, Dr. Robert Hoover of the National Cancer Institute sent Wyeth the manuscript of an article he planned to publish in the New England Journal of Medicine revealing that long-term use of estrogen therapy more than doubled the risk of breast cancer. He told Wyeth his results warranted further study (A-I-000192). Wyeth responded with proposals to refute and mitigate the effects of the report (A-I-000177), because "[Wyeth] cannot afford to wait for the axe to begin its descent before we give serious attention to how we might blunt its edge" (A-I-000190; also A-I-000183).

2. The Pike study

At a 1989 "Premarin Advocate Meeting," Dr. Malcolm Pike "took his usual position" on E+P and breast cancer and discussed a new study that showed a doubling of breast cancer risk (A-II-000507). Wyeth's immediate reaction was not to invite Dr. Pike to future seminars (A-II-000508). Although Wyeth ultimately relented, given Dr. Pike's reputation in the field, (T-X-1928:24-1929:10) this memo confirms that Wyeth's leaders considered blacklisting a respected researcher because he called attention to the breast cancer link.

3. The FDA advisory committee meeting

The 1990 FDA Advisory Committee meeting concluded that insufficient data was available on the breast cancer risk of E+P (A-I-000212). Wyeth celebrated that it had attained its goal to "ensure that this meeting was a 'non-event.'" (A-I-000209).

4. The Colditz study

In 1990, world-renowned breast cancer epidemiologist Dr. Graham Colditz planned to present findings on hormone drugs and breast cancer. Rather than assist, Wyeth had spokespeople at the meeting to counteract any negative press coverage and assembled a press kit that would distract participants and the press from the risks of HT by shifting attention to its purported benefits (A-II-000427-000428).

5. Oncologists chairing meetings: "NO, NO, NO"

In December, 1994, a Wyeth executive issued a memo indicating that a prominent oncologist would chair a Wyeth consultants' meeting (A-II-000571-000573; T-X-1942:8-1944:23), not an OB/GYN. Oncologists are physicians who treat breast cancer, (T-V-715:7-13) and were historically far more skeptical of HT and its risks than OB/GYNs. A handwritten note responding to the memo says, "No way having an oncologist chair this. NO, NO, NO, NO & NO" (A-II-000571; T-X-1944:4-6).

6. IARC task force

The International Agency for Research on Cancer (IARC) is the branch of the World Health Organization charged with identifying cancer-causing agents in the environment (A-III-000782 at 63:15-64:7). During 1990, the same year it successfully manipulated the FDA advisory committee meeting to be a "non-event," Wyeth created a task force "to ensure that IARC does not develop a position on a definitive relationship between breast cancer and estrogen replacement therapy" (A-I-000216) (emphasis in original).

7. The Seasons magazine campaign

Wyeth published a magazine for its consumers called "Seasons." This magazine was a blatant attempt to disguise marketing as science, *dismiss* adverse data and *distract* consumers from the breast cancer issue. The FDA rejected the initial magazine's proposed message for numerous reasons, including the fact that it "intentionally misleads the reader into thinking that her physician is somehow responsible for providing it to her" (A-I-000217) (emphasis in original) and contains "articles" that illegally promote off-label (unapproved) benefits of HT (A-I-000218-000219). In sum, the FDA wrote:

> "We view this campaign in its entirety to be a form of extremely insidious hidden persuasion....[It is] an insidious marketing ploy masquerading as concern for the health of post-menopausal women" (A-I-000219).

Wyeth was forced to alter the campaign. (T-XV-2749:5-2750:21).

8. The Cummings study

Dr. Steve Cummings' work involved a 10-year prospective study of older women, sponsored by the National Institutes of Health (T-IV-568:2-8). The results, revealed in 1996, showed that a woman's bone mineral density affected her chance of developing breast cancer. Since E+P was being prescribed to prevent osteoporosis, Dr. Cummings concluded that "the risk of breast cancer associated with HT may have been substantially underestimated" (A-II-000352). Wyeth admitted this study could call into question previous information the company had given to doctors (T-IV-567:9-12).

Such important study findings should have led to immediate dissemination of the information with new warnings. Wyeth did the exact opposite. First, Wyeth established a Breast Cancer Working Group led by executive Jeff Buchalter who distributed the Cummings abstract to the group with a memo warning: "Please keep this confidential -- Do not discuss w/ anyone outside of W-A [Wyeth-Ayerst]" (A-II-000359) (emphasis in original). In a handwritten document relating to the Cummings memo, Buchalter wrote: "Dismiss/Distract" after outlining Wyeth's strategy to avoid bad press: "Keep US press busy" (A-II-000361).

Wyeth's breast cancer task force followed Buchalter's directive. Its strategies for downplaying the Cummings findings included: encouraging third-party allies to dismiss the data, downplaying the study, creating press material to

counteract and discredit the data and retaining spokespeople to counterbalance the breast cancer risk (A-II-000350; A-II-000356; T-III-470:12-18; T-IV-569:5-571:10; T-IV-572:9-14).

Even Dr. Lisa Rarick, Wyeth's regulatory expert, acknowledged that such tactics were improper (T-XII-2340:24-2341:13).

9. Criticism of horse estrogen: "Letting sleeping dogs lie"

In 2000, Dr. T.H. Lippert of Germany reported that the majority of studies showing a breast cancer risk from hormone therapy involved horse urine estrogen (Premarin). In discussing how Wyeth should respond, Victoria suggested internally that there may be advantage to "letting sleeping dogs lie." He warned that Wyeth should avoid any discussion of the composition of its product (A-II-000372).[5] Rather than study the issue, Wyeth intentionally chose to ignore it and downplay it.

10. Ghostwriting

One notorious tactic Wyeth used to dismiss and distract attention from adverse data was ghostwriting articles to combat the data. The steps involved in an article purportedly written by Dr. John Eden best exemplify the strategy. Ghostwriting occurs when a drug company creates the idea for an article, hires a company to write the manuscript and retains a physician to publish the "ghost-

[5] The Lippert article attached to this memo was deemed a learned treatise that would not go back with the jury.

written" paper under his name alone, allowing the paper to maintain the appearance of independent support from a scientist.

For the Eden paper, Wyeth decided on an article concluding that progestin's addition to estrogen does not cause breast cancer (A-II-000376). Wyeth selected Dr. Eden to act as the "author" (A-II-000373; A-II-000375). Wyeth hired DesignWrite, a technical writing company, to create a manuscript for Wyeth's approval and editing, which could then be sent to the named author (A-II-000378; A-II-000380; A-II-000382; A-II-000383). DesignWrite's "writer," an English major (not a scientist), was paid to write the article (A-II-000377). Dr. Eden made a few "technical changes" to the manuscript (A-II-000384-000413; T-VII-1341:11-1343:3) and DesignWrite arranged for the article to be published in the Journal of Obstetrics and Gynecology, a journal widely read by OB/GYNs (T-VII-1339:20-24).

DesignWrite prepared the submitting cover letters for the named author's signature (A-II-000414). Dr. Eden's article, "Progestins and Breast Cancer," (A-II-000384; A-II-000417-000425) made no mention at all of Wyeth's or DesignWrite's involvement but did conclude that there was no evidence that progestins cause breast cancer. Other authors then cited the Eden ghostwritten article as authority, including Wyeth's Dr. Ginger Constantine in an article she

wrote later (T-X-1935:7-21). Eventually, ghostwritten articles become part of scientific parlance, their origins unknown to the doctors relying upon them.

What was the motive behind this dismiss-and-distract policy? Money. E+P was very important financially to Wyeth. Indeed, at the Prempro launch meeting in April, 1995, soon-to-be CEO Robert Essner announced that Premarin had become Wyeth's biggest-selling product. Hormone therapy was the company's most important asset and priority. Essner characterized the product's marketing plan as "a Holy War, a Crusade, more than a typical pharmaceutical marketing effort" (A-II-000525). To Essner, the company's future depended on the success of marketing of these drugs (A-II-000533). Wyeth's goal was to create a "revolution" in women's health "where the majority of women will start HRT at menopause and continue on it for the rest of their lives" (A-II-000532). A billion dollars in sales would just be the starting point (A-II-000532). In stark contrast, Wyeth spent nothing on studies to investigate Prempro's suspected risk of breast cancer.

D. Prempro's Approval: the WHI Study Begins

Wyeth's paper application for a two-pill E+P package eventually became an application for a single pill containing E and P called "Prempro" (T-VII-1307:22-1308:2). Since the 1970's, the FDA had urged Wyeth to conduct studies to establish the safety and efficacy of E+P (T-VII-1310:20-1311:5). Wyeth had done

nothing. By 1993, the use of E+P by doctors was rampant. The FDA was left with only two choices: continue not to approve E+P because of the lack of data, even though doctors were using the combination at risk to women, or grant a conditional approval that would finally require Wyeth to conduct a breast cancer study. The FDA lacked power to order Wyeth to study E+P (as that was a combination therapy made up of two already approved drugs being used off-label), thus it chose option two (T-VII-1313:14-23). In December 1994, FDA approved Prempro on condition that Wyeth conduct a post-marketing "comprehensive investigation of the breast cancer risk".[6] (A-II-000344; T-IV-558:15-17). Specifically, the FDA recommended that Wyeth conduct a case-control study in areas of greatest use of E+P (T-III-480:3-13; T-XII-2332:11-2333:8).[7]

While the Prempro application was pending, the National Institutes of Health (NIH) decided to perform a randomized clinical trial on E+P to determine whether the drug provided the cardiovascular benefits Wyeth had long touted. This study was named the "Women's Health Initiative" (WHI). Though the cardiovascular results of the WHI were highly anticipated, the FDA did not believe the study would answer the breast cancer question. A randomized trial on

[6] A Phase IV study like this is conducted after product approval to obtain more safety data the FDA feels is needed (T-VII-1309:19-25).

[7] A case-control study looks at population groups and official reports of cancer to ascertain commonalities among those acquiring the disease (T-VII-1246:5-10).

therapeutic *benefits* is often not powerful enough to quantify *side effects* such as breast cancer (T-III-465:15-25; T-XI-2173:21-2174:2; T-XII-2331:16-19). Nevertheless, Dr. Rarick, an FDA official at the time, approved Wyeth's 1997 request to have the company's support for WHI satisfy its Phase IV commitment to get comprehensive answers to the breast cancer question (A-II-000363). Dr. Rarick now works for Wyeth as an expert and testified at this trial. So, despite agreeing to the conditional approval of Prempro, Wyeth never performed a Phase IV case-control study. Instead, Wyeth continued marketing E+P as safe while waiting for the taxpayer-funded WHI study to provide some answers.

E. Wyeth's Old Labels: A Reassurance to E+P Users

Because Wyeth failed to conduct studies that would reveal the true breast cancer risk of E+P, the Premarin and Prempro breast cancer warnings were milquetoast. Any caution expressed in one sentence of the label was taken away or neutralized in the next sentence. Mild warnings were counteracted by reassuring statistics. Consider the Premarin label. It noted that the "majority of studies" showed no breast cancer risk with the usual doses of estrogen. The only studies that had shown a risk involved higher doses of estrogen and prolonged duration of use (A-III-000841; T-VII-1345:10-15). Significantly, the Premarin label did not even discuss the risk of E+P; its warnings were limited to estrogen alone (T-III-440:5-16).

Dr. Suzanne Parisian was a chief medical officer for the FDA in the division that included reproductive devices (T-VII-1226:5-1227:3; A-III-000746-000766; T-VII-1227:12-17). When Dr. Parisian worked in the Office of Compliance, she reviewed product labeling to ensure compliance with FDA regulations (T-VII-1250:12-18). She testified that the language of the Premarin label would not have conveyed a risk of breast cancer to physicians or patients like Ms. Scroggin, who were using E+P (T-VII-1345:1-23). Dr. Irving Kuperman, Ms. Scroggin's prescribing physician, testified that he did not perceive a risk of breast cancer from the Premarin label (T-V-765:13-767:7).

The Prempro label provided no stronger warning. Like the Premarin label, it noted that "most studies" showed no higher risk in women who have ever used ***estrogens*** (A-III-000838; T-IV-688:3-15) (emphasis added). Dr. Parisian testified that this suggested no real risk (T-VII-1303:16-20). Dr. Kuperman confirmed that the language suggested no risk to him (T-V-777:13-778:15; T-V-780:6-17). The label also said that the effect of adding progestins was "unknown," with some studies suggesting a risk and others showing no risk (A-III-000838; T-IV-688:3-15). Dr. Kuperman testified this language suggested there is no unique risk to E+P

(T-V-778:24-779:10). The label had no black box warning on breast cancer (T-III-479:16-22).[8]

Particularly reassuring to Dr. Kuperman was the Prempro label's claim that Wyeth's clinical study established that the rate of breast cancer among E+P users was no greater than the rate among the general population (T-IV-700:14-21; T-V-799:11-780:13). Even Victoria admitted that a reasonable physician could view this language as suggesting no risk of breast cancer (T-III-478:23-479:3). The referenced study lasted only one year, much shorter than the lengthy duration of use Wyeth encouraged, and was not designed as a breast cancer study (T-III-469:9-22; T-IV-694:22-24; T-X-1909:21-22).

Wyeth's witnesses did not deny that the labels failed to convey the actual risk of breast cancer; they claimed that the labels accurately reflected the science of the time (E.g., T-XIII-2440:11-17 (Stovall)). But the point is that the science of the time was inadequate because of defendants' unreasonable failure to study. The issue is not whether Wyeth failed to warn of the risk it knew, but whether Wyeth failed to warn of the risk it should have known, had it behaved as a reasonably-prudent pharmaceutical company and studied known uses of its product as well as clearly unanswered risk questions.

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[8] A black box includes particularly strong warnings and draws the attention of physician to the risks (T-V-760:23-761:8; T-XII-2328:24-2329:6). The current label identifies the breast cancer risk, among other risks established by the WHI, in a black box appearing at the beginning of the label (A-III-000845).

II. UPJOHN'S STRATEGY: DO NOTHING AT ALL

Wyeth's conduct is akin to the lifeguard who climbed his chair, but ignored the pleas for help from the pool. Upjohn is the lifeguard who didn't even get out of bed that day. The above facts regarding the inadequacy of studies on the risk of E+P apply equally to Upjohn. Dr. Constantine testified that Upjohn had the same access to medical literature that Wyeth had (T-X-1961:6-9). At trial, Ms. Scroggin showed that Upjohn was under a heightened obligation to study yet did nothing at all.

Upjohn manufactured Provera, a synthetic progestin. Provera was approved for sale in 1959 for the treatment of abnormal uterine bleeding (T-VII-1350:17-25) Provera was not approved for use with estrogen to treat menopausal symptoms until 1998 (A-III-000872 at 226:9-24). Yet, Upjohn repeatedly applied for precisely such a menopause indication and, despite repeated FDA rejections, continually advertised Provera for this unapproved use. But Upjohn never studied the breast cancer risk of which it was well aware.

Upjohn knew by 1963 that Provera may cause breast cancer, when a published article reported the risk (T-XI-2198:18-2201:1). Undeniably, Upjohn was aware of the risk by 1970 when Upjohn withdrew Provest, an oral contraceptive containing both E and P, from the market based on a study showing that progestin caused mammary nodules in beagle dogs. (A-II-000522; T-XV-

2731:15-2732:7). The beagle dog study and Provest's removal put Upjohn on notice of the need to study the breast cancer potential of Provera (especially when used with Premarin, because the combination would contain the same active ingredients as Provest). Upjohn knew that Provera was 36 times more potent than endogenous progesterone (A-III-000704). Yet, as late as 1992, Upjohn's internal memos confirmed that the breast cancer risk of E+P was still unknown (A-III-000830-000832).

A. FDA Rejections of Upjohn's Applications

Upjohn first applied for a menopausal indication for use of Provera with estrogen in 1966. The FDA rejected the application due to lack of study on E+P (A-III-000714). Upjohn applied again in 1986, despite never conducting or even supporting a single long-term study. Again, the FDA denied the application due to the lack of adequate study (A-III-000706-000707). Upjohn claimed at trial that the FDA only sought studies establishing the efficacy of Provera in protecting the uterus but did not ask for safety studies. That is false. In 1986, the FDA expressly told Upjohn that "the potential risks [of E+P] are not yet resolved" (A-III-000713). The FDA was concerned about the lack of evidence of both safety and efficacy (T-VII-1376:13-1377:11).

B. Upjohn's Illegal Advertising of the Unapproved Combination

Despite the FDA's rejection of Upjohn's applications and Upjohn's failure to conduct a single safety study, Upjohn illegally advertised Provera for menopausal use repeatedly, even after the FDA told Upjohn to stop. Upjohn began advertising Provera for use with Premarin in the 1960's. The FDA consistently demanded that Upjohn stop such advertising (T-VII-1359:19-1360:2). In January 1984, the FDA instructed Upjohn to withdraw a Provera ad and cease advertising combination use because it had not been approved (A-III-000705). Upjohn agreed to confine its advertising to treatment of abnormal bleeding (A-III-000708). Yet, nearly two years later, Upjohn was still promoting Provera for combination use. The FDA noted that Upjohn breached the agreement and must stop promoting off-label use, declaring it inappropriate for Upjohn to claim E+P was safe and effective. The FDA warned: "Further attempts to promote this product beyond your approved indications will cause us to seek stronger regulatory relief" (A-III-000708).

But Upjohn's illegal campaign continued unabated. In 1990, Upjohn submitted several ads for FDA approval that promoted Provera for use with estrogen in post-menopausal women. Over the next several months, the FDA repeatedly disapproved of these ads and instructed Upjohn to withdraw them. Upjohn ran the ads anyway. (A-III-000709-000710; A-II-000510; A-III-000712).

C. Upjohn's Refusal to Study the Breast Cancer Risk

Upjohn never conducted a study on the risk of breast cancer from E+P. Dr. Parisian, the aforementioned FDA medical officer, is a board-certified physician who began practicing medicine in 1979 (T-VII-1224:4-15; A-III-000746-000766). Her work at the FDA included the review of epidemiological studies (T-VII-1270:14-20). Dr. Parisian reviewed the epidemiological studies involved in this case (T-VII-1270:21-1271:3) and testified that, from the 1960s to the present, Upjohn conducted no breast cancer study on E+P (T-VIII-1563:24-1564:3). Plaintiffs' expert, Dr. Austin, after reviewing the literature, found no Upjohn breast cancer studies (T-II-241:24-242:2).

Upjohn's own witnesses concurred. Dr. Rodney Carlson, Upjohn's former Director of Medical Affairs, testified that Upjohn never studied or sponsored a study on the breast cancer risk of E+P (A-III-000716-000717 at 24:1-6; A-III-000723-000724 at 54:22-55:1; 55:12-15; 58:20-59:23; A-III-000736 at 141:15-142:9). Dr. Heidi Jolson, Upjohn's regulatory expert, admitted that her client conducted no breast cancer study of any type (T-XI-2195:5-11). Nor did Upjohn encourage or cooperate with others to conduct such studies (T-XI-2214:9-17). Upjohn did not even propose a protocol to the FDA for such a study (T-XI-2197:5-12).

Upjohn certainly knew how to conduct studies. From 1982 to 1994, Upjohn performed 34 different studies designed to establish Provera's efficacy in reducing the endometrial effects of estrogen. None of these studies was designed to look for breast cancer and none was large enough or long enough to identify the breast cancer risk (T-XI-2214:18-2215:9). Michael Schoenfeld, a clinical trials specialist at Upjohn for 20 years (A-III-000859-000860 at 159:16-19; 165:4-7), testified that none of the studies Upjohn conducted on E+P lasted more than two years (A-III-000877 at 256:13-257:4). Carlson agreed and admitted that two years is an insufficient period to detect a breast cancer risk (A-III-000732 at 98:9-18).

During the 50 years Provera has been on the market, the only act Upjohn ever undertook to examine the product's potential breast cancer risk was to retain the Degge Group to review the epidemiological literature in preparation for the 1990 FDA advisory committee meeting (A-III-000718-000719 at 30:21-32:24). The Degge Group's review concluded that more studies were needed. (A-II-000607). Yet Upjohn intentionally ignored the conclusion and recommendations of its own consultant and never supported or conducted a study to assess breast cancer risk.

D. The Upjohn Label: No Breast Cancer Warning at All

Amazingly, until 2007 Upjohn never warned of any risk of breast cancer from Provera or E+P (E.g., A-III-000853-000855; A-III-000856-000858; A-II-

000593-000594; A-II-000595-000596). Dr. Jolson admitted that Upjohn did not warn of the risk of breast cancer during the time Ms. Scroggin ingested the product (T-XI-2195:12-18). Dr. Kuperman likewise found no warning of breast cancer in the label (T-V-883:8-12). One section of the Provera label noted that beagle dogs treated with progestin developed mammary nodules, but then established that the significance of this finding to humans was unknown (A-II-000594; A-II-000596; T-VII-1375:6-21). Even the 1999 label contained no human breast cancer warning (T-V-866:15-18).

Upjohn never petitioned the FDA for a warning on breast cancer -- or even drafted such a warning. Upjohn did not seek to incorporate the Degge Group's findings into the label (A-III-000724 at 56:15-58:13). Nor did Upjohn send a Dear Doctor letter discussing the Degge Group report (A-III-000724 at 58:15-19).

III. E+P CAUSED DONNA SCROGGIN'S BREAST CANCER

As noted above, the WHI clinical trial was designed to determine whether E+P provides cardiac benefits (T-X-1821:4-20). A safety alarm was built into the study that would sound if breast cancer rates exceeded a predetermined level. The cancer rates surpassed that level before the study group had averaged even five years use. The study was abruptly stopped and the results were published on July 9, 2002 (T-XIII-2436:20-2437:5; T-XV-2739:3-7; T-XVI-2857:13-21), long before the study's planned termination.

found a 256% increased risk (RR 3.56) for E+P use of five years (T-II-202:11-203:9; T-VI-950:11-951:1). An analysis by Wyeth revealed an even higher risk, 361% (RR 4.61) for women using E+P for five to 10 years (T-X-1934:23-1935:4).

The proof is indisputable:

- The aforementioned Dr. Colditz, world-renowned breast cancer epidemiologist (A-III-000768 at 16:24- 18:2), author of over 700 peer-reviewed articles (A-III-000769 at 20:19-21:7), professor of medicine at Harvard Medical School (A-III-000768-000769 at 19:3-20:3), and, currently, associate director for cancer prevention and control at the Siteman Cancer Center at Washington University School of Medicine in St. Louis (A-III-000768 at 18:19-19:4) testified that epidemiological studies have **confirmed the causative relationship** between E+P and breast cancer (A-III-000783 at 73:19-74:5).

- At least a dozen epidemiological studies have now established a 2.0 or greater relative risk (A-III-000791-000792 at 108:8-109:2). Indeed, the epidemiological data now consistently establishes increased risk of breast cancer with long duration of E+P use (A-III-000783-000785 at 74:6-77:3). This body of evidence establishes a general causal relationship (A-III-000772-000773 at 34:23-35:10; A-III-000783 at 73:7-18; A-III-000790-000791 at 105:16-106:12). Dr. Colditz developed and published this opinion long before this litigation began (T-III-403:13-404:8; T-III-406:8-10).

- Dr. Austin, reviewed a "sizable portion of the world literature," and agreed that the epidemiological data strongly shows a causal relationship (T-II-176:12-177:15; T-II-214:11-21). Animal studies likewise confirm the link (T-II-227:7-18). Dr. Austin testified that the available scientific data confirms that E+P causes breast cancer (T-II-178:24-179:3; T-III-276:8-277:11).

- Dr. Elizabeth Naftalis, a board-certified, licensed breast surgeon, (T-VI-922:6-10; T-VI-924:11-18; T-VI-929:16-18; A-II-000582-000592) who teaches, researches and publishes on the subject (T-VI-925:3-

928:14; T-VI-929:19-930:9; T-VI-932:7-14), testified that E+P causes breast cancer (T-VI-945:22-946:2).

- Dr. Brian MacMahon, a world-renowned expert on breast cancer who chaired the epidemiology department at the Harvard School of Public Health, (A-III-000781 at 61:16-23), published that there are three known causes of breast cancer, including hormone therapy use (A-III-000781 at 62:8-16). Dr. Colditz testified that Dr. MacMahon's findings are both authoritative and reliable (A-III-000781 at 61:24-62:4).

- The IARC, the international organization charged with identifying cancer causes, now classifies E+P as a known carcinogen of the breast (A-III-000782 at 64:8-18; A-III-000785-000786 at 80:22-81:2).

- Dr. Colditz testified that a causal relationship is generally accepted (A-III-000780-000781 at 61:5-61:12). Dr. Austin testified there is no longer any serious debate about the causative effect (T-II-179:4-6).

E+P causes breast cancer through promotion. Dr. Colditz explained E+P promotes the growth of abnormal, benign cells into malignant tumors (A-III-000773-000776 at 43:6-43:14; 48:13-49:4). E+P causes abnormal cells in the breast to proliferate and grow more rapidly than they would otherwise (A-III-000773-000775 at 42:4-43:5; 46:18-48:12; A-III-000779 at 58:9-59:2). Using layman's terminology, E+P is like fertilizer on plants and is essential to the growth of hormone-sensitive breast cancer (A-III-000776 at 49:15-21; A-III-000780 at 59:12-61:4). A hormone-sensitive cancer tests positive for the presence of estrogen receptors (ER) and progesterone receptors (PR). An ER+/PR+ tumor is one that requires hormones to fuel its growth (T-VI-972:25-973:6; T-VI-1077:7-8).

Stated differently, the presence of hormone receptors establishes that hormones are responsible for the cell's growth (T-VI-973:7-15; A-III-000809 at 174:11-175:4).

Everyone has abnormal cells in the body (A-III-000780 at 60:4-21). Autopsy studies have shown that it is common for women who die of causes other than breast cancer to have benign abnormal cells or lesions in their breasts -- lesions that were unknown and undetected (T-VI-974:19-975:5). Those lesions grow into cancer only under the right conditions (A-III-000780 at 60:11-61:4). Absent hormones, lesions that would have grown into hormone receptor-positive tumors will die or remain dormant (A-III-000780 at 59:12-60:2).

As Drs. Colditz, Austin and Naftalis testified, E+P does not initiate the first bad or abnormal cell. E+P promotes the growth of preexisting abnormal cells or lesions into cancer (A-III-000776 at 49:6-14; T-II-227:19-23; T-III-279:7-14; T-VI-937:16-938:6; T-VI-939:2-9; T-VI-975:12-24). A patent application filed by Dr. Lewis Chodosh (Wyeth's cell biology expert) in 1999 states: "A wealth of epidemiological evidence indicates that ovarian hormones play a crucial role in the etiology of breast cancer" (T-XI-2063:25-2064:22). Dr. Kevin Fox, a professor at the Abramson Cancer Center of the University of Pennsylvania, the very center where Dr. Chodosh works, acknowledged that estrogen receptor-positive tumors must have estrogen to grow (T-XI-2085:5-24).

The promotion effect is described and defended in both textbooks and the medical literature (T-VI-975:6-11; T-XI-2074:20-2075:15). The scientific community generally accepts promotion as the means by which E+P causes breast cancer. Similarly, the scientific community agrees that promotion is the way E alone caused the endometrial cancer crisis (A-III-000776 at 49:22-50:14; A-III-000786-000787 at 91:24-92:24). Even Dr. Chodosh was forced to concede that E alone causes endometrial cancer by promotion, given the short time period involved (T-XI-2064:23-2065:3; T-XI-2071:15-19).

Ecological data provides strong evidence of promotion.[10] Ecological data reveals that breast cancer rates are directly affected by E+P. Increased prescriptions have corresponded to increased rates of breast cancer (A-III-000787 at 93:2-15). Conversely, the precipitous drop in prescriptions that occurred after WHI resulted in a dramatic decline in breast cancer incidence (T-VI-980:2-981:2; A-III-000787-000788 at 93:17-95:20). Dr. Peter Ravdin, a world-renowned cancer expert independent of this litigation, published the results of his study in the New England Journal of Medicine (T-II-254:5-18), concluding that breast cancer rates decreased dramatically in the year following announcement of the WHI results and continued to decline thereafter. This decline corresponded precisely to decreased prescriptions of E+P (T-II-254:19-256:10). It mirrored the decline in endometrial

[10] "Ecological data" shows trends in the prevalence of events in a population (T-II-174:2-175:2).

cancer following decreased use of E-alone when studies linked the drug to that disease (A-III-000789-000790 at 102:14-103:4). The almost-immediate effect on breast cancer rates occurring after changes in use suggest that causation is by "promotion" rather than "initiation" (T-II-251:3-253:3).

The post-WHI decline in breast cancer rates was most dramatic in postmenopausal women (A-III-000789 at 100:7-22) and occurred only for hormone receptor-positive tumors. The rate of hormone-negative cancer remained steady during this time period (T-II-258:5-19; T-VI-981:3-982:2; A-III-000789 at 100:7-22).

This correlation of prescriptions and breast cancer rates going up and down, in lock step, is strong support of a causal relationship between E+P and breast cancer (T-III-280:2-11; T-VI-981:3-982:2). The only explanation for this dramatic decline in cancer was the equally dramatic drop in E+P use (T-II-262:1-9). Based on this ecological data, Dr. Karla Kerlikowske estimated that E+P was responsible for 17,500 new cases of breast cancer in this nation annually (T-XV-2722:7-24).

E+P caused Donna Scroggin's cancer. The tumors in her breasts were estrogen receptor-positive and progesterone receptor-positive (A-III-000834-000836). Dr. Mariann Harrington, a board-certified, 28-year oncologist who treated Ms. Scroggin's cancer (T-V-714:20-716:8), testified that the tumors in both breasts were 100 percent ER+/PR+ (T-V-719:24-720:4; T-V-720:5-6).

The hormones fueling the growth of Ms. Scroggin's tumors came from E+P, not her own body. Ms. Scroggin suffered from menopausal symptoms (T-VI-957:7-16), including hot flashes (T-VI-974:4-11; T-VI-1092:10-1093:14) and vaginal atrophy (T-VI-1079:5-13). That is why she took E+P for 11 years (T-VI-1096:2-4). The type and degree of menopausal symptoms from which she suffered led Dr. Naftalis to conclude Ms. Scroggin was estrogen-deficient (T-VI-957:20-958:2).[11] Thus, more likely than not, exogenous (externally administered) hormones -- E+P -- fueled the growth of her tumors, rather than endogenous (her own natural) hormones, because she was deficient of natural hormones after menopause (T-VI-974:12-18).

Dr. Kuperman acknowledged that hot flashes are caused by low levels of estrogen (T-V-753:8-14). Before this litigation, Wyeth always agreed. In fact, a study Wyeth funded showed that menopausal symptoms are the product of estrogen deficiency (T-VI-1077:22-1079:4). Wyeth's own literature confirms that estrogen deficiency is responsible for menopausal symptoms (T-III-410:9-411:11). The reason hormone therapy effectively treats menopausal symptoms is because those symptoms are caused by lack of estrogen (T-VI-1080:1-17). There was no

[11] While non-symptomatic women may continue to produce tangible levels of estrogen after menopause (T-IX-1589:5-19), post-menopausal women produce, at most, trivial levels of progesterone (A-III-000807-000808 at 151:7-12).

dispute at trial that vaginal atrophy is the result of estrogen deficiency (T-VI-1079:5-13).

Based on these facts, and her own differential diagnosis, Dr. Naftalis concluded that Donna Scroggin's approximately 11-year-ingestion of E+P was the "but/for" cause of her cancer, based on reasonable medical probability (T-VI-977:18-25). Absent her use of E+P, Ms. Scroggin would not have developed bilateral breast cancer (T-VI-972:2-9; T-VI-981:22-982:2; T-VI-1076:8-20). This is particularly true because the tumor in Ms. Scroggin's left breast was tubular (T-X-717:18-718:8 (Dr. Harrington); T-VI-940:25-942:3; T-VI-951:2-8 (Dr. Naftalis)). The 5.0 relative risk of developing tubular cancer from E+P is so high that it, alone, is sufficient evidence that E+P caused the tumor in Ms. Scroggin's left breast (T-VI-951:9-14).

IV. THE DIFFERENCE ADEQUATE STUDY WOULD HAVE MADE

Defendants could have performed studies in the 1980s that would have evaluated, quantified and confirmed the breast cancer risk. Wyeth admitted that the most feasible study would have been a case-control study (T-IV-558:18-559:4), the type of study the FDA requested from Wyeth in its conditional approval of Prempro (T-IV-560:13-561:14). Adequate data existed in the late '70's and early '80's for a case-control study (T-VII-1246:11-19). Because a case-control study looks retrospectively at existing data, a case-control study begun in 1980 could

have been completed in approximately two years (T-II-224:6-17), But it could have looked at duration of use in excess of 10 years because the study would have examined data that already existed (T-VII-1245:23-1246:4).[12] Case-control studies in the 1970's produced the data establishing that E alone causes endometrial cancer (T-XI-2187:5-2188:5; T-XII-2315:25-2316:7). Further, either defendant could have performed a WHI-like clinical trial during the same time frame, using separate E and P pills (T-XV-2702:2-2703:2). Wyeth stipulated that such a study would have been financially feasible (T-IX-1593:7-19).

If these studies had been conducted, the warnings for E+P would have been dramatically different (T-VIII-1385:4-7). The appropriate product label after such study would have imparted precisely the same warnings that the post-WHI labels conveyed. It would have conveyed the breast cancer warning in a black box. The black box would have contained warnings of the risk of myocardial infarction (heart attacks), blood clots, DVTs and pulmonary emboli, at a minimum. The label would have advised that long-term use of over five years is particularly risky. And it would have identified alternative treatments (T-VIII-1385:8-1386:8).

More likely than not, such a label would have averted Donna Scroggin's breast cancer. Dr. Kuperman would likely not have prescribed the drug for a

[12] This contrasts sharply with the clinical trials Upjohn performed on Provera to determine whether the drug would be profitable. Those studies involved only two years use of the drug (SOF, II(C), *supra*).

duration that would have injured her. Dr. Kuperman acknowledged that his prescriptions of E+P declined after WHI (T-V-790:5-6). He now tries to wean patients off the drug (T-V-789:5-16; T-V-871:9-16) prescribes the product only in severe cases involving "significant" symptoms, and then, for the shortest duration (T-V-787:1-7). Dr. Kuperman no longer automatically prescribes or encourages E+P; he simply discusses the option with his patients (T-V-801:16-19; T-V-821:13-18). After WHI, he told Wyeth's sales representatives that he was averse to E+P and wanted no more Prempro samples (T-V-871:21-872:3). Around the same time, he told his colleague, Dr. Hagler, that he was strong in his skepticism of the combination (T-V-871:17-20).

Dr. Kuperman would likely have removed Ms. Scroggin from the drug many years before she developed cancer. In the 1990's, his practice was to prescribe E+P long-term (T-V-775:7-21), for even 10 to 15 years (T-V-787:8-12). Today, most of the time, he prescribes E+P for fewer than five years (T-V-787:13-15). Such a duration would not have caused Ms. Scroggin's cancer. As shown above, the risk of cancer plummets upon cessation of E+P use. It took 11 years of use for Ms. Scroggin to develop breast cancer. Dr. Naftalis testified that, had Ms. Scroggin used the drug for five years, she would not have developed cancer (T-VI-972:16-24).

At the very least, Dr. Kuperman would have honored Ms. Scroggin's wishes that he refrain from prescribing the product. Dr. Kuperman testified he would have passed on all information he learned to Ms. Scroggin (T-V-755:10-17; T-V-767:22-25). Dr. Kuperman would not have prescribed E+P to a patient who told him she didn't want the drug after they discussed its risks and benefits (T-V-787:19-788:5). He would have respected a patient's wish not to take the drug, or to take it no more than five years (T-V-788:11-19). Ms. Scroggin would have stopped taking the drug had she been given the facts about the panoply of harms it creates (T-VII-1145:10-17). She would not have taken the drug long-term (T-VII-1145:10-17).

Donna Scroggin would therefore still have both her breasts and her peace of mind. Because of her use of E+P, Ms. Scroggin developed multiple tumors in both breasts (T-IX-1755:22-24). Her surgeon, Dr. Hagans, testified that at least one tumor in each breast was invasive (T-IX-1754:21-25). He therefore recommended a double mastectomy (T-VI-1106:4-12). Ms. Scroggin had both breasts surgically removed (all the way down to the muscle) as well as the lymph nodes under both arms (T-VI-943:18-24). Ms. Scroggin was afraid of additional surgery, so she

declined reconstruction and is now dramatically scarred for life (T-VI-943:25-944:7; T-VII-1145:2-5).[13]

Ms. Scroggin experienced six months of "scary" chemotherapy that involved administration of drugs through a port in her chest. The procedure caused nausea, anxiety, hot flashes, severe fatigue and, paradoxically, difficulty sleeping (T-V-736:19-25; T-VI-1109:2-1110:6). Ms. Scroggin was then placed on Tamoxifen, a drug that stripped her body of estrogen, for five years (T-VI-1110:7-17). This brought back the very menopausal symptoms that hormone therapy was supposed to alleviate (T-V-737:1-8; T-VI-1110:7-17). No drug could treat the night sweats she experienced (T-V-739:1-4).

Ms. Scroggin incurred necessary and reasonable medical expenses for her cancer treatment (T-VI-979:17-980:1 & cited exhs.). She will be at risk for return of cancer for the rest of her life (T-V-729:7-13). Her mental state has never returned to normal (T-VI-1111:6-24).

[13] To protect Ms. Scroggin's privacy, photographs of her disfigurement were placed in a manila envelope during the trial so individual jurors could decide whether to view them (T-VII-1143:12-114:5). They have been removed from the envelope and appear at A-III-000743-000745.

SUMMARY OF THE ARGUMENT

In July 2002, the National Institutes of Health abruptly terminated the largest clinical trial ever performed on women. The Women's Health Initiative study was designed to determine whether postmenopausal combination hormone therapy -- estrogen with progestin (E+P) -- offered cardiovascular benefits. Just a few years into the study, no heart benefits were seen but breast cancer incidence became unacceptable. News of the results caused prescriptions of the drugs to plunge. The rate of breast cancer then plummeted. The medical community learned that E+P had caused thousands of women to develop cancer every year. One of those women was Donna Scroggin.

Ms. Scroggin's plight is the result of two drug companies putting profits over public health. Wyeth and Upjohn have been aware for decades of the breast cancer potential of E+P. The FDA and scientists alike repeatedly urged the companies to study the risk. The companies ignored red flag after red flag because they feared the inevitable – loss of a lucrative product when the truth of its cancer-causing effect emerged.

Wyeth went to great lengths to suppress, downplay and deflect continued findings of the breast cancer risk of its product. Wyeth used friends, allies, public relations firms and internal containment groups to dismiss and distract from the risk of breast cancer, even though Wyeth had never studied that risk for E+P.

Upjohn repeatedly applied for an E+P indication, ignoring the FDA's multiple demands for study, repeatedly advertised E+P, ignoring the FDA's multiple demands to stop, and declined to place any breast cancer warning at all in its label. Yet, at no time, did Upjohn ever conduct or even support a study on the breast cancer risk.

After hearing four weeks of testimony about the willful disregard for women's health these defendants exhibited, the jury awarded Ms. Scroggin compensatory damages and levied substantial punitive damages against Wyeth and Upjohn. The district court denied defense motions to set aside or retry the liability findings and compensatory award. But the court vacated the punitive award, issuing an opinion that relies on evidence and inferences from the evidence against the verdict (including the interested testimony of defendants' own witnesses) and ignores a plethora of evidence supporting the verdict. The court's failure to follow the applicable standard for review of a jury verdict warrants reversal and reinstatement of the punitive award.

ARGUMENT

The granting of judgment as a matter of law is reviewed *de novo*. *Marti v. City of Maplewood, Mo.*, 57 F.3d 680, 683 (8th Cir. 1995). The remedy is appropriate only if the evidence, viewed in the light most favorable to the verdict, is such that no reasonable juror could have returned a verdict for Donna Scroggin. *Minn. Supply Co. v. Raymond Corp.*, 472 F.3d 524, 536 (8th Cir. 2006). Appellate review of the jury's verdict is "extremely deferential." *Day v. Toman*, 266 F.3d 831, 836 (8th Cir. 2001) (citation omitted). The presumption is that the jury made the right inferences from, and properly weighed, the evidence. *Id.* All conflicts must be resolved and all reasonable inferences made in favor of Ms. Scroggin. *See Schooley v. Orkin Extermination Co.*, 502 F.3d 759, 764 (8th Cir. 2007).

Arkansas law allows punitive damages for "malicious" conduct, *Ellis v. Price*, 990 S.W.2d 543, 548 (Ark. 1999) or conduct done with a "wanton and conscious disregard for the rights and safety of others." *Dalrymple v. Fields*, 633 S.W.2d 363, 363 (1982) (*both cited in Boerner v. Brown & Williamson Tobacco Co.*, 394 F.3d 594, 601 (8th Cir. 2005)). "[M]alice is not necessarily personal hate. It is rather an intent and disposition to do a wrongful act greatly injurious to another." *Fegans v. Norris*, 89 S.W.3d, 919, 925 (Ark. 2002) (citations omitted).

Defendants engaged in a decades-long course of action that reflected conscious indifference to women's health. Both knew that E+P risked breast

cancer, yet both declined to study the product for over two decades to protect their bottom lines.

In addition, Wyeth engaged in a deliberate, comprehensive campaign to dismiss evidence of the breast cancer risk and distract the media and public alike from that risk. Wyeth's conduct is akin to the defendant's actions in *Boerner*, 394 F.3d at 601, where, like the instant case, the defendant's product caused cancer. The *Boerner* defendant was aware of the risk, yet downplayed and misrepresented it, attempting to suppress evidence revealing the risk. *Id.* at 601. Similarly, Wyeth was aware that its first HT product (E-alone) caused endometrial cancer and deliberately misrepresented that fact to every OB/GYN in the country. Even after the FDA chastised Wyeth for such blatant misrepresentation, Wyeth continued to practice deceit after discovering that its second product (E+P) increases the risk of breast cancer. Wyeth not only refused to study this risk, but consistently undermined reports of the risk by others. This Court found similar evidence sufficient to justify a punitive award in *Boerner* and it should find the evidence sufficient here. *Id.* at 601.

Upjohn's misconduct and omissions were equally reprehensible. Upjohn repeatedly ignored admonitions by the FDA to refrain from marketing Provera with estrogen until the safety and efficacy of the combination was established. Upjohn marketed the product in violation of the law without ever performing a

breast cancer study. Upjohn failed to include any human breast cancer warning with its product.

Arkansas courts have consistently awarded punitive damages in cases involving comparable and, frankly, far less egregious conduct. *See, e.g., Pac. RR Co. v. Barber*, 149 S.W.3d 325, 343, 346-47 (Ark. 2004) (failing to correct dangerous condition at railroad crossing); *D'arbonne Const. Co. v. Foster*, 123 S.W.3d 894, 900 (Ark. 2003) (failing to make truck repairs); *Advocate, Inc. v. Saner*, 111 S.W.3d 346, 358-59 (Ark. 2002) (understaffing nursing home); *So. Farm Bureau Cas. Ins. Co. v. Allen*, 934 S.W.2d 527, 530 (Ark. 1996) (misrepresenting availability of insurance coverage); *Walt Bennett Ford, Inc. v. Keck*, 768 S.W.2d 28, 30 (Ark. 1989) (retaining car after nonpayment of disputed rental vehicle charges); *Petrus Chrysler-Plymouth v. Davis*, 671 S.W.2d 749, 752 (Ark. 1984) (selling vehicle with known wiring problem); *Growth Properties I v. Cannon*, 669 S.W.2d 447, 449 (Ark. 1984) (constructing equipment transport road in cemetery and exposing several gravesites); *Aon Risk Services v. Mickles*, 242 S.W.3d 286, 294 (Ark. Ct. App. 2006) (inserting misrepresentation in insurance policy after it was filled out); *Ray Townsend Farms, Inc. v. Smith*, 207 S.W.3d 557, 567 (Ark. Ct. App. 2005) (engaging in corporate self-dealing); *King v. Powell*, 148 S.W.3d 792, 798-99 (Ark. Ct. App. 2004) (trespassing and destroying neighbor's trees).

In this case, the defendants acted with literally no regard for public safety.

I. Substantial Evidence Supports the Jury's Punitive Award Even Without Dr. Parisian's Testimony.

The court below struck Dr. Parisian's expert testimony and all exhibits referenced while she was on the stand (A-V-001403-001404). The court had no basis for striking the documentary evidence. Independently, defendants waived any objection to Dr. Parisian's testimony by failing to timely object. Further, Dr. Parisian's testimony was appropriately admitted. Finally, the most the court could have granted was a new trial, not judgment as a matter of law.

A. The Documents Were Independently Admissible and Sufficient to Support the Verdict.

The sole concern of the court below was that Dr. Parisian's area of expertise was FDA regulations and practices. Yet, according to the court, Dr. Parisian merely read documents the jury was capable of reading, without connecting them to regulatory issues. Thus, the court concluded it should have excluded both Dr. Parisian's testimony AND the exhibits that were admitted into evidence while she was on the stand (A-V-001359-001370).

The first error is that NONE of the exhibits reviewed while Dr. Parisian held the witness chair depended on any testimony from Dr. Parisian for their admissibility. They were defendants' internal documents and correspondence, and

every one of them was admitted before Dr. Parisian testified. The court identified 15 documents that it claimed should have been excluded (A-V-001358-001368, § II(A)(2)(a-n)). The chart below cites the page/line designations of the transcript where each document was admitted before Dr. Parisian had even begun discussing it.

a	Endo. cancer & FDA response (A-I-000171-000172, A-I-000173-000176)	T-XV-2681:1-7
b	Prempak study memo (A-I-000195-000208)	T-XV-2685:12-21
c	Seasons campaign (A-I-000217-000219)	T-XV-2689:1-20
d	Premarin marketing plan (A-II-000429-000506)	T-XV-2700:1-15
e	Essner Prempro launch speech (A-II-000535-000541, A-II-000523-000534)	T-XV-2704:22-2705:1; T-XV-2708:1-9
f	Burson-Marsteller memo (A-II-000556-000570)	T-XV-2709:11-22
g	George Mills e-mail (A-II-000542-000543)	T-XV-2720:1-7
h	Budget proposal (A-II-000574-000578)	T-XV-2720:1-7
i	Kerlikowske article (A-V-001465-001470)	learned treatise (not admitted) T-XV-2724:1-25
j	CME handout (A-II-000364-000371)	T-XV-2725:3-10
k	Grant authorization (A-II-000512-000520)	T-XV-2727:11-16
l	Ghostwriting	No document referenced
m	Upjohn Dear Dr. ltr (A-II-000521-000522)	T-XV-2729:24-2730:5

n	Exec. Session summary (A-III-000830-000831, A-III-000832-000833)	T-XV-2736:21-25

Defendants' objections were overruled before Dr. Parisian ever entered the courtroom. The punitive damages phase of this trial occurred one week after the liability phase. During the interim, Ms. Scroggin submitted her proposed exhibit list (A-V-001413-001419, A-V-001420-001421, A-V-001423-001429, A-V-001435-001438),[14] defendants objected (A-III-001002-001029 (Wyeth); A-III-000986-001001 (Upjohn)), and the Court ruled on all objections (A-IV-001036-001039). None of the objections, or any of the Court's rulings, were based on Dr. Parisian's knowledge (A-IV-001036-001039). The documents could have been introduced *en masse* or through another witness.

The documents confirm conscious disregard, even though they do not specifically mention FDA regulations. The trial court never determined that violations of FDA rules were the sole basis for punitive damages. While Dr. Parisian was arguably constrained to opine about FDA regulations (based on the court's perception of her expertise), the jury was free to find violations of common law duties that extended beyond regulatory requirements. Indeed, the trial court expressly instructed the jury during the liability phase that defendants could be

[14] Ms. Scroggin submitted three different lists because the Court ordered her to pare down her first two (A-V-001422, A-V-001430-001434).

found culpable even if they complied with FDA standards (A-III-000980).[15] This Court has held that FDA regulations are "minimal standards" that common-law requirements can supplement. *Hill v. Searle Labs*, 884 F.2d 1064, 1068 (8th Cir. 1989).

B. Defendants Waived Any Complaint about Dr. Parisian's Testimony by Failing to Object.

The trial court's order states that defendants adequately preserved their objections to Dr. Parisian's testimony (A-V-001356 & n. 16-18). In support, the court cited five motions filed long after Dr. Parisian's testimony (A-IV-001040-001041, A-IV-001042-001043, A-IV-001044-001046, A-IV-001047-001049, A-IV-001183-001248), two motions filed before Dr. Parisian's testimony in the compensatory damages phase (A-IV-001030-001032, A-IV-001033-001035) and two motions filed more than five months before any of Dr. Parisian's testimony (A-III-000933-000935; A-III-000936-000937). The court resolved the latter two motions by issuing an order limiting Dr. Parisian's testimony (A-III-000957-000965). Thereafter, defendants were obliged to object if they believed the testimony failed to comply with the order.

[15] The court informed the jury during the punitive-phase that it was to follow the instructions given in the liability phase (A-IV-001050).

Defendants' failure to object to the testimony at issue when it was elicited means their objections were waived. *See Marmo v. Tyson Fresh Meats, Inc.*, 457 F.3d 748, 761 n. 5 (8th Cir. 2006).

> The rule is well settled in this circuit that for an objection to be timely it must be made at the earliest possible opportunity after the ground of objection becomes apparent, or it will be considered waived.

Terrell v. Poland, 744 F.2d 637, 638-39 (8th Cir. 1984).

Defendants did not independently object that Dr. Parisian's testimony was not focused on FDA regulations[16] a single time during Dr. Parisian's punitive damages testimony. Thirty-six pages into the testimony, the trial court, *sua sponte*, expressed concern that Dr. Parisian was reading from documents rather than discussing regulations. Wyeth's counsel latched onto the judge's words, objecting to a single comment Dr. Parisian had made about a particular Wyeth act being "indifferent" (T-XV-2713:14-2714:17). Neither Wyeth nor Upjohn made any further objection regarding Dr. Parisian's testimony extending beyond FDA regulations during the remainder of Dr. Parisian's testimony. The court below cited four objections (A-V-001356 & n. 17), but none occurred during Dr. Parisian's direct examination (the only testimony at issue).

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[16] Wyeth once objected that Dr. Parisian did not have the scientific expertise to opine about a document. The court overruled the objection when Plaintiff's counsel indicated scientific testimony would not be elicited (T-XV-2683:24-2684:8).

Defendants also failed to object to Dr. Parisian's testimony that cited Dr. Kerlikowske's conclusion that 17,500 women annually have developed breast cancer due to E+P (T-XV-2722:7-24). The court noted that defendants previously moved to exclude this evidence (A-V-001365). But those motions had nothing to do with Dr. Parisian; they claimed the prejudicial nature of the evidence outweighed its probative value (A-V-001439-001440, A-V-001441-001448, A-V-001449-001451, A-V-001454-001455, A-V-001456-001463). The court agreed during the compensatory phase (A-V-001452-001453) but denied the motions in the punitive phase, assuming the evidence was accompanied by a limiting instruction (which it was) (A-V-001464). Thus, any objection to Dr. Parisian testifying about the evidence was waived. (Though academic, the court's statement that Dr. Parisian was not qualified to opine about Dr. Kerlikowske's work is irrelevant because Dr. Parisian did nothing more than recite Dr. Kerlikowske's conclusion. Dr. Austin, an epidemiologist, testified that the article was a peer-reviewed published learned treatise earlier in the trial (T-III-281:19-24).

One of the purposes of requiring contemporaneous objections is to permit the witness to clarify her answers. Had either defendant objected that Dr. Parisian had not cited a federal regulation as the basis for a conclusion, Dr. Parisian could have cited that regulation in her ensuing answer. That is precisely what happened during the liability phase. On those rare occasions when Wyeth objected, Dr.

Parisian cited precisely the regulation that served as the basis of her testimony (E.g., T-VII-1241:15-1246:4).

C. Dr. Parisian's Testimony Was Appropriately Based Upon FDA Regulations and her Experiences as an FDA Medical Officer.

The court criticized Dr. Parisian for citing only a few CFR provisions in the punitive phase and not referring to those regulations when discussing each exhibit (A-V-001357-001370). No order required Dr. Parisian to cite the code during her testimony. The order limiting her testimony merely stated that she may testify based on her "observations over the years and her understanding of the regulations" (A-III-000966, A-V-001357). During trial, the Court indicated that Dr. Parisian's testimony would be admissible so long as it was grounded in FDA regulations (T-VII-1318:25-1320:2). In other words, Dr. Parisian's conclusions were to be based on the FDA regulatory framework; there was no requirement that she identify a CFR provision proscribing each action by defendants. Furthermore, the bulk of Dr. Parisian's testimony about the defendants' violations of FDA regulations came during the first phase of trial, and the court specifically instructed the jury to consider the evidence presented in both phases in assessing punitive damages (A-IV-001053).

Dr. Parisian testified that both defendants' persistent failure to study E+P violated FDA requirements as follows:

- FDA regulations require that drug labels contain essential scientific information about safety and efficacy and be based on human data wherever possible (T-VII-1242:15-1243:14 (*citing* 21 C.F.R. § 201.56)). Defendants did no human breast cancer studies, and Upjohn's label never even mentioned human breast cancer.

- FDA regulations obliged defendants to verify the risks and benefits of long-term use of E+P before applying for a combination indication (T-VII-1283:24-1284:15) and require drug labels to warn about any risks from long-term use (T-VII-1244:13-1245:12 (*citing* 21 C.F.R. § 201.4)). Defendants did no long-term studies even though it was clear that the risks of hormone therapy increase with duration of use (SOF, III, *supra*).

- FDA regulations prohibit labeling claims that are based on inadequate data, hence a drug company must study its products before changing its label or getting a new product approved (T-VII-1242:12-1243:14 (*citing* 21 C.F.R. § 201.56)).

- FDA regulations require labels to identify the risks of foreseeable uses of a drug (T-VII-1244:13-1245:12 (*citing* 21 C.F.R. § 201.57)). Defendants were thus obliged to study combination use. Defendants knew their drugs were being used together but chose to treat the grandmothers of this country as guinea pigs rather than conduct necessary studies.

- Wyeth's dismiss-and-distract strategy - specifically, its public relations tactics -- violated the "fair and balanced" information requirement of FDA regulations (T-XV-2678:18-2679:20; T-XV-2719:18-25).[17] The FDA would have expected Wyeth to take the 1990 Advisory Committee seriously and not attempt to dismiss it as a "non-event" (T-VII-1295:13-15).

- Upjohn's failure to honor an FDA officer's demand to cease its inappropriate advertising was improper (T-XV-2735:11-2736:22) and its advertising of unapproved benefits constituted misbranding under the regulations (T-VII-1361:10-1362:8; SOF, II(C), *supra*).

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[17] Wyeth and the court below noted that Dr. Parisian identified the CFR section at issue as 201.105 which deals with veterinary drugs (A-V-001357 at n. 22). The actual section is 201.5. The error was clearly inadvertent. Dr. Parisian had previously identified two different subsections of 201.5 during the liability phase (T-VII-1242:9-14; T-VII-1244:2-25).

Dr. Parisian concluded that defendants' abject refusal to study throughout the '70s, '80s and '90s breached their obligations under FDA regulations (T-VII-1320:10-1321:14).

Undeniably, in the process of presenting her conclusions, Dr. Parisian read portions of documents so the jury would have a frame of reference. She should hardly be faulted for this. Approximately 300 exhibits were admitted during this four-week trial, many of them voluminous. The notion that the jury could figure out which documents, and specifically, which excerpts, had been the focus of Dr. Parisian's testimony is unrealistic. *See, e.g., Flanagan v. Altria Group, Inc.*, 423 F. Supp. 2d 697, 699 (E.D. Mich. 2005) (expert opinion about voluminous documents admissible where it adds to the history and occasionally interjects opinions); *In re Welding Fume Products Litigation*, 2005 WL 1868046, at *17 (N.D. Ohio Aug. 8, 2005) (expert testimony that helps jury understand voluminous documents is admissible).[18]

[18] The court cited *In re Rezulin* for the contrary position (A-V-001372 & n. 86, *citing* 309 F. Supp. 2d 531, 555 (S.D.N.Y. 2004)). Rezulin was on the market just three years, and the issues surrounding its marketing were not complex. By contrast, hormone therapy has been sold, in various incarnations, for over a half-century.

D. Defendants Admitted They Owed the Duties upon which Dr. Parisian's Testimony Was Based.

Defendants' motion to limit Dr. Parisian's testimony was based on the requirement that expert opinion be based on objective criteria and not the *ipse dixit* of the expert (A-III-000938-000939). However, defendants acknowledged each of the duties of care cited by Dr. Parisian. Thus, defendants provided the objective criteria.

Both defendants admitted they had a duty to ensure that any product they sold was adequately studied. Both defendants acknowledged a duty to investigate their products' risks when used in combination with other products (T-III-427:5-12 (Victoria); T-XI-2196:12-22 (Jolson)). Both defendants agreed they were obliged to ensure that high-quality studies were performed on their products, whether by them or third parties, both before and after approval (T-XI-2185:25-2186:17 (Jolson); T-X-1788:5-8; T-X-1854:20-1855;11 (Constantine); T-III-424:8-425:9; T-IV-537:9-538:1; T-IV-564:24-563:3 (Victoria); T-XII-2303:10-21 (Rarick).

Victoria acknowledged that a drug company has the duty to refrain from off-label promotion (the marketing of unapproved benefits). While physicians may prescribe off-label, drug companies may not market off-label (T-IV-632:18-633:5).

Victoria also admitted that a drug company has a duty to provide a fair and balanced portrayal of its products' risks -- precisely the duty upon which Dr.

Parisian based her criticism of Wyeth's dismiss-and-distract policy (T-III-425:22-426:23).

Simply put, defendants admitted each of the duties that formed the basis of Dr. Parisian's opinion that they acted recklessly.

E. At Most, any Prejudice Would Warrant a New Trial on Punitive Damages, Not Judgment as a Matter of Law.

This point is academic because Dr. Parisian's testimony was appropriate and, according to the trial court, at worst, constituted a mere reading of otherwise admissible documents. Given the strong evidence of egregious misconduct in this case, it is implausible that her testimony was so prejudicial as to create an unfair trial. But if it were, the remedy would be a new trial, not judgment as a matter of law. *See Rottlund Co. v. Pinnacle Corp.*, 452 F.3d 726, 730-31 (8th Cir. 2006). Despite the potentially prejudicial nature of Dr. Parisian's testimony, the documents introduced during the punitive phase stand on their own. As the court below repeatedly noted, the jury was just as capable of reading and understanding them as Dr. Parisian (E.g., A-V-001359). Those documents support an award of punitive damages, making judgment as a matter of law improper.

Arkansas law permits a new trial on punitive damages alone, with the compensatory damages findings remaining in tact. *Rose Care, Inc. v. Ross*, 209 S.W.3d 393, 408 n. 5 (Ark. Ct. App. 2005).

II. The Trial Court Substituted Its Judgment for that of the Jury.

Reviewing judgment as a matter of law, courts must consider all the evidence presented, but they "must disregard all evidence favorable to the moving party that the jury is not required to believe." *Reeves v. Sanderson Plumbing Prods Inc.*, 530 U.S. 131, 151 (2000). In other words, courts may give credence only to evidence favoring the movant "that is uncontradicted and unimpeached, at least to the extent that the evidence comes from disinterested witnesses." *Id.* at 155 (emphasis added); *Ohrujlik v. Univ. of Ark.*, 395 F.3d 872, 878 (8th Cir. 2005) ("The court may not substitute its own judgment for that of the jury"). Courts must draw all reasonable inferences in favor of the nonmovant and not weigh the evidence. *Reeves*, 530 U.S. at 150. The court may not discount an inference from the evidence that favors the plaintiff based on the testimony of an interested defense witness. *See, e.g., Wilson v. Brinker Int'l, Inc.*, 382 F.3d 765, 770 (8th Cir. 2004) ("because Wilson is an interested party, her testimony alone does not permit entry of judgment as a matter of law in her favor, because the jury was not required to accept it") (*citing* 9A CHARLES ALAN WRIGHT & ARTHUR R. MILLER, FED. PRAC. & PRO. § 2527 (2d ed. 1995 & Supp. 2004) (collecting cases and observing that juries are not required to accept interested parties' testimony as true, even if uncontradicted)).

A. The Trial Court Weighed the Evidence Against Wyeth, Adopting Interested Testimony the Jury Was Not Required to Accept.

The court below substituted its evaluation of evidence for the jury's evaluation. It handpicked interested testimony from defendants' own witnesses and adopted those biased explanations as the only plausible inferences from the evidence. The court became a "super-jury," giving credence to evidence supporting the movants, evaluating witness credibility and deciding inferences in favor of the movants. This practice is unsupported by the rules.

--- **The trial court's adoption of Wyeth's biased remarks**

Throughout its witness testimony and documents, Wyeth referred to the information it disseminated on breast cancer as "complete" and "balanced" (E.g., A-V-001389 & n. 176). These are nothing more than judgment-laden buzzwords reflecting a biased viewpoint. Yet, repeatedly, when a witness or document mentioned Wyeth's desire to present a "balanced" approach or provide "complete" information, the trial court latched onto these statements as literal truths, even though an objective observer may rightfully view them as one-sided.

The court noted: "The record is replete with evidence that Wyeth wanted the media to present 'balanced' information" (A-V-001389) (quotation in original). Translated: Wyeth papered its files and prepped its witnesses with claims that its approach was balanced. The jury had the right to see through the subterfuge; the trial court had no basis, let alone jurisdiction, to white-wash the evidence.

The evidence the court cited favoring the movant is not evidence the jury had to accept, and cannot serve as the basis for judgment as a matter of law (A-V-001389 & n. 176 & evidence cited therein).[19] For example, the court cited the testimony of Justin Victoria, who said Wyeth strived to present a balanced response to the Hoover study (T-IV-619, T-IV-625[20]). A long-term Wyeth executive, Victoria had a clear incentive to defend Wyeth's dismiss-and-distract policies and to protect the company from litigation. (T-IV-577:9-25) (T-III-417:19-20).

The court also cited the testimony of Dr. Rarick who said Wyeth sought to respond to the Colditz study with "balanced" information (T-XII-2323, T-XII-2340). The jury had many reasons to discount Dr. Rarick's credibility. She is Wyeth's retained expert who has charged the company at least $220,000 for her work in this litigation (T-XII-2271:4-13; T-XII-2275:25-2276:13). Since leaving the FDA, Dr. Rarick has become a professional drug company consultant (T-XII-2270:20-2271:3), testifying, for example, that Merck violated no FDA rules or common law standards in its handling of the Vioxx debacle (T-XII-2338:1-16; T-XII-2271:14-25).

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19 This citation includes each piece of testimony discussed in this section.

20 The trial court did not provide line designations in its citations.

While at the FDA, Dr. Rarick reviewed Wyeth's Prempro application (A-II-000346-000348). Many events of this case occurred on her watch. Indeed, she was the FDA official who decided that Wyeth did not have to follow through on its commitment to perform a Phase IV case-control study (A-II-000362-000363). Clearly, Dr. Rarick is not an "uninterested" witness the jury was required to believe.

The court cited Dr. Michael Dey's response to many damning documents by insisting Wyeth's goal was to provide fair and balanced information (T-XVI-2928, T-XVI-2932, T-XVI-2935, T-XVI-2956-57). Dr. Dey is Wyeth's President of Scientific Affairs and Women's Healthcare (T-XVI-2842:11-18). He was formerly responsible for the marketing of Wyeth's HT products (T-XVI-2842:19-2843:2). With an incentive to defend the activities in his own department, he was hardly a disinterested witness (T-XVI-2842:18-2843:2).

--- **The Hoover study** (A-V-001375-001376)

Here, again, the trial court engaged in its own inferences and relied on biased Wyeth testimony. The Hoover study showed a 2.0 RR of breast cancer from estrogen that Dr. Hoover told Wyeth warranted more study (SOF, II(C)(1), *supra*). The court said Wyeth reacted with more study, citing the biased testimony of Wyeth executive, Victoria (A-V-001375 & n. 97).

The court ignored that Wyeth's own internal memorandum discussed strategies to refute and mitigate the study months before Wyeth had even seen the results (A-I-000177; A-I-000191-000192). Instead, the court cited a passage from the memo saying Wyeth should keep abreast of those studies that had been done (which Wyeth knew even then were inadequate) (A-I-000177). That suggestion came under the heading of "Refutation and Mitigation" (A-I-000177-000178). Certainly a plausible inference is that Wyeth's intent to review the other studies was merely to find some data to help minimize Hoover's study.

The court further noted that, in June 1976, Wyeth reported that studies had not shown breast cancer causation (A-V-001375). This very memo acknowledges that hormone receptor positive breast cancer "can, and does, respond to the presence of estrogen" and that the effect of progesterone on the etiology of breast cancer needs further study (A-I-000185-000188). The court claimed that this memo does not establish definitive evidence that P increases the risk of breast cancer (A-V-001376-001377 & n. 105). The court missed the point: defendants' reckless conduct was the failure to investigate the effect of adding P to E despite obvious signals of potentially serious risk.

--- **The endometrial cancer crisis** (A-V-001376-001377)

The court also erred by excluding key evidence of notice. Wyeth responded to the estrogen-induced endometrial cancer epidemic by implementing its dismiss-

and-distract policy. The FDA rebuked Wyeth for doing so and demanded a more proactive response in the future (A-V-000171-000172, A-V-000173-000176). These documents confirmed that Wyeth knew what was required to protect patient safety yet chose to do nothing. The court failed to confront this evidence other than to note that these documents were admitted when Dr. Parisian was on the stand and therefore should have been excluded (A-V-001377). These documents were independently admissible and confirmed that Wyeth's consistent downplaying of any adverse data was deliberate.

--- **The PremPak study** (A-V-001378-001379)

A 1983 Wyeth memo revealed the company was concerned that if Wyeth actually did a study on E+P, the study might prove costly, unsuccessful and embarrassing (A-I-000193-00194). The trial court adopted the position taken by Wyeth executive, Victoria, that this memo merely expressed concern that the FDA might expect E+P studies to prove additional menopausal benefits beyond what estrogen alone provided (A-V-001379). Aside from the obvious self-interest of this testimony (and the impropriety of the trial court relying on it), the analysis is implausible. OB/GYNs had known since the 1970's that the sole purpose of adding P to E was to prevent endometrial cancer (A-II-000426; T-IV-564:20-23). No one expected P to provide any actual menopausal benefit. Wyeth feared doing studies because it was worried studies would prove E+P's significant risks.

The court disputed Plaintiff's claims that Wyeth discontinued the Prempak study without justification. It cited Dr. Constantine as claiming enrollment problems were to blame (A-V-001380). Dr. Constantine is hardly an "uninterested" witness whose testimony should establish facts as a matter of law. She was Wyeth's Vice-President of Women's Health (T-X-1778:14-17) and became responsible for the company's HT products in 2000 (T-X-1782:19-21). She is literally Wyeth's lead spokesperson in the HT litigation, having testified for Wyeth in multiple trials (T-X-1856:10-1857:8)

More significantly, abundant evidence disputes Dr. Constantine's claim about enrollment. The year the PremPak study began, physicians wrote 10 million prescriptions for Premarin and one million prescriptions for Provera (T-VIII-1557:12-17). Dr. Rarick, Wyeth's regulatory expert, acknowledged that Wyeth and Upjohn could have found suitable candidates for study from among this pool of users (T-XII-2308:11-2310:6). Dr. Austin testified there were ample users of E+P during this time frame to conduct a breast cancer study (T-II-223:7-224:5). The court offered no explanation for adopting Dr. Constantine's unsupported assertion over Plaintiff's contrary evidence. In fact, the court did not even mention Plaintiff's evidence.

--- **The ECOG study** (A-V-001380-001381)

Shockingly, documents reveal that Wyeth had "a company policy" against supporting breast cancer studies. Wyeth refused to provide drugs for a study by ECOG, even though other manufacturers were supporting this endeavor (A-I-000223-000224, A-I-000225-000226). Victoria claimed Wyeth refused to support the study because HT is contraindicated for breast cancer survivors. The court adopted Victoria's self-interested testimony even though he is a Wyeth executive (A-V-001381). If Victoria's position were true, one would expect at least one Wyeth document to say so. But the court found that it was Ms. Scroggin's burden to prove Victoria had been untruthful (A-V-001381), even though a plausible inference from the documents is precisely what the documents say -- Wyeth had a "company policy" against funding breast cancer studies (A-I-000223-000224; A-I-000225-000226).

--- **The Cummings study**

Despite the extensive emphasis this evidence received at trial and in post-trial briefing, the court ignored it altogether. Dr. Cummings' study threatened the profitability of E+P because it suggested women using the combination for osteoporosis were at the greatest risk of breast cancer. In secret meetings, Wyeth reiterated its "Dismiss/Distract" policy in two handwritten notes by a Wyeth executive. Wyeth encouraged third-party allies to dismiss the data, downplayed

the study, created press material to counteract and discredit the data and retained spokespeople to counterbalance the breast cancer risk. Even Wyeth's regulatory expert agreed these actions were improper. The trial court skipped right over this evidence (SOF at I(C)(8), *supra*).

--- **The *Seasons* magazine campaign** (A-V-001386)

The *Seasons* campaign was Wyeth's effort to manipulate consumers into thinking its magazine, replete with off-label benefit claims and ghostwritten articles minimizing the risk of breast cancer, was actually sponsored by their doctors or pharmacies. The FDA ordered Wyeth to revise the campaign (SOF, III(C)(7), *supra*). The court below suggested that Wyeth's capitulation to the FDA's demand nullified this evidence (A-V-001387). The jury could have determined that Wyeth's conduct in this context was further proof of its deliberate and reckless disregard for women's health. Certainly, the jury's potential interpretation was entitled to deference rather than dismissal.

--- **Ghostwriting** (A-V-001389-001390)

The court acknowledged that Wyeth sought to deflect attention from breast cancer findings by creating purportedly scholarly articles without disclosing that the company was behind them. The court simply said there was no evidence that this practice was inappropriate (A-V-001389). This position is incredible. Physicians rely upon medical articles when making important health decisions.

The scientific community has publicly criticized ghostwriting as a misleading and unacceptable means for drug companies to influence medical opinion. Here, the trial evidence confirmed that Wyeth deliberately concealed its involvement in the writing of articles, thereby undermining a physician's ability to evaluate the articles' messages. This conduct reflects a conscious disregard for women's health.

Dr. Thomas Stovall is an OB/GYN and Wyeth's expert on specific causation. Dr. Stovall was also an editorial advisory board member for the very journal that published the Eden ghostwritten article. He testified that medical journals like his expect any entity's involvement in the drafting of an article to be revealed because disclosure facilitates evaluation of bias (T-XIII-2458:2-16).

The court also claimed there was evidence that ghostwriting may be a common practice (A-V-001390), citing Dr. Rarick, Wyeth's expert. Given her biased status, the jury was not required to accept Dr. Rarick's testimony. More fundamentally, the relevance of the court's statement is unclear. Does the common occurrence of a dishonest practice make it any less reckless? Off-label promotion and withholding of information from the FDA may be common pharmaceutical practices, but the frequency with which these illegal acts occur does not diminish their reprehensibility. The fact that the tobacco industry, as a whole, manipulated nicotine levels in cigarettes hardly made that practice acceptable.

These are just some of the examples in which the Court adopted the testimony of Wyeth's witnesses and Wyeth's inferences to disregard the jury's verdict for Ms. Scroggin.

B. The Trial Court Weighed the Evidence Against Upjohn, Declining to Make Reasonable Inferences in Ms. Scroggin's Favor.

Upjohn repeatedly sought a menopausal indication for Provera. The FDA consistently said "no" and told Upjohn it could not market Provera for such use until Upjohn established the safety and efficacy of the indication. Upjohn ignored the FDA and advertised the product anyway as a menopausal drug. The FDA repeatedly ordered Upjohn to cease and desist, again telling the company it must establish Provera's safety and efficacy. Upjohn initially withdrew its inappropriate advertising but then published more illegal ads. The court interpreted this evidence as showing only that the FDA disapproved of Upjohn's promotion of Provera as "safe and effective" for the treatment of endometrial hyperplasia and not for claiming the product was "the other half of estrogen replacement therapy" (A-V-001398-001399). This is a distinction without meaning. The FDA made clear that Provera had not been proven safe or effective and therefore could not be advertised as such. Upjohn did it anyway.

The court stated that the FDA's repeated orders to stop, and Upjohn's repeated defiance, simply reflected "a dialogue" between the two that the "sum of the testimony" suggested was the "normal course of business" (A-V-001398).

Ignoring for a moment that the sum of evidence need not support the jury verdict, it is impossible to reconcile the court's finding with FDA statements such as: "Further attempts to promote this product beyond your approved indications will cause us to seek stronger regulatory relief" (A-III-000708).[21]

Still further, for decades, Upjohn was aware of the need to study the breast cancer risk of E+P but did nothing. Indeed, until 2007, Upjohn never warned of any human breast cancer risk of Provera or E+P. The court found no reckless disregard because Upjohn conducted some E+P studies; it just failed to perform the "right" studies (A-V-001398). Upjohn's failure to do the "right studies" was not inadvertent. The only studies Upjohn ever performed were efficacy studies, designed to confirm that Provera was beneficial to the endometrium and would thus increase profits. Upjohn deliberately avoided conducting any studies designed or powered to ascertain a breast cancer risk (SOF, II(C), *supra*). Upjohn's sole concern was for the bottom line.

Finally, the court found that Upjohn was not obliged to conduct its own studies if it relied on breast cancer studies performed by others (A-V-001398). That is true. But Upjohn did not rely on any adequate breast cancer studies on E+P

[21] The court further noted that Dr. Parisian's testimony that Upjohn's advertising violated FDA regulations on labeling was false because advertisements are not labels (A-V-001398). Yet, the United States Supreme Court has long held that FDA regulations on labeling encompass advertising as well. *Kordel v. U.S.*, 335 U.S. 345, 349-50 (1948).

by others, and there is no evidence in the record (much less, evidence the jury was required to accept) to suggest otherwise. The Degge Group, which Upjohn finally retained in 1990, found only seven studies on E+P and all were inadequate (SOF, II(B), *supra*). The group also found that the ongoing studies failed to correct the methodological defects of the prior studies (A-III-000661). Yet, Upjohn did no follow-up.

C. At Most, the Court's Reservations about Plaintiff's Evidence Warrant a New Trial on Punitive Damages.

The Court's conclusions involved assessing witness credibility, weighing the evidence and adopting inferences contrary to the verdict. For the reasons given above, the Court's findings were without merit. But if they were, at most, they would warrant on new trial on punitive damages, not judgment as a matter of law. *See Powell v. TIP Petroleum, Inc.*, 510 F.3d 818, 822 (8th Cir. 2007).

CONCLUSION

For the foregoing reasons, Plaintiff/Appellant, Donna Scroggin respectfully requests that this Court reverse the trial court order granting judgment as a matter of law (and, alternatively, a new trial) on punitive damages, reinstate the jury's punitive damages award, affirm the trial court judgment in all other respects and provide Plaintiff all other relief to which she is entitled.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I, Erik B. Walker, certify that on October 22, 2008, a copy of the Brief for Appellant, Donna Scroggin, a copy of the Appendix and CD-Rom were served upon the following counsel for Appellees by DHL, as follows:

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CERTIFICATE OF COMPLIANCE

1. This brief complies with the type-volume limitations of Fed. R. App. P. 32(a)(7)(B) because this brief contains 13,813 words, excluding the parts of the brief exempted by Fed. R. App. P. 32(a)(7)(B)(iii).

2. This brief has been prepared in a proportionally spaced typeface using Microsoft Word, Times New Roman font face in font size 14.

Erik B. Walker
Attorney for Appellant, Donna Scroggin

Dated: October 22, 2008.

The WHI study showed that overall breast cancer incidence among E+P users was 24 percent higher than placebo users (T-XIII-2436:20-2437:5). Had the study continued, the rate would have been greater because the risk was increasing with duration of use (T-II-214:22-215:10; T-VIII-1545:18-24; A-III-000792 at 109:5-20; T-III-368:21-369:6; T-X-1969:16-1970:2). Dr. Austin noted that the 1.24 relative risk (RR)[9] underestimates the risk for those using the product more than five years (T-II-214:4-10).

Further, the WHI's 1.24 RR fails to account for the number of women who ceased using E+P during the study. The figure is based on the "intent to treat" group, meaning all women originally supposed to take E+P (T-II-195:22-197:20; T-III-290:7-15). A staggering 40 percent of those placed on E+P discontinued use during the study, thus severely skewing the study results (T-II-197:11-198:25).

The WHI investigators later reanalyzed the data to ascertain what effect continued use for a long duration would have. The investigators discovered that some of the women given E+P during the study had used the combination prior to the study. Accounting for this prior use and the drop out figures, the investigators

[9] "Relative risk" refers to the ratio of increased incidence of an event among those exposed to the variable being studied to the incidence among those who are not exposed (T-X-1804:22-1905:6). The baseline risk is 1.0, hence a relative risk (RR) equal to or less than 1.0 means there was no greater incidence of the event among those exposed (T-II-235:15-21; T-III-474:4-7). A 2.0 RR means a doubling of the risk (twice as much incidence) among those exposed whereas a 5.0 RR refers to five times greater risk (a 400 percent increase in incidence) among those exposed (T-II-204:6-12).

UNITED STATES COURT OF APPEALS
FOR THE EIGHTH CIRCUIT

Case No. 08-2555
CIVIL

DONNA SCROGGIN,

Plaintiff/Appellant

v.

WYETH, WYETH PHARMACEUTICALS, INC.
AND PHARMACIA & UPJOHN COMPANY, LLC,

Defendants/Appellees

On Appeal from the United States District Court
for the Eastern District of Arkansas,Western Division
Judge William R. Wilson, Jr., Presiding

APPELLANT'S ADDENDUM

List of Documents

ADDENDUM NO. 1

JURY VERDICT FORM

QUESTION NO. 1:
Has Ms. Scroggin proven by the greater weight of the evidence that Wyeth inadequately warned about a known or knowable risk of Premarin or Prempro and that such failure proximately caused her breast cancer?

Yes: X No: _____

QUESTION NO. 2:
Has Ms. Scroggin proven by the greater weight of the evidence that Upjohn inadequately warned about a known or knowable risk of Provera and that such failure proximately caused her breast cancer?

Yes: X No: _____

QUESTION NO. 3:
Have Defendants proven by the greater weight of the evidence that Ms. Scroggin knew, or by the exercise of reasonable diligence, should have discovered that her claim accrued before April 7, 2001.

Yes: _____ No: X

If you answered "Yes" to Questions 1 or 2 and "No" to Question 3, answer Question No. 4:

QUESTION NO. 4:
What amount of money, if any, would fairly and reasonably compensate Ms. Scroggin for the damages caused by the conduct of Defendant(s).

$ 2,750,000.00

Please inform the Court that you have reached a verdict.

Presiding Juror

ADDENDUM NO. 2

VERDICT FORM

1. Do you find that Ms. Scroggin has proven by clear and convincing evidence that Wyeth knew, or should have known, in light of the surrounding circumstances, that its failure to warn would naturally and probably result in breast cancer and that Wyeth continued such conduct (i) with malice or (ii) in reckless disregard of the consequences from which malice may be inferred and, therefore, that Wyeth should be required to pay her punitive damages?

X YES _____ NO

2. If you answered "yes" to Question Number 1, state the amount of punitive damages, if any, Wyeth should be required to pay Ms. Scroggin:

$ 19 million three hundred sixty thousand/
19,360,000.00

3. Do you find that Ms. Scroggin has proven by clear and convincing evidence that Upjohn knew, or should have known, in light of the surrounding circumstances, that its failure to warn would naturally and probably result in breast cancer and that Upjohn continued such conduct (i) with malice or (ii) in reckless disregard of the consequences from which malice may be inferred and, therefore, that Upjohn should be required to pay her punitive damages?

X YES _____ NO

4. If you answered "yes" to Question Number 3, state the amount of punitive damages, if any, Upjohn should be required to pay Ms. Scroggin:

$ 7 million seven hundred sixty thousand
7,760,000

Rodney J. Scroggin
PRESIDING JUROR

ADDENDUM NO. 3

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF ARKANSAS
WESTERN DIVISION

In re:	:	**MDL Docket No. 4:03CV1507-WRW**
	:	**4:04CV01169**
PREMPRO PRODUCTS LIABILITY LITIGATION	:	
	:	
	:	
DONNA SCROGGIN	:	**PLAINTIFF**
	:	
v.	:	
	:	
WYETH, et. al.	:	**DEFENDANTS**

AMENDED JUDGMENT

This action came on for jury trial Monday, February 4, 2008, the Honorable William R. Wilson, Jr., United States District Judge, presiding.

The issues having been duly tried, the jury rendered a verdict in the liability / compensatory damages phase on Monday, February 25, 2008 and a verdict in the punitive damages phase on Thursday, March 6, 2008. Now, therefore, pursuant to the verdicts:

Judgment is entered in favor of the Plaintiff Donna Scroggin and against Defendants Wyeth, Wyeth Pharmaceuticals Inc. and Pharmacia & Upjohn Company LLC, jointly and severally in the sum of $2,750,000.00 with post-judgment interest at the rate of 1.35% per annum.

Judgment is further entered in favor of the Plaintiff Donna Scroggin and against Defendants Wyeth and Wyeth Pharmaceuticals Inc. in the additional sum of $19,360.000.00 with post-judgment interest at the rate of 1.35% per annum.

Judgment is further entered in favor of Plaintiff Donna Scroggin and against Pharmacia & Upjohn Company LLC in the additional sum of $7,760,000.00 with post-judgment interest at the rate of 1.35% per annum.

As the prevailing party, Plaintiff may be entitled to recover attorneys' fees and costs from Defendants. Plaintiff should refer to Local Rule 54 regarding her petition for attorneys' fees and bill of costs.

IT IS SO ORDERED this 9th day of April, 2008 (*nunc pro tunc* as of March 26, 2008).

/s/ Wm. R. Wilson, Jr.
UNITED STATES DISTRICT JUDGE

ADDENDUM NO. 4

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF ARKANSAS
WESTERN DIVISION

In re:	:	**MDL Docket No. 4:03CV1507-WRW**
	:	**4:04CV01169**
PREMPRO PRODUCTS LIABILITY LITIGATION	:	
	:	
DONNA SCROGGIN	:	**PLAINTIFF**
v.	:	
WYETH, et. al.	:	**DEFENDANTS**

ORDER[1]

Pending are Defendants' Motion for Judgment as a Matter of Law, or for New Trial, or Remittitur of Punitive Damages Awards (Doc. Nos. 637, 642). Plaintiff has responded and Defendants have replied.[2] The parties presented oral arguments on May 9, 2008.

I. BACKGROUND

Following a trial of nearly three weeks, the jury, on February 25, 2008, found that Plaintiff proved by the greater weight of the evidence that Wyeth and Upjohn inadequately warned about a known or knowable risk of Premarin, Prempro, and Provera, and Defendants' failure to warn resulted in Plaintiff's breast cancer.[3] The jury awarded compensatory damages of $2,700,000.00.[4]

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[1]United States Magistrate Judge Henry L. Jones, Jr. is also assigned to this case and entered some of the orders referenced in this Order.

[2]Doc. Nos. 651, 652, 654, 655.

[3]Doc. No. 552.

[4]*Id.*

The punitive damages phase of the trial commenced on March 3, 2008, and lasted three days. On March 6, 2008, the jury found Defendants liable for punitive damages; Wyeth in the sum of $19,360,000.00 and Upjohn in the sum of $7,760,000.00.[5]

Following the entry of the judgment,[6] Defendants filed Motions for Judgment as a Matter of Law or for a New Trial on both compensatory and punitive damages. As to compensatory damage issues, the motions were denied on April 10, 2008, and the parties were directed to focus their attention on the issue of punitive damages.[7]

II. STANDARD OF REVIEW

A motion for judgment as a matter of law following a jury verdict -- a.k.a. motion for judgment notwithstanding the verdict ("JNOV") -- is governed by Federal Rule of Civil Procedure 50. Judgment as a matter of law is appropriate when the evidence, viewed in the light most favorable to the verdict, was such that no reasonable juror could have returned a verdict for the nonmoving party.[8] "Judgment as a matter of law is proper when the record contains no proof beyond speculation to support the verdict."[9] A court should review all of the evidence in the record, including any evidence unfavorable to the non-moving party that "the jury is required to believe."[10]

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[5]Doc. No. 616.

[6]Doc. Nos. 629, 636 (correcting the post-judgment interest rate).

[7]Doc. No. 647.

[8]*Minnesota Supply Co. v. Raymond Corp*, 472 F.3d 524, 536 (8th Cir. 2006).

[9]*Larson by Larson v. Miller*, 76 F.3d 1446, 1452 (8th Cir. 1996).

[10]9B CHARLES A. WRIGHT & ARTHUR R. MILLER, FEDERAL PRACTICE AND PROCEDURE § 2529 (3d ed. 2008) (citing *Reeves v. Sanderson Plumbing Products*, 530 U.S. 133 (2000)).

When considering a Motion for JNOV, a court may reconsider evidence that was erroneously admitted, strike the evidence, and then make the determination as to whether, based on the properly admitted evidence, there was sufficient evidence to support the verdict.[11]

Additionally, a trial judge who grants a JNOV should rule conditionally on an alternative motion for new trial.[12]

III. DISCUSSION

A. Dr. Parisian's Punitive Damages Stage Testimony

Plaintiff designated Dr. Parisian as her "regulatory expert," and asserted that Dr. Parisian would establish that the duty to test is part of the ordinary care required of pharmaceutical companies.[13] To support her opinions, Dr. Parisian was to rely on her observations over the years as a former FDA medical officer and her understanding of the regulations referenced in her expert report, her deposition and the supplemental briefs."[14]

Defendants repeatedly argued that Dr. Parisian's punitive damages phase testimony should be stricken. Because a court may "satisfy its gatekeeper role" under *Daubert* on a post-

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[11]*Weisgram v. Marley Co.*, 528 U.S. 440, 455-456 (2000) (Finding no abuse of discretion when the appellate court found expert testimony inadmissible and instructed that judgment be entered as a matter of law, since, without the erroneously admitted testimony, there was insufficient evidence to support the jury verdict. The Supreme Court rejected Plaintiff's assertion "that allowing courts of appeals to direct the entry of judgment for defendants will punish plaintiffs who could have shored up their cases by other means had they known their expert testimony would be found inadmissible." The Court recognized that "although [Plaintiff] was on notice every step of the way that [Defendant] was challenging his experts, he made no attempt to add or substitute other evidence.").

[12]*Montgomery Ward & Co. v. Duncan*, 311 U.S. 243, 253-54 (1940).

[13]Doc. No. 175.

[14]Doc. No. 389.

trial motion,[15] I will now consider Defendants' Motions to Strike. Incidentally, any assertion by Plaintiff that Defendants did not properly reserve their objections to Dr. Parisian's testimony is without merit. Defendants submitted motions to exclude,[16] lodged numerous objections during the punitive damages stage, and requested, both orally[17] and in writing,[18] that Dr. Parisian's punitive damages testimony be stricken or excluded. On an occasion or two, Defendants may have failed to reassert a specific objection contemporaneously, but their specific points had been made and were well-known to me and Plaintiff's counsel.

1. Pre-Trial Limitations on Testimony

Following several rounds of briefing and a hearing, an Order outlining permissible testimony from Dr. Parisian was entered:

> A purely factual recitation of the history of Provera, and its progression as a drug to be used in conjunction with estrogen to treat menopausal symptoms is relevant to show the environment in which Upjohn operated. Use of the specific advertising or promotional pieces is not necessary to make this point. Plaintiff has conceded that Dr. Parisian will not give an opinion on Upjohn's intent or whether Upjohn's advertisement influenced either Plaintiff or any treating physician.
>
> Also Dr. Parisian's testimony is relevant, because she is attempting to show that off-label promotion, without testing, is a violation of pharmaceutical company's duty to use ordinary care . . . Plaintiff's attempt to use Dr. Parisian to establish that the duty to test is part of the ordinary care required from pharmaceutical companies, is relevant to the claims in this case. . .
>
> Dr. Parisian has recited her experience in the FDA and the history of Provera, but she has not set out what standards or "standards of the industry" she relies on. As Judge Wilson requested [in his] November 1, 2007 Order, Plaintiff must provide some citation to authority, whether it is legislative or historical, that Dr. Parisian relies on. I have not been able to find such a reference after reviewing her report in the record.

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[15]*Goebel v. Denver and Rio Grande Western R.R. Co.*, 215 F.3d 1083, 1087 (10th Cir. 2000).

[16]Doc. Nos. 66, 101, 577, 594.

[17]See March 3, 2008, Tr. at 2714; March 3, 2008, Tr. at 2740-41; March 5, 2008, Tr. at 2835; March 6, 2008, Tr. at 2974.

[18]Doc. Nos. 605, 607, 610, 611, 643.

> If Plaintiff can provide a specific reference to the standards relied upon by Dr. Parisian, I will reconsider this ruling and address the remaining issues raised in Upjohn's motion.[19]

In response, Plaintiff submitted supplemental briefing, and this order was entered:

> While I agree that Dr. Parisian's citations leave a bit to be desired, I believe she has met the *Daubert* threshold. Defendants' remaining criticism of Dr. Parisian's testimony and report can be addressed during cross-examination.
>
> Dr. Parisian can give her opinions on the reasonableness of a pharmaceutical company's actions based on her observations over the years and her understanding of the regulations referenced in her expert report, her deposition, and the supplemental briefs. Dr. Parisian will not be permitted to talk about or refer to what an "ethical" or "responsible" pharmaceutical company does or would do.[20]

2. Trial Testimony on Regulations

Although she is Plaintiff's "regulatory expert," Dr. Parisian mentioned only three FDA regulations during the punitive damages stage of trial. At the beginning of the punitive damages stage, Plaintiff asked Dr. Parisian whether she had "run across documents that would violate rules that the FDA has regarding how information is to be handled," and she responded, "Yes, sir."[21] Next, Dr. Parisian cited three C.F.R. statutes -- two of which Defendants claim were cited erroneously[22] -- and summarized the regulations:

> you're supposed to have adequate instructions for use, adequate warnings . . . truthful advertisement, reprints, [and] information that you would provide to your physician . . . marketing information is supposed to be truthful . . . and you're not allowed to have labeling that's false, not fair and balanced.[23]

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[19]Doc. No. 340 (The Order was entered by Judge Jones).

[20]Doc. No. 389.

[21]March 3, 2008, Tr. at 2678.

[22]See Doc. No. 643 ("But section 201.105 has to do with veterinary drugs, and section 203 with the reimportation and wholesale distribution of prescription drugs.").

[23]March 3, 2008, Tr. at 2679.

Following this cursory review of FDA regulations, Dr. Parisian and Plaintiff's counsel commenced addressing specific exhibits.

a. December 1975 Dear Doctor Letter (Plaintiff's Ex. 22) and January 1976 Response from FDA (Plaintiff's Ex. 24)

Plaintiff questioned Dr. Parisian about the December 1975 Wyeth "Dear Doctor" letter and the FDA's January 1976 summary of a meeting between Wyeth and the FDA, which discussed this letter.[24] In briefing,[25] Plaintiff asserted that these documents were necessary to "show Wyeth's policy to dismiss and distract, even outright deny, that Premarin causes cancer."[26]

After Dr. Parisian read lengthy passages from the exhibits, Plaintiff's counsel asked "Now, from your expert standpoint, what do those two letters . . . say with regard to Wyeth's knowledge of how to handle scientific data that pertains to their products?"[27] Defendants objected that the question called for speculation and was beyond the scope of Dr. Parisian's report. At the sidebar, I overruled the objection after Plaintiff asserted that Dr. Parisian could "certainly opine about what information FDA requires," how Wyeth responded, and "whether or not that's appropriate under the FDA guidelines."[28] Next, Plaintiff asked Dr. Parisian whether Wyeth "display[ed] a similar attitude as it relates to breast cancer."[29] Again Defendants objected, and it was overruled. Dr. Parisian testified that rather than "doing scientific studies

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[24]*Id.* at 2681-2685; Plaintiff's Exs. 22 and 24.

[25]Before the punitive damages stage commenced, the parties filed several motions and responses regarding witness, exhibits, *etc*.

[26]Doc. No. 588.

[27]March 3, 2008, Tr. at 2683.

[28]*Id.* at 2684.

[29]*Id.*

and addressing the risks [of endometrial cancer, Wyeth] took another route in terms of trying to deal with the problem," and based on the documents she reviewed, there was a similar pattern with breast cancer.[30]

But, Dr. Parisian's testimony did not align with Plaintiff's assurances at the sidebar. Instead Dr. Parisian summarized the document:

> The letter shows that there has been a scientific discussion at the advisory panel meeting and the FDA anticipated that the company, since they are the primary provider of this product, would have pursued a scientific course or some kind of response about a clinical trial doing some kind of study. And that's why the FDA referred to this as a passive position. The company instead chose to tell physicians that it was simplistic and that there was no relation to their product and rather downplayed the risk in terms of addressing it as a responsible manufacturer.[31]

The testimony was simply a regurgitation of an exhibit, absent any expert analysis or opinion. Also missing was any reference to FDA requirements. Despite the assurances of Plaintiff's counsel, Dr. Parisian mentioned neither guidelines nor requirements in her assessment of these two exhibits. Regarding Plaintiff's Exhibits 22 and 24, the record is devoid of any testimony that Wyeth's actions violated FDA regulations or any other defined standard.[32] Instead, Dr. Parisian simply read and summarized the documents, as any layperson could have done. The promised expert testimony simply was not delivered, so I should have struck this testimony at the time.

b. Prempak Study Memo (Plaintiff's Ex. 95)

Next, Dr. Parisian addressed Wyeth's internal minutes of discussions about Prempak and its Prempak Study. Again, she and Plaintiff's counsel took turns reading the document into the

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[30] *Id.* at 2685.

[31] *Id.* at 2684.

[32] Notably, Dr. Parisian could hardly testify that Wyeth's action violated FDA regulations, because this position would have been contrary to the exhibit. The exhibit reads: "This letter is borderline in terms of violating the Food, Drug and Cosmetic Act." The FDA disagreed with Wyeth's actions, but believed only that Wyeth's actions had come close to crossing the line.

record. And, again, Dr. Parisian provided no testimony as a "regulatory expert." As best I can tell, the only reason this document was introduced was to point out that someone at Wyeth wanted to "peek at the data" of the ongoing study. There was no testimony that this would violate any regulations -- Dr. Parisian did not testify that this was inappropriate behavior -- she stated only that you "have to be careful peeking at the data" so as not to introduce bias.[33] I should not have permitted this evidence.

c. *Seasons* Magazine Proposal (Plaintiff's Ex. 154)

Plaintiff claimed Wyeth's proposal to the FDA regarding *Seasons* magazine established that "Wyeth pushed unapproved long term benefits of E and E+P" but did not study the potential risks of long-term use.[34] According to Plaintiff, the document "show[ed] Wyeth dismissed and distracted ERT/HRT breast cancer risk and overshadowed any risk of breast cancer with significant long term benefits."[35] Once again, Dr. Parisian read into evidence excerpts from the exhibit and summarized -- but her summary required no expertise.

When asked about the letter's meaning "from the FDA's standpoint," Dr. Parisian responded that all manufacturers are supposed to have fair and balanced labeling that's not misleading."[36] Dr. Parisian also testified that when pharmaceutical companies distribute information, it should be clear that the pharmaceutical company is the source of the information, rather than a doctor or pharmacist.[37] Essentially, her testimony mirrored the language in the document. Plaintiff's argument for introducing the document -- to show that "Wyeth pushed

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[33]March 3, 2008, Tr. at 2688.

[34]Doc. No. 588.

[35]*Id.*

[36]March 3, 2008, Tr. at 2693 (emphasis added).

[37]*Id.* at 2693.

unapproved long term benefits of E and E+P," but did not study the potential risks of long-term use -- was not established by Dr. Parisian. I should have struck the testimony and exhibit, because Dr. Parisian provided no expert analysis.

d. 1993 Premarin Marketing Plan (Plaintiff's Ex. 1565)

According to Plaintiff, the 1993 Premarin marketing plan "show[ed] Wyeth's awareness of long term use of its drugs by many consumers yet Wyeth never chose to study E or E+P long term to evaluate the risks . . . which goes squarely to notice, duty to test, and subsequent failure to warn."[38] Defendants suspected that Plaintiff actually intended to use the document to discuss marketing,[39] which is what happened. Dr. Parisian testified that the marketing plan exemplified when a pharmaceutical company's "marketing takes the first seat as opposed to the science."[40] Dr. Parisian's testimony about the document is devoid of any reference to the FDA or reliance on her expertise as an regulatory expert -- she provided an editorial about pharmaceutical companies putting sales and marketing before science, but gave no testimony from her position as a regulatory expert. The exhibit should have been excluded.

e. Essner's Prempro Launch Speeches (Plaintiff's Exs. 6776 and 6558)

Plaintiff contended that Bob Essner's April 4, 1995 and April 2, 1995 Prempro "launch" speeches showed "Wyeth's corporate policy to support and push E+P benefits long term without every [sic] studying E+P long term" and how Wyeth treated Prempro "from a risk and benefit perspective."[41]

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[38]Doc. No. 588.

[39]Doc. No. 2703-2704.

[40]March 3, 2008, Tr. at 2704.

[41]Doc. No. 588.

Basically, Dr. Parisian again read selected excerpts from the documents, but provided no analysis which would require regulatory expertise -- or any expertise. There was no mention of FDA regulations, nor any opinion based on her experience as an FDA medical officer. Plaintiff's primary critique of Essner's speeches was that they do not mention short-term use, breast cancer risk, or studies[42] -- this was not connected with FDA regulations.

Plaintiff also asked Dr. Parisian about Wyeth's "position with regard to how the product will be treated from a marketing standpoint."[43] In response, Dr. Parisian simply read the exhibit. Had she provided an actual opinion on this topic, it would have been beyond Dr. Parisian's expertise as a regulatory expert. I should have struck the testimony and exhibit.

f. Burson-Marsteller Account Overview (Plaintiff's Ex. 8019-A)

According to Plaintiff, the June 6, 1994 "Burson-Marsteller Premarin & Wyeth-Ayerst Women's Health: Account Overview" exemplified "Wyeth's policy of dismiss and distract of the concerns about the risk of HRT and breast cancer . . . [and] absolutely show[ed] Wyeth was on notice of breast cancer risks but did not study E+P and breast cancer and as a result did not warn of the risk."[44]

Dr. Parisian testified that if a company knew there was a link between its product and breast cancer, neutralizing that information would not be fair and balanced. She continued, "[I]t's the duty of the manufacturer to ensure that the product is safe for that indication and for those women who are using the product."[45]

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[42]March 3, 2008, Tr. at 2707.

[43]*Id.* at 2708.

[44]Doc. No. 588.

[45]March 3, 2008, Tr. at 2712-2713.

Following this testimony, I requested a sidebar, and voiced concern that Dr. Parisian was testifying outside the scope permitted by the pretrial orders. Plaintiff responded:

> [A]s to everything that I've put on thus far, I believe that I've linked it to the FDA regulations. And the concern that's been pointed out by Wyeth even in this most recent document was FDA regulatory concerns. And she went through and described, you know, what would be improper about the approach to neutralizing that evidence. So I don't think I've put in anything that doesn't fit within her area of expertise.[46]

Defendants responded that Dr. Parisian had "gone beyond both her report and her designation for this case and the limits of [pre-trial] ruling[s] regarding her testimony."[47] Plaintiff replied, "Your Honor, this is my only witness. I don't have any other witnesses. You struck Dr. Hollon."[48] Plaintiff's reason for eliciting testimony from Dr. Parisian that was outside of her report was not well founded. If a court strikes one expert, a party may not use another expert to give the same testimony if it is beyond the expert's expertise and designation. I should have struck this testimony.

g. George Mills Email on Breast Cancer Issues (Plaintiff's Ex. 7423)

Plaintiff introduced George Mills's (a Wyeth employee) February 25, 2000 email, which set out his idea for handling breast cancer issues. In the pretrial briefs, Plaintiff asserted that this exhibit "show[ed] Wyeth's policy of dismiss and distract of the concerns about the risks of HRT and breast cancer," and that Wyeth was on notice of a breast cancer risk, but neither studied nor warned of the risk.[49]

Plaintiff's counsel mentioned that he'd previously read the exhibit to the jury, and asked Dr. Parisian if it would "ever be appropriate . . . to withhold information about breast cancer risk

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[46] *Id.* at 2713.

[47] *Id.* at 2714.

[48] *Id.*

[49] Doc. No. 588.

from users of the product . . . ."[50] I am unsure as to why a regulatory expert would be needed to explain this document to the jury. The jury was equally capable of assessing the document and making the conclusions offered by Dr. Parisian. In pre-trial motions, Wyeth objected on various grounds,[51] and although a specific objection was not interposed during the punitive stage, I should have excluded this exhibit, which was clearly inadmissible via Dr. Parisian (Wyeth repeatedly objected that her testimony was not connected to FDA regulations).

h. February 28, 2000 Budget Proposal (Plaintiff's Ex. 8151)

According to Plaintiff, the February 28, 2000 budget proposal "show[ed] Wyeth's policy of funding to dismiss and distract the risk of breast cancer of E+P while expounding on the long-term benefits of E+P . . . ."[52] Counsel read a section of the exhibit: "In addition, media attention on two recent publications have raised consumer awareness about the relative risk of breast cancer . . . Additional funds are needed to minimize the impact on growth or programs which focus on the role of estrogen in disease prevention and help put the small potential risk of breast cancer in perspective."[53] Plaintiff's counsel asked Dr. Parisian, "Would it be appropriate to fund to this degree a campaign that seeks to cut down any media suggestion that there's a breast cancer risk."[54] Dr. Parisian responded, "No. It would not be appropriate from a public health point of view in terms of women's safety."[55] But where was the "regulatory" testimony promised from Dr. Parisian? Wyeth did not lodge a specific objection at this point, but had

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[50]March 3, 2008, Tr. at 2720.

[51]Doc. No. 566.

[52]Doc. No. 588.

[53]March 3, 2008, Tr. at 2721-2722.

[54]*Id.* at 2722.

[55]*Id.*

objected to the exhibit in a pre-trial motion.[56] I should not have permitted the exhibit to be admitted through Dr. Parisian, because she did not connect it with any FDA regulations.

i. Dr. Karla Kerlikowske Study

This is an August 14, 2007 article titled "Declines in Invasive Breast Cancer in Use of Postmenopausal Hormone Therapy in a Screening Mammography Population," by Dr. Karla Kerlikowske, which was published in the Journal of the National Cancer Institute.[57] After Dr. Parisian indicated that she had seen the document before, Plaintiff asked "can you tell us what Dr. Kerlikowske said regarding the potential risk" of breast cancer.[58] Dr. Parisian read the following to the jury:

> Based on an estimated 211,300 breast cancer cases in 2003, 75 percent of these diagnosed in postmenopausal women, 85 percent of them are ER positive, and an annual decline of 13 percent in ER-positive disease. The impact of declining use of postmenopausal hormone therapy could account for an estimated 17,500 fewer ER-positive invasive breast cancer cases annually among women aged 50 to 69 years.[59]

This testimony on "excess breast cancers" was the subject of numerous oral and written motions. At the close of Dr. Parisian's punitive damages phase testimony, Defendants argued that this "learned treatise" was not properly authenticated by Dr. Parisian.[60] Plaintiff argued that the article was authenticated by Dr. Austin -- an epidemiologist and Plaintiff's "general causation

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[56]Doc. No. 566.

[57]Karla Kerlikowske, et al., *Declines in Invasive Breast Cancer and Use of Postmenopausal Hormone Therapy in a Screening Mammography Population*, 100 J. OF THE NAT'L CANCER INST. 599 (2008).

[58]March 3, 2008, Tr. at 2722.

[59]March 3, 2008, Tr. at 2722.

[60]March 5, 2008, Tr. at 2837-2838

expert" -- during the compensatory damages phase of trial.[61] While the article may have been authenticated by Dr. Austin, Plaintiff did not establish that Dr. Parisian was qualified to interpret it.[62] The evidence from this learned treatise is epidemiologically based and relates to causation; both are outside the scope of Dr. Parisian's qualifications -- again, FDA regulations were her designated forte.[63]

"A scientist, however well credentialed he may be, is not permitted to be the mouthpiece of a scientist in a different specialty. That would not be responsible science."[64] According to the Advisory Committee notes to Federal Rule of Evidence 803(18), a learned treatise may be admitted as substantive evidence only when "an expert is on the stand and available to explain and assist in the application of the treatise . . . ."[65] As a regulatory expert, Dr. Parisian could not "explain and assist in the application" of the Kerlikowske article to this case. Additionally, Dr. Parisian gave no indication that she relied on the article in forming her regulatory opinions. Accordingly, Dr. Parisian should not have been permitted to read portions of the Kerlikowske article into evidence, and her testimony regarding the Kerlikowske article should have been excluded.

j. CME "Myths and Misperceptions" Handout (Plaintiff's Ex. 427)

This exhibit is a CME course handout titled "Myths and Misperceptions, Breast Cancer and HRT" from September, 1998. Dr. Parisian testified that the FDA would have no ability to

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[61]Doc. No. 652.

[62]During a sidebar, I responded that Defendants' objections made me very uncomfortable and made me think I had made pretty clear error. I concluded "I'm going to overrule your motion at this time. I've got it under advisement still." See March 5, 2008, Tr. at 2838.

[63]An expert must establish the trustworthiness of a treatise as viewed by professionals in that field.

[64]*Dura Automotive Systems of Indiana v. CTS Corp.*, 285 F.3d 609, 613 (7th Cir. 2002).

[65]FED. R. EVID. 803(18).

restrict these types of CME activities. Since the FDA could not restrict these activities, there was no evidence that Wyeth's actions violated FDA regulations. Accordingly, Dr. Parisian's interpretation of the exhibit was unnecessary.

Furthermore, when Plaintiff used this exhibit, Wyeth objected to "lack of foundation" because the exhibit was "not a Wyeth document."[66] The objection was sustained, but Plaintiff continued to use the document. Allowing further testimony after I sustained the objection was error. It appears that I had my mind in neutral at this point. The testimony regarding this document should not have been admitted.

k. March 4, 1999 Grants Authorizations (Plaintiff's Ex. 5733)

Through Dr. Parisian, Plaintiff introduced Wyeth's finance committee's March 4, 1999 authorization for awards and grants, but all Plaintiff's counsel did with the exhibit was read a few of the names of the organizations on the list.[67] There was no connection between this exhibit and FDA regulations. In fact, the "FDA doesn't have regulations about unrestricted grants."[68] I should have excluded this testimony by Dr. Parisian.

l. Ghostwriting

Dr. Parisian testified that the FDA would not be aware of ghostwriting,[69] and she provided no testimony linking FDA regulations and ghostwriting. Accordingly, I should not have permitted Dr. Parisian to testify on this topic.

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[66]March 3, 2008, Tr. at 2726.

[67]*Id.* at 2728.

[68]Feb. 20, 2008, Tr. at 2345.

[69]March 3, 2008, Tr. at 2729.

m. 1970 Upjohn "Dear Doctor" Letter (Plaintiff's Ex. 5785)

This November 19, 1970 Upjohn "Dear Doctor" letter informed physicians that Upjohn's oral contraceptive, Provest, had been shown to be connected with the "appearance of mammary nodules in beagle dogs exposed to multiples of the human dose of the progestational component for a prolonged period of time."[70] Upjohn relayed to physicians that "[a]ll available clinical data suggest no reason to predict human extrapolation of this finding nor is there any way of disproving that this can occur in the human."[71] Using this exhibit, Dr. Parisian testified only that Upjohn could have arrived at a different conclusion based on the data, and Upjohn could have done its own study to determine the validity.[72] This is more argument than expert testimony. Furthermore, there was no testimony that Upjohn's decision not to conduct a study to refute the beagle dog findings violated any FDA regulations or breached any duty Upjohn might have to test. Dr. Parisian's assessment of this document lacked any regulatory expertise, and I should have excluded the testimony.

n. July 21, 1992 HRT Scientific Review: Executive Session Summary (Plaintiff's Exs. 11011 and 11012)

Through Dr. Parisian, Plaintiff introduced an Upjohn internal memorandum and attachment that described the company's desire to get indications for HRT uses and its strategy going forward. Dr. Parisian simply read a few sections from the document. Since she provided no testimony regarding FDA regulations,[73] the testimony should have been excluded.

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[70]Plaintiff's Ex. 5785.

[71]*Id.*

[72]March 3, 2008, Tr. at 2731-2732.

[73]March 3, 2008, Tr. at 2736-2739.

3. Necessity of Expert to Distill of Voluminous Documents

In pre-trial briefs and hearings, Plaintiff argued that an expert like Dr. Parisian was necessary to review and summarize documents and "give the jury the tools they need to look at those documents, [and] understand them in the context of a regulatory background."[74] Plaintiff asserted that "Dr. Parisian's testimony and use of internal company document [would] educate the jury, not merely duplicate counsel's closing argument."[75] Plaintiff pointed out that in other bellwether trials I ruled that this was acceptable for trial.[76] In this case, the Court[77] ruled: "A purely factual recitation of the history of Provera, and its progression as a drug to be used in conjunction with estrogen to treat menopausal symptoms is relevant to show the environment in which [Defendants] operated."[78] The purpose for allowing such testimony was efficiency, and the summary of the documents was to be "purely factual."

Repeatedly, Plaintiff has argued that "[d]istilling voluminous documents is proper" for an expert -- but I do not believe the 22 or so documents introduced through Dr. Parisian during the punitive damages stage can be considered "voluminous." But more importantly, and contrary to Plaintiff's position during the *Daubert* hearing, and during he punitive damages stage, Dr. Parisian, generally, did not "give the jury the tools they need to look at those documents, [to] understand them in the context of a regulatory background"[79] -- she simply read the documents to the jury.

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[74]Nov. 5, 2007, Tr. at 113.

[75]Doc. No. 175.

[76]Nov. 5, 2007, Tr. at 113 and Doc. No. 175.

[77]I say "the Court," because this Order was entered by Judge Jones.

[78]Doc. No. 340.

[79]Nov. 5, 2007, Tr. at 113.

I cannot accept Plaintiff's position that Dr. Parisian "didn't just read a document," but "tie[d] pieces of the puzzle together."[80] To the contrary, Dr. Parisian usually read selected portions of documents in evidence, without further comment. I did not anticipate that documents would be admitted via Dr. Parisian so that she could simply engage in recitation of those exhibits; jurors are capable of reading documents. Ironically, on cross-examination, Dr. Parisian, on at least one occasion, took the position that the document "speaks for itself."[81]

If an expert does nothing more than read exhibits, is there really any point in her testifying as an expert? As was seen during the punitive damages stage, the use of the "regulatory expert" to deal with large volumes of documents is subject to abuse. The expert did not explain the documents, provide summaries, or tie them in to her proposed regulatory testimony. Dr. Parisian did not provide analysis, opinion, or expertise.

4. Applying FDA Regulations to the Facts

In response to Defendants' Motion to Exclude Dr. Parisian's testimony regarding FDA regulations -- filed before Dr. Parisian testified during the punitives phase -- Plaintiff asserted that Dr. Parisian "will testify further, what those [FDA] regulations require in a particular set of facts and circumstances. Dr. Parisian will also testify that the regulations were violated under this set of facts."[82] She did neither. As discussed in detail above, Dr. Parisian often did nothing, or little, more than read exhibits.

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[80]May 9, 2008, Tr. at 41.

[81]March 3, 2008, Tr. at 2794.

[82]Doc. No. 589 (emphasis in original).

5. Summary

Federal Rule of Evidence 702 permits expert testimony to assist a jury in understanding technical or scientific evidence. Dr. Parisian was designated to testify on regulations and the standards and practice in the industry based on her experience. Yet, Dr. Parisian's punitive damages stage testimony was hardly expert in nature. The question and answer sessions merely paid lip service to Dr. Parisian testifying from an expert standpoint.

The Advisory Committee notes to Federal Rule of Evidence 702 read: "If the witness is relying . . . primarily on experience, then the witness must explain how that experience is a sufficient basis for the opinion and how that experience is reliably accurate to the facts." In pretrial hearings, Judge Jones and I both expressed concern regarding whether Dr. Parisian met this requirement (as evidenced by the repeated requests for citations and explanations[83]). After hearing Dr. Parisian's testimony in the punitive damages phase and reviewing it post-trial, I realize that our concerns were warranted.

Dr. Parisian's punitive damages stage testimony reveals "how vital it is that judges not be deceived by the assertions of experts who offer credentials rather than analysis."[84] "An expert who supplies nothing but a bottom line supplies nothing of value to the judicial process."[85] Expert opinion must be just that -- expert opinion drawn from a special expertise. Opinion given through the mouth of an expert does not necessarily make it expert opinion.

During the punitive damages stage of the trial, Dr. Parisian's testimony tracked Plaintiff's legal arguments, and there was very little significant analysis. On numerous occasions, Dr. Parisian declared "this isn't fair and balanced," but she provided no explanation. Dr. Parisian,

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[83]Doc. Nos. 340, 389, and Nov. 14, 2008 email Correspondence from the Court.

[84]*Minasian v. Standard Chartered Bank, PLC*, 109 F.3d 1212, 1216 (7th Cir. 1997) (citations omitted).

[85]*Id.*

no doubt has special knowledge and skill regarding FDA operations and regulations, but she did not apply this knowledge and skill to her testimony.

When Dr. Parisian actually elaborated on documents, her testimony did "no more than counsel for plaintiff [did] in argument, *i.e.*, propound a particular interpretation of [defendant]'s conduct."[86] Having an expert witness simply summarize a document (which is just as easily summarized by a jury) with a tilt favoring a litigant, without more, does not amount to expert testimony. Because Dr. Parisian's testimony -- or reading -- invaded areas that required no expert assistance, it was inappropriate "expert" testimony.[87]

Since Dr. Parisian testified as to the bottom line without any explanation, failed to provide expert analysis, testified beyond limitations established by pretrial orders, testified in areas beyond her expertise, and invaded areas that required no expert testimony, most of Dr. Parisian's punitive damages testimony should have been excluded.

B. Sufficiency of Evidence During Punitive Damages Stage

Excluding the testimony I erroneously allowed in through Dr. Parisian, Plaintiff did not produce sufficient evidence to create an admissible issue under the clear and convincing standard required for punitive damages.

The Arkansas Supreme Court has approached punitive damages with caution: "If punitive damages are improperly awarded, the defendant suffers far more than a plaintiff does if the jury incorrectly fails to give him a windfall."[88] In Arkansas, "an award of punitive damages is justified only where the evidence indicates that the defendant acted wantonly in causing the

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[86] *In re Rezulin*, 309 F. Supp. 2d 531, 551 (S.D.N.Y. 2004) ("[E]xperts should not be permitted to 'supplant the role of counsel in making argument at trial, and the role of the jury in interpreting the evidence.'").

[87] *Id.* at 541.

[88] *Nat'l Bank of Commerce v. McNeill Trucking Co., Inc.*, 828 S.W.2d 584, 589 (Ark. 1992) (Dudley, J., concurring).

injury or with such a conscious indifference to the consequences that malice may be inferred."[89] To justify an award of punitive damages, "it must appear that the negligent party knew, or had reason to believe, that his act of negligence was about to inflict injury, and that he continued in his course with a conscious indifference to the consequences, from which malice may be inferred."[90] Arkansas law requires an "element of willfulness or such reckless conduct on the part of the defendant as is equivalent thereto."[91] "Gross dereliction of duty does not warrant punitive damages."[92]

In the punitive damages stage, Plaintiff's burden was to establish, by clear and convincing evidence, that Defendants knew or should have known that their negligent failure to warn (which, based on the compensatory damages phase testimony, included a duty to test) of the risks associated with ERT/HRT use and breast cancer would result in injury, and that Defendants continued the conduct with wantonness or reckless disregard from which malice can be inferred.

During opening statements of the punitive damages stage, Plaintiff's counsel argued the evidence would establish that:

> Wyeth and Upjohn failed to follow up on the red flags that showed that this product was causing breast cancer, they failed to get the proper answers by going out and studying the drugs, and they failed to give the doctors and the women accurate information. And then finally, they failed to market the product appropriately.[93]

Yet, the evidence Plaintiff presented was an extension of the liability arguments that amounted to no more than negligence. The record, absent erroneously admitted information,

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[89] *Union Pacific R.R. Co. v. Barber*, 149 S.W.3d 325, 343 (Ark. 2004) (citing cases).

[90] *Id.*

[91] *Id.*

[92] *Orsini v. Larry Moyer Trucking, Inc.*, 833 S.W.2d 366, 368 (Ark. 1992); see also *Alpha Zeta Chapter of Pi Kappa Alpha Fraternity by Damron v. Sullivan*, 740 S.W.2d 127, 132 (Ark. 1987) ("Negligence alone, however gross, is not enough to sustain punitive damages.").

[93] March 3, 2008, Tr. at 2649.

reflects insufficient evidence of wantonness, willfulness, or reckless disregard from which malice could be inferred.

1. Summary of Punitive Damages Evidence Against Wyeth.

Plaintiff's argument for punitive damages can be summarized as follows: In 1976 Wyeth was aware of the Hoover Study, which suggested a link between estrogen use and breast cancer. The endometrial cancer crisis also occurred around this time, and Wyeth should have seen it as a wake-up call to commence looking into the relationship between estrogen use and breast cancer. Wyeth knew that physicians were prescribing estrogen and progestin together, and it should have realized that if E-alone causes cancer in one reproductive organ, the addition of progestin could cause cancer in similar organs. Wyeth "knew" adding progestin to estrogen could increase the risk of breast cancer.

Wyeth knew more study was needed, but took a passive role in conducting studies. When Wyeth considered initiating the Prempak Study, Wyeth was concerned that the study might not be successful and could be "embarrassing." Wyeth never completed the Prempak Study.

Wyeth responded to studies associating ERT and HRT use with breast cancer by downplaying the studies and promoting the benefits of ERT and HRT. Specifically, Wyeth used public relations firms, "friendly organizations to which it gave millions of dollars, friends who spoke favorably about its products, marketing, press manipulation or even ghostwriting" to counter studies (and media) reporting a link between HRT and breast cancer.[94]

[94]Doc. No. 652.

a. Wyeth Knew About Studies Linking Breast Cancer and Estrogen

Plaintiff argued that in 1976 Wyeth was aware that the Hoover Study[95] suggested a link between estrogen use and breast cancer, but "did nothing" in response.[96] This argument is contrary to the evidence in the record. Wyeth acknowledged the Hoover Study and determined that the suggestion of a link between estrogen use and breast cancer "required further evaluation and monitoring, which is what [Wyeth] did."[97] Additionally, Wyeth took the position that it "need[ed] to know all there is to know, both good and bad, about all available studies having a bearing" on the connection between estrogen use and breast cancer.[98] Wyeth recognized that it may need to "shift their efforts to the development of a protocol for a study on mammary cancer."[99]

Three months later, in June of 1976, Wyeth noted that "there have been and are numerous epidemiological studies on the clinical effects of long term estrogen therapy," but concluded that the "studies on estrogen-breast cancer relationships . . . show[ed] no significant increase in the relative risk."[100] Wyeth concluded that "[t]he fact that no recent significant increase in breast cancer has been reported can be taken as an indirect indication that estrogens do not cause an

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[95]Dr. Hoover wrote a letter to Wyeth that reads:

> Enclosed is a confidential copy of a manuscript which will be published . . . This study forms the basis for my . . . statement that I had evidence which I interpreted as indicating that menopausal estrogens may be a risk factor for breast cancer as well as for endometrial cancer. As you can see, the findings for breast cancer are certainly not as clear-cut as those for endometrial cancer . . . I believe it does indicate that there may be a problem, that certainly needs more intensive study.

Plaintiff's Ex. 31.

[96]Doc. No. 652.

[97]Feb. 7, 2008, Tr. at 504.

[98]Plaintiff's Ex. 26.

[99]*Id.*

[100]Plaintiff's Ex. 28.

increase in breast cancer" and that "[e]strogen use does not appear to bring about an increased risk of breast cancer."[101]

In sum, Wyeth's response to the 1976 study suggesting a link between estrogen use and breast cancer -- recognition of a possible connection and follow-up research -- illustrated neither a passive response nor reckless indifference that would infer malice.

b. Endometrial Crisis Should Have Been A Wake-Up Call

In post-trial briefing, Plaintiff asserted that the "endometrial cancer crisis should have been a wake-up call to Wyeth. If E-alone cause[d] cancer in one reproductive organ, the addition of a new hormone, progestin, could cause cancer in another such organ."[102] I do not recall any expert testifying that, because Wyeth was aware that hormones may cause cancer below the waist, it should have known that hormones could cause cancer above the waist. Without scientifically supported evidence, this statement is nothing more than argument. Even if Plaintiff's position was supported by some evidence, the record reflects that Wyeth reviewed the available science and considered the issue.[103]

c. Wyeth Knew That Adding Progestin Could Increase Risk

In its post-trial brief, Plaintiff argued that "Wyeth knew that the addition of a progestin could increase the incidence of breast cancer";[104] but the brief lacked a citation to evidence that Wyeth "knew" progestins could increase the incidence of breast cancer. Based on the record, what Wyeth "knew" was that "[t]he possible role of progesterone in the etiology of breast cancer

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[101]Plaintiff's Ex. 28 (emphasis in original).

[102]Doc. No. 652.

[103]Plaintiff's Exs. 28, 117, and 1057.

[104]Doc. No. 652.

is another area that need[ed] clarification."[105] Additionally, the fact that as late as the mid-1990s the medical community believed that adding a progestin to an estrogen would protect against breast cancer, in the same way it protected the uterus, rebuts Plaintiff's unsupported assertion that Wyeth "knew" just the opposite.[106] Accordingly, Plaintiff's argument that Wyeth knew the addition of a progestin could increase the incidence of breast cancer was unsupported by any significant evidence.

d. Wyeth Knew More Study Was Needed, But Took a Passive Role

Plaintiff asserted that in 1977, Wyeth knew that "more study was needed on the combination product."[107] Dr. Parisian testified that Wyeth took a "passive role" in response to the endometrial cancer crisis.[108] She also testified that Wyeth had a passive attitude in its response to breast cancer: "Instead of doing scientific studies addressing the risks, they took another route in terms of trying to deal with the problem."[109] Notably, Wyeth objected that Dr. Parisian was "not competent to talk about Wyeth's attitude,"[110] and I overruled the objection. On reflection, this was error.

Plaintiff relied on Plaintiff's Exhibits 22 and 24 for this testimony. However, above I determined that since Dr. Parisian did not connect her testimony on these documents to FDA regulations, the testimony and exhibits should not have been admitted. That being so, there is no evidence to support Plaintiff's position.

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[105]Plaintiff's Ex. 28.

[106]Feb. 6, 2008, Tr. at 458-459; Feb. 8, 2008, Tr. at 850-852; Feb. 15, 2008 Tr. at 1811-1812.

[107]Doc. No. 652.

[108]March 3, 2008, Tr. at 2685.

[109]*Id.*

[110]*Id.* at 2684-2685.

e. The Prempak Study

Wyeth began studies of the estrogen and progestin combination in the early 1980s.[111] Specifically, in 1983, Wyeth initiated the Prempak Study. Plaintiff's critique of the Prempak Study was minimal -- she introduced speculative evidence regarding "embarrassment," pointed out that someone wanted to peek at the data, and emphasized that the study was not completed. I will address each of these in turn.

i. Study Results Could be Embarrassing

A September 22, 1983, Wyeth internal correspondence titled "PREM-PAK: Desired Labeling and Indications" reads, in part:

> An underlying consideration concerning our overall approach to the FDA concerning PREM-PAK has been the importance of avoiding the problems which could arise if the FDA were to take the position that PREM-PAK is equivalent to a combination drug product of the type requiring demonstration that the combination does more than its components in regard to each indication for the combination product. To attempt such demonstration would be very costly, would take many years, and might in the end not prove successful. In fact, the results of the studies that would be needed could turn out to be embarrassing.[112]

Plaintiff asserted that this exhibit "goes to the heart of this issue of whether or not [Wyeth] had reckless disregard."[113] However, Dr. Parisian's testimony about the exhibit, given during the compensatory damages stage, was limited:

> Q: And what could be embarrassing, from your standpoint as an FDA reviewer, if they did studies?
> A: Well, it would be embarrassing, perhaps, if the results weren't positive and you didn't get approved.[114]

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[111]Feb. 6, 2008, Tr. at 441-442.

[112]Plaintiff's Ex. 69.

[113]March 3, 2008, Tr. at 2649.

[114]Feb. 12, 2008, Tr. at 1286.

Plaintiff argued that this exhibit established that Wyeth was aware that a study might reveal that breast cancer could result when progestin is added to estrogen;[115] however, she provided no evidence to support this position. During trial, Wyeth explained that the exhibit:

> is talking about the FDA combination drug policy, which typically when you combine two products together into a combination, the first product has a certain degree of benefit or efficacy and the second product has a certain degree of benefit or efficacy. The expectation is that the combination would have a greater benefit, more efficacy, faster efficacy, better efficacy. In this instance, we were not putting the MPA or the progestin component to estrogen to make it more efficacious, to give it better effect, to relieve vasomotor symptoms faster or better, to improve bone better. It was there to protect the endometrium only.
>
> So what Dr. Perdue is saying is that if FDA or anyone were to expect that this particular combination would have better efficacy, it wouldn't, and so if one were to have that expectation, the results of the study might be embarrassing because it didn't provide greater efficacy. That was never the intent and was not the expectation.[116]

When considering the exhibit in context and based on the evidence as a whole, Plaintiff's position appears to be speculation. This evidence that Plaintiff claimed went "to the heart of this issue of whether or not [Wyeth] had reckless disregard," provided no support for her position on punitive damages.

ii. Someone Suggested Peeking at the Data

The Prempak Study's goal was to show that adding progestin to an estrogen would reduce the risk of endometrial hyperplasia.[117] Wyeth's summary of minutes -- from a meeting held in mid to late 1987[118] -- discussing the progress of the Prempak Study reads:

> Objective was to demonstrate that the presence of a progestogen did not add to the detriment of the product . . . Hope [the hyperplasia] is showing up in estrogen alone

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[115]May 9, 2008, Tr. at 44.

[116]Feb. 7, 2008, Tr. at 641.

[117]March 3, 2008, Tr. at 2687.

[118]The document is not dated, but the following is included: "No meeting on this project has been held in the last 12 months (May 1986)." Plaintiff's Ex. 95.

> group. If not, can [sic] kiss the product good-bye . . . Somebody should peek at the data when you reach a certain point. [Wyeth] hides the randomization code.[119]

Regarding testing, Plaintiff's counsel suggested that "it looks like [Wyeth] was doing the right thing, but somebody else within this system wanted to peek at the data."[120] As for peeking at the data, as noted above, Dr. Parisian testified only that "[w]e have to be careful peeking at the data because you can introduce bias . . . ."[121] She did not contend that "peeking at the data" was inappropriate or a violation of any regulations; she suggested only that you must be careful. Additionally, there was no testimony that Wyeth either peeked at the data or introduced bias.

iii. The Prempak Study Was Not Completed

Plaintiff pointed out that the Prempak Study was not completed. In 1988, the Prempak Study ended because of on-going difficulty obtaining participants.[122] No reckless disregard can be inferred from the fact that the study was never completed.

f. Refusal to Provide Drugs to ECOG (Plaintiff's Exs. 251 and 265)

During the compensatory damages stage, Plaintiff presented two internal Wyeth memos, dated December 8, 1993 and February 9, 1994, regarding Wyeth's refusal to supply Premarin in support of a proposed study by the Eastern Cooperative Oncology Group.[123] According to the documents, Wyeth would not provide drugs for the ECOG study "consistent with company policy."[124] While discussing the December 8, 1993 memo, Plaintiff's counsel argued that Wyeth's "company policy" in 1993 was "not to provide drugs to people that were doing studies

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[119]Plaintiff's Ex. 95.

[120]March 3, 2008, Tr. at 2688.

[121]*Id.*

[122]Feb. 15, 2008, Tr. at 1864.

[123]Plaintiff's Exs. 251 and 265.

[124]Plaintiff's Ex. 251.

on breast cancer."[125] The witness "absolutely disagree[d]" with this statement.[126] Using the February 9, 1994 memo, Plaintiff's counsel again attempted to get the witness to agree that Wyeth had a policy of not supporting breast cancer studies; again, the witness disagreed.[127] The witness later testified that Wyeth's "company policy" at the time was to not study ERT or HRT in patients who had previously been diagnosed with breast cancer, because this was a "contraindication"[128] for the products.[129]

In its post-trial brief, Plaintiff asserted that since Wyeth provided no document laying out "company policy," a jury has the right to infer that the policy was to not give drugs to breast cancer studies.[130] Plaintiff had the burden of proof, and the testimony was that Wyeth's "company policy" in 1993 was to not support the study because it involved a contraindication. Plaintiff presented no evidence to contradict Wyeth's explanation of the "company policy." Accordingly, the ECOG evidence provided no support for Plaintiff's claim that Wyeth took a passive role in conducting studies.

g. Prempro Pivotal Trial

In 1988, Wyeth submitted a draft to the FDA for what would become the Prempro Pivotal Trial.[131] The Prempro Pivotal Trial "monitored for safety risks, including breast cancer . . . ."[132]

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[125]Feb. 7, 2008, Tr. at 552.

[126]*Id.* at 553.

[127]*Id.* at 554.

[128]According to the Merriam-Webster on-line dictionary, in medicine, a contraindication is a condition or factor "that makes a particular treatment or procedure inadvisable." Available at: http://www.merriam-webster.com/dictionary/contraindication

[129]Feb. 7, 2008, Tr. at 625.

[130]May 9, 2008, Tr. at 45.

[131]Feb. 7, 2008, Tr. at 642. This study was a one-year, randomized controlled trial designed to "assess the impact on endometrial hyperplasia of the combination product." Feb. 7,

Plaintiff conceded that the Prempro Pivotal Trial studied for breast cancer, but argued that it was not long enough.[133] While this may be true, I do not believe this is evidence from which reckless disregard can be inferred.

h. Reaction to Adverse Studies and Media

According to Plaintiff, Wyeth's reactions to studies that suggested a link between breast cancer and hormone replacement therapy demonstrated Wyeth's conscious indifference. Plaintiff pointed out that Wyeth used public relations firms, "friendly organizations to which it gave millions of dollars," marketing, press manipulation, and ghostwriting to counter studies (and press reporting on the studies) that suggested a link between HRT and breast cancer.[134]

i. Public Relations Firms

Burson-Marsteller is a public relations firm that has worked for Wyeth since the 1980s.[135] Plaintiff devoted considerable time discussing numerous marketing and public relations suggestions that Burson-Marsteller submitted to Wyeth over the years.

According to Plaintiff, Burson-Marsteller's June 6, 1994 "Premarin & Wyeth-Ayerst Women's Health: Account Overview"[136] showed Wyeth's strategy of "pre-empting negative

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2008, Tr. at 644.

[132]*Id.* at 644.

[133]Feb. 7, 2008, Tr. at 590.

[134]Doc. No. 652.

[135]March 5, 2008, Tr. at 2897-2898.

[136]Plaintiff's Ex. 8019-A.

press [and] offer[ing] the media balanced information."[137] According to the document, this approach "[n]eutralized [the] impact of negative news linking ERT to range of health issues."[138] Dr. Parisian testified that if it were true that there was a link between the product and breast cancer, this approach would not be "fair and balanced . . . [and] it's the duty of the manufacturer to ensure the product is safe for that indication . . . ."[139] This exhibit referenced activities that occurred from 1989-1991, but, according to another Burson-Marsteller proposal, as late as 1995, there was "no definitive evidence associating breast cancer with estrogen . . . [and] the majority of epidemiological studies [showed] no association between the usual low doses used for ERT and breast cancer."[140]

In 1997, Burson-Marsteller suggested that "[i]n the world of ERT and breast cancer, misperceptions and confusion dominate the emotional issues surrounding breast cancer,"[141] and they wanted "to impact existing attitudes about breast cancer by promoting reality and debunking myths surrounding the issues," to get users or potential users away from the "misperceptions linking HRT and breast cancer."[142] The goal was to provide women with "the correct information on the relationship between breast cancer and HRT . . . ."[143] Dr. Parisian testified that Burson-Marsteller's proposal "wanted to create the desired perception of HRT and breast cancer was not known [sic], but I'm supposedly getting so many benefits that I will not

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[137]Plaintiff's Ex. 8019-A; March 3, 2008, Tr. at 2928.

[138]Plaintiff's Ex. 8019-A.

[139]March 3, 2008, Tr. at 2711-2712.

[140]Plaintiff's Ex. 5677.

[141]*Id.*

[142]*Id.*

[143]*Id.*

fear breast cancer anymore."[144] She said that the proposal "would not be acceptable" to the FDA because it was not "fair and balanced."[145]

In the proposal, Burson-Marsteller designated the Nurses' Health Study as one of "four primary barriers distorting reality" between breast cancer and HRT.[146] According to Dr. Parisian, if this was how Wyeth viewed the Nurses' Health Study, it should have updated its labeling and marketing to physicians or done a study to determine if there was a link between breast cancer and HRT.[147] Again, however, Dr. Parisian did not bottom her opinion upon FDA regulations -- her designated area of expertise.

Plaintiff also introduced an August 22, 1997 Burson-Marsteller proposal titled "Premarin Pre-emptive Plan."[148] Plaintiff's counsel pointed out that the plan wanted to "redefine Premarin's risk profile, [sic] breast cancer, demonstrate that Premarin is not a carcinogen."[149] Yet, there was no testimony explaining what this meant, or why it might be malicious.

Plaintiff presented a July 25, 1994 letter from Burson-Marsteller to Wyeth titled "Breast Cancer & ERT: Risk in Perspective Campaign -- Preliminary Recommendations."[150] However, the testimony relating to this document was not relevant to a punitive damages issue (I'm still puzzled as to why it was introduced).[151]

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[144]March 3, 2008, Tr. at 2715.

[145]*Id.*

[146]Plaintiff's Ex. 5677.

[147]March 3, 2008, Tr. at 2716-2717.

[148]Plaintiff's Ex. 1448.

[149]March 5, 2008, Tr. at 2829.

[150]Plaintiff's Ex. 1030.

[151]See March 5, 2008, Tr. at 2816-2820.

Plaintiff introduced Wyeth's 1991 "Premarin crisis preparedness plan."[152] According to the testimony, the document was a "mock exercise" for how "Wyeth could respond to issues."[153] There appears to be nothing per se wrong when a company prepares to respond to negative press.

Essentially, Plaintiff used the Burson-Marsteller documents to suggest that Wyeth's responses to negative media are inappropriate. But the evidence in the record established that Wyeth believed the "media sensationalize[d] negative events,"[154] and that the science conflicted with the media reports. Employing a public relations firm to counter the media is not, in itself, evidence of reckless disregard by the company; rather, it may be a business model employed by most corporations. According to the documents, Wyeth's goal was to put the "risk in perspective" and assure that the media provided "balanced" reports on the science regarding the link between HRT and breast cancer. This seems to be in line with Dr. Parisian's repeated phrase that the FDA requires information to be "fair and balanced." Plaintiff's point is that Wyeth countered the media, rather than embracing it and conducting studies. If true, on this record, it is evidence of, at most, negligence -- not clear and convincing evidence of reckless indifference by Wyeth.

ii. Donations to Friendly Organizations

According to Wyeth's finance committee's March 4, 1999 authorization, Wyeth authorized $18,114,725 for awards and grants as part of the annual budget.[155] The exhibit also listed each of the organizations receiving the awards and grants. Plaintiff emphasized the quantity and scope of Wyeth's donations, but Dr. Parisian conceded that Wyeth's support of

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[152]Plaintiff's Exs. 1187, 1188, 1190. See March 5, 2008, Tr. at 2898-2903, 2924-2925.

[153]March 5, 2008, Tr. at 2924.

[154]Plaintiff's Ex. 8019-A.

[155]Plaintiff's Ex. 5733.

ACOG, NAMS, and other medical associations was appropriate.[156] So, this exhibit provides no evidence of reckless indifference. And, as discussed above, I should not have permitted the exhibit to be introduced through Dr. Parisian.

iii. *Seasons* Magazine (Plaintiff's Ex. 154)

Wyeth's *Seasons* magazine was intended for "women taking Premarin with incentives to continue taking Premarin."[157] Plaintiff claimed that Wyeth used *Seasons* magazine to downplay the breast cancer risk while promoting the benefits of HRT.[158] According to Plaintiff, this evidence also goes to Wyeth's state of mind.[159]

In a February 25, 1991 letter, the FDA responded to Wyeth's *Season* magazine proposal, which Wyeth "plan[ned] to use in a direct-to-consumer program . . . ."[160] The "draft [was] submitted to the FDA in advance of and requesting permission to publish it."[161] The FDA believed that the proposed draft was "misleading in that the sponsorship [was] not clearly stated. It intentionally misleads the reader into thinking that her physician [was] somehow responsible for providing it to her."[162] The FDA also pointed out that there were "a number of other potentially false and misleading points in the submitted material."[163]

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[156]Feb. 13, 2008, Tr. at 1534-1535.

[157]Plaintiff's Ex. 154.

[158]Doc. No. 588.

[159]May 9, 2008, Tr. at 32.

[160]Plaintiff's Ex. 154.

[161]March 3, 2008, Tr. at 2749.

[162]March 3, 2008, Tr. at 2690.

[163]Plaintiff's Ex. 154.

According to Dr. Parisian, if "Wyeth wanted to do something like [the *Seasons* magazine ad campaign], they would have to clearly indicate that they are the source, and they are trying to sell their own products to the woman."[164] Wyeth responded to the FDA on February 25, 1991:

> It was not our intent to imply to consumers that Seasons [sic] magazine is a commercially available magazine being provided by her physician or pharmacist. We have, therefore, revised all components of the program to clearly state that the program and magazine are produced and distributed by Wyeth-Ayerst.[165]

Wyeth revised the *Seasons* magazine draft and resubmitted it to the FDA.[166] On August 19, 1991, the FDA informed Wyeth that it had "further discussed the revised [*Seasons* magazine] campaign," and had "no objections to [Wyeth] proceeding with this campaign."[167] In the ten years that Wyeth published *Seasons* magazine, the FDA never complained about an issue of *Seasons* magazine "as it was published to the public."[168]

Dr. Parisian only testimony on this exhibit was that when pharmaceutical companies distribute information, it should be clear that the pharmaceutical company was the source of the information, rather than a doctor or pharmacist.[169] The document did not provide proof of reckless indifference. Additionally, the April 16, 1991 letter from Wyeth to the FDA[170] reveals Wyeth's state of mind -- there's no need to speculate. Wyeth revised the draft to conform with

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[164]March 3, 2008, Tr. at 2693.

[165]Wyeth's Ex. 368.

[166]March 3, 2008, Tr. at 2750.

[167]Wyeth's Ex. 700; March 3, 2008, Tr. at 2750.

[168]March 3, 2008, Tr. at 2750-2751.

[169]*Id.* at 2692.

[170]Wyeth's Ex. 368.

the FDA's request, and "endeavored to clearly state throughout these pieces that the program and magazine are published and provided by Wyeth-Ayerst Laboratories, makers of Premarin."[171]

If this exhibit suggests malice or reckless disregard, the suggestion is weaker than a $2.00 suitcase -- it is not enough standing alone or with the other admissible evidence to create a submissible issue on punitive damages. Furthermore, I unable to discern or divine how this omission (failing to show who wrote the articles) relates to a failure to warn allegation. Regardless, as discussed in Section III(A)(2)(c) of this Order, I should have struck the exhibit and Dr. Parisian's testimony about the exhibit.

iv. Press Manipulation

In early 1990, Wyeth discovered that Dr. Graham Colditz was going to present a study relating Premarin and increases in the risk of breast cancer. Plaintiff introduced evidence that Wyeth's proposed strategy in response to the study was to "[b]e reactive on the cancer issue. Be prepared to take a responsive stance towards media covering the cancer story with accurate, full and balanced information on the issues presented in proper context."[172] Wyeth also considered "plans for publishing breast cancer study."[173] Neither of these actions, without more, support any inference of reckless disregard by Wyeth.

Plaintiff contended that the February 28, 2000 "Premarin -- Additional Marketing Budget" "show[ed] Wyeth's policy of funding to dismiss and distract the risk of breast cancer of E+P while expounding on the long term benefits of E+P . . . ."[174] Additional funds were needed because the current budget did

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[171]*Id.*

[172]Plaintiff's Ex. 1265.

[173]*Id.*

[174]Doc. No. 588.

> not adequately support the additional tactics needed to drive growth, particularly in light of the introduction of four new competitors . . . In addition, media attention on two recent publications have [sic] raised consumer awareness about the relative risk of breast cancer . . . Additional funds are needed to minimize the impact on growth or programs which focus on the role of estrogen in disease prevention and help put the small potential risk of breast cancer in perspective.[175]

This document does not bolster Plaintiff's claim for punitive damages. The fact that Wyeth increased the Premarin budget in an effort to "put the small potential risk of breast cancer in perspective" does not support a claim that Wyeth acted with reckless indifference. While "putting the risk of breast cancer in perspective" rather than doing an independent study may support a claim for negligence, it does not rise to the level required for punitive damages.

The record is replete with evidence that Wyeth wanted the media to present "balanced" information.[176] No malice or reckless indifference can be inferred from a company's desire to attempt to assure the media presents "balanced" information, especially when there is on-going debate on an issue.

v. Ghostwriting

Plaintiff focused heavily on the fact that Wyeth, through DesignWrite, collaborated with authors to have articles written about HRT in a process called "ghostwriting." In closing argument, Plaintiff asserted that ghostwriting is "exactly the type of conduct that necessitates punitive damages."[177] However, there is no evidence that this practice is inappropriate or that Wyeth supported articles that it knew were false or misrepresented the science. Rather, the articles supported Wyeth's position on the state of the science. Additionally, there was evidence

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[175]Plaintiff's Ex. 8151.

[176]Plaintiff's Ex. 1265; Feb. 7, 2008, Tr. at 619, 625; Feb. 12, 2008, Tr. at 1294, 1305; Feb. 20, 2008, Tr. at 2323, 2340; March 3, 2008, Tr. at 2711; March 5, 2008, Tr. at 2928, 2932, 2935, 2956-2957.

[177]March 6, 2008, Tr. at 3025.

that ghostwriting was a common practice in the industry.[178] In fact, Dr. Parisian conceded that she had done ghostwriting on behalf of Johnson & Johnson.[179]

Regardless of the bad inference Plaintiff placed on ghostwriting, it is apparently the norm in the industry,[180] and without evidence that Wyeth lied or misrepresented the science it chose to support, this evidence does not establish malicious behavior that would permit punitive damages. Additionally, this testimony was introduced through Dr. Parisian, but has no link to FDA regulations -- Dr. Parisian's area of expertise. And, if the inference of reckless disregard is raised, it is very weak. There is not enough to support submission to the jury taken alone or considered with all the other admissible evidence.

vi. Essner Launch Speech (Plaintiff's Exs. 6558, 6776)

Plaintiff contended that Bob Essner's (a Wyeth executive) April 4, 1995 Prempro "launch speech"[181] to the Wyeth sales team and his April 2, 1995 Prempro "launch speech"[182] showed "Wyeth's corporate policy to support and push E+P benefits long term without ever studying E+P long term" and how Wyeth dealt with "Prempro from a risk and benefit perspective."[183] During post-trial briefing, Plaintiff asserted that the launch speeches showed how "Wyeth illegally tried to hook postmenopausal women on E+P for the rest of their lives."[184] However,

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[178]Feb. 20, 2008, Tr. at 2343.

[179]Feb. 13, 2008, Tr. at 1533-1534.

[180]"[H]iring third-party professional writers and asking authors to sign those and asking those authors to be responsible for their content is very common practice." Feb. 20, 2008, Tr. at 2343.

[181]Plaintiff's Ex. 6776.

[182]Plaintiff's Ex. 6558.

[183]Doc. No. 588.

[184]Doc. No. 652.

when the Essner launch speeches are reviewed in context, they provides little support for Plaintiff's claims for punitive damages.

First, Plaintiff pointed out that nowhere in these launch speeches does Mr. Essner mention short-term use, breast cancer risk, or studies;[185] but, Plaintiff presented no evidence as to why these speeches would require reference to these specific topics. Additionally, according to the testimony, the sales organization "spent the next five days learning about the safety and efficacy of the product."[186]

Second, Plaintiff argued that Mr. Essner instructed the sales force to "thumb its nose at the FDA" and "improperly, if not illegally promote lifetime use for all women."[187] This conclusion is not supported by the evidence. Mr. Essner's comments were:

> [Dr. Healy] made the prediction that in the very near future there is going to be a revolutionary increase in the use of hormones to prevent and treat a variety of conditions in older women . . . [Dr. Healy said] that women starting on HRT at menopause and staying on it for the rest of their lives will become the rule, and that this will have a dramatic and positive effect on women's health . . . We have an opportunity to start the HRT revolution that Dr. Healy predicted. We can make real the full promise of HRT to create in the near future a world where the majority of women will start HRT at menopause and continue on it for the rest of their lives. A world where women will get the full medical benefit of replacing the estrogen lost after menopause and the full protective effect of MPA."[188]

Mr. Essner was quoting Bernadine Healy, the former head of NIH, and her opinion that all women should be on HRT. Additionally, nowhere in the speech does he tell the sales force to promote Prempro in this manner; rather, he's suggesting that things look good for Prempro in view of Dr. Healy's predictions on the future of HRT.

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[185]March 3, 2008, Tr. at 2707.

[186]March 5, 2008, Tr. at 2888.

[187]Doc. No. 652.

[188]Plaintiff's Ex. 6558.

Plaintiff also pointed out that Mr. Essner referenced Carrie Smith-Cox's (from Wyeth's marketing department) comments that "for Prempro and Premphase there are no boundaries, no limits."[189] The unrequited testimony regarding the meaning of "no boundaries, no limits" is that Mr. Essner wanted to get the sales force "fired up" about going all-out to promote Prempro;[190] the phrase was about the sales force's "selling effort."[191]

But, as discussed earlier in detail, I should have struck these two exhibits and Dr. Parisian's testimony about the exhibits.

vii. IARC Document (Plaintiff's Ex. 146)

Plaintiff contended that Wyeth wanted to "ensure that IARC [did] not develop a position on a definitive relationship between breast cancer and estrogen replacement therapy . . . ."[192] Plaintiff argued that this is "not appropriate,"[193] but Plaintiff provided no testimony to support this position -- only argument of counsel. In fact, the only point Plaintiff made with this exhibit (that wasn't in opening statement or closing argument -- which are not evidence) was that it referred to estrogen therapy alone.

There is no testimony that Wyeth's forming a task force to "provide the necessary information to IARC"[194] to support Wyeth's position that there was no definitive relationship between estrogen therapy and breast cancer is improper. If Wyeth believed that there was no "definitive association" between estrogen replacement therapy and breast cancer, why wouldn't

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[189]March 3, 2008, Tr. at 2707.

[190]March 5, 2008, Tr. at 2887.

[191]Plaintiff's Ex. 6776.

[192]Plaintiff's Ex. 146 (emphasis in original).

[193]March 3, 2008, Tr. at 2650.

[194]Feb. 7, 2008, Tr. at 547-548.

it attempt to gather science and convince IARC that there was no "definitive association" between the two?

2. Summary of Punitive Damages Evidence Against Upjohn

Plaintiff contended that Upjohn was liable for punitive damages because it conducted no studies and proposed no warnings to the FDA regarding the possible connection between Provera use and breast cancer. Plaintiff's position was:

As early as 1963, Upjohn should have been aware of the breast cancer risk related to Premarin, based on an abstract that was released. In 1966, the FDA rejected Upjohn's supplemental new drug application for "revised labeling to include the adjunctive use of [Provera] in hypoestrogenic states."[195] According to Plaintiff, when the FDA informed Upjohn that the "supplemental application [was] incomplete" because it "failed to include adequate clinical data . . .,"[196] Upjohn was on notice of its duty to test the relationship between Provera and breast cancer. In 1970, Upjohn knew that animal toxicology studies, involving a product that was different from Provera, but that contained medroxyprogesterone, reported that the subjects developed mammary nodules. But rather than test, Upjohn informed doctors that "[a]ll available clinical data suggest no reason to predict human extrapolation of this finding nor is there any way of disproving that this can occur in the human."[197] In the 1980s and 1990s, Upjohn promoted Provera as "the other half of estrogen replacement therapy," and the FDA scolded Upjohn when some advertisements attempted to promote Provera for indications (prevention of endometrial hyperplasia, osteoporosis) for which it was not approved. During this

[195]Plaintiff's Ex. 10388.

[196]*Id.*

[197]Plaintiff's Ex. 5785.

entire time, Upjohn never conducted its own study addressing the breast cancer in connection with HRT.[198]

a. 1963 Upjohn Memo (Plaintiff's Ex. 10388)

Plaintiff asserted that "Upjohn knew of the potential breast cancer risk at least by 1963,"[199] and should have started studying the drug. In June, 1963, Upjohn analyzed an abstract titled "Provera-induced hypercalcemia in women with advanced breast cancer."[200] But this document does not support Plaintiff's suggested inference. The uncontradicted testimony is that the report suggested progestin may have raised calcium levels in women who already had breast cancer.[201]

b. "The Other Half of Estrogen Replacement Therapy"

During the punitives stage, Plaintiff's punitive damages evidence against Upjohn focused primarily on correspondence between the FDA and Upjohn regarding advertising campaigns for Provera. Plaintiff argued that this evidence established a duty to test -- *e.g.*, "If a drug company advertises its products to be used in combination with another product, the company has a duty to study the two drugs in operation together."[202] The evidence was:

- **January 5, 1984 FDA Letter** -- The FDA requested "immediate cancellation" of an advertisement that "impl[ied] the use of Provera with estrogen replacement therapy except in those situations as described in [the] approved package insert."[203] The FDA also informed Upjohn that it recognized that the concurrent

[198]March 3, 2008, Tr. at 2738-2739; March 5, 2008, Tr. at 2813.

[199]Doc. No. 651.

[200]Plaintiff's Ex. 10910.

[201]Feb. 19, 2008, Tr. at 2199-2201 and 2226.

[202]Doc. No. 651.

[203]Plaintiff's Ex. 10154.

use of estrogen and progestin was becoming a more common practice, but that Upjohn needed to update its package insert before promoting Provera for such a use.[204]

- **September 10, 1985 FDA Letter** -- The FDA wanted ads titled "The other half of estrogen replacement therapy" removed from circulation, because the ads "present[ed] Provera as being safe and effective for the treatment and reversal of endometrial hyperplasia which [was] not an approved indication . . . ."[205] Plaintiff argued that this exhibit establishes that in 1985 Upjohn was aware that its product was being used with estrogen and was under a duty to test.
- **July 10, 1986 Letter** -- Upjohn informed the FDA that it planned to submit a proposal for a "convenience pack" for concomitant estrogen and progestin administration.[206] The FDA informed Upjohn that "there [was] not yet an indication for such combinations and the potential risks [were] not yet resolved."[207]
- **January 15, 1988 FDA Letter** -- Upjohn wanted Provera approved to oppose the endometrial effects of estrogen in menopausal women receiving estrogen replacement therapy. The FDA informed Upjohn that it "failed to provide substantial evidence consisting of adequate well-controlled studies . . ." that

[204] *Id.*

[205] Plaintiff's Exs. 10178 and 10155 (same document).

[206] Plaintiff's Ex. 10342.

[207] *Id.*

Provera will have this effect.[208] Dr. Parisian testified only that the FDA believed that there was insufficient evidence to support the indication Upjohn wanted.

- **October 30, 1990 FDA Letter**[209] -- This exhibit was admitted into evidence, but Plaintiff never discussed it with a witness.
- **October 31, 1990 FDA Letter**[210] -- The FDA informed Upjohn that it should voluntarily withdraw a promotional piece that suggested that combination estrogen and progestin therapy is indicated to reduce the risk of postmenopausal osteoporosis, because Provera was not indicated for that use.
- **November 13, 1990 FDA Letter** -- The FDA rejected Upjohn's proposed ads based on the ads' "emphasis . . . on 'menopausal therapy' rather than on an approved product indication."[211] On November 9, 1990, Upjohn informed the FDA that "the relevant promotion pieces and reprints [were] no longer being distributed by sales representatives."[212]
- **December 9, 1991 FDA Letter**[213] -- In response to a proposed advertisement from Upjohn, the FDA reminded Upjohn that Provera was not "indicated for use in postmenopausal replacement therapy for the prevention of endometrial hyperplasia."[214]

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[208]Plaintiff's Ex. 10166.

[209]Plaintiff's Ex. 10180.

[210]Plaintiff's Ex. 10179.

[211]Plaintiff's Ex. 3401.

[212]Upjohn's Ex. 928.

[213]Plaintiff's Ex. 10189.

[214]Plaintiff's Ex. 10189.

- **December 13, 1991 FDA Letter** -- The FDA informed Upjohn that referring to a postmenopausal patient as a candidate for using Provera is "potentially misleading to the reading regarding the indication for use of the product."[215]

Plaintiff asserted several purposes for this evidence. In pre-trial responses to Upjohn's objections to the exhibits, Plaintiff argued that the exhibits showed Upjohn's policy of promoting "Provera to be used in combination with Premarin without an indication or approval to do so."[216] According to Plaintiff, the advertisements "demonstrate[d] Upjohn's failure to study and to warn, and tie[] directly to FDA violations."[217] Plaintiff repeatedly argued that Upjohn calling Provera "the other half of estrogen [replacement] therapy" after being reprimanded by FDA amounted to conscious disregard on the part of Upjohn to follow the rules of the FDA.[218] And, again during the hearing on Defendants' Motions for JNOV, Plaintiff argued that the FDA "repeatedly admonished" Upjohn for advertisements promoting Provera as "the other half of hormone therapy" [sic].[219] But, in its opposition to Defendant's Motion for JNOV, Plaintiff argued that the advertisements "simply triggered Upjohn's duty to study."[220] Regardless of the intended purpose of the evidence, the evidence was merely an extension of the liability phase. At best, this evidence went to a duty to test, which was a compensatory damages stage issue.

If Plaintiff's final position is that the exhibits established a duty to test, then the exhibits are no help in determining punitive damages. First, as stated, this is a compensatory damages

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[215]Plaintiff's Ex. 10189.

[216]Doc. No. 588.

[217]Doc. No. 588.

[218]Feb. 19, 2008, Tr. at 2216; Feb. 14, 2008, Tr. at 1604-1605.

[219]May 9, 2008, Tr. at 55.

[220]Doc. No. 651.

stage issue. Second, Plaintiff conceded that "Upjohn was doing studies during this time frame of the endometrial effects of the combination drugs,"[221] but argued that Upjohn was not conducting the "right" studies.

To the extent that these exhibits are intended to establish Upjohn's alleged reckless indifference, the inference is not supported by the record. A review of the exhibits shows that the FDA's criticisms were quite specific. Never did the FDA criticize Upjohn's use of the phrase "the other half of estrogen replacement therapy"; rather, the FDA criticized the indications for use suggested by the advertisements. Specifically, the FDA scolded Upjohn for suggesting progestin prevented endometrial hyperplasia,[222] provided protection against osteoporosis,[223] and was safe and effective for treatment and reversal of endometrial hyperplasia.[224]

In summarizing these exhibits, Dr. Parisian testified that Upjohn was "ignoring the FDA" and "providing labeling that's misleading, that's false and misleading, with inadequate instruction for use."[225] This testimony is also essentially unsupported by the evidence. First, the documents involve advertising, not labeling. Second, there is no evidence establishing that Upjohn ignored the FDA. These letters were a dialogue between the FDA and Upjohn regarding appropriate advertising. The FDA informed Upjohn that an ad was "potentially misleading," and Upjohn changed the advertisements. Based on the sum of the testimony at trial, this is the normal course of business.

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[221]March 3, 2008, Tr. at 2734.

[222]Plaintiff's Ex. 10189.

[223]Plaintiff's Ex. 10179.

[224]Plaintiff's Exs. 10178 and 10155.

[225]March 3, 2008, Tr. at 2736.

Dr. Parisian elaborated that "Upjohn is not doing the clinical trials. If you want that indication, you need to do the clinical trials to support that indication and get approved . . . ."[226] But this doesn't establish malice, without evidence that Upjohn knew or should have known that ingesting progestin would cause breast cancer. At this time (mid 1980s) it was the standard of care in the medical community to prescribe Provera to prevent uterine bleeding and uterine cancer.[227] Although this was the standard of care, prevention of uterine cancer was not an approved indication.[228]

According to Dr. Parisian, if Upjohn "wanted that indication," it needed "to do a clinical study and submit an application to the FDA for approval."[229] Plaintiff asked "while we know that Upjohn was doing studies during this time frame of the endometrial effects of the combination, in all of the documents that you've reviewed, did Upjohn ever do any breast cancer studies during that time frame"; Dr. Parisian responded "No."[230] However, if Upjohn was relying on other breast cancer studies or data, this would not establish malice or reckless disregard.

Finally, if these exhibits were submitted under the negligence standard, they might pass muster for jury consideration, but not under the clear and convincing standard.

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[226]March 3, 2008, Tr. at 2736.

[227]*Id.* at 2790.

[228]*Id.* at 2791.

[229]*Id.* at 2733.

[230]*Id.*

c. Response to the Degge Group Findings

Plaintiff argued that Upjohn's response to the Degge Group findings "is the most telling proof of Upjohn's abject refusal to examine the breast cancer issue . . . ."[231] Following the release of the Bergkvist article,[232] Upjohn retained the Degge Group to conduct a review of the literature on the link between breast cancer and estrogen and progestin use.[233] Based on their review of the literature, the Degge Group determined that the "ultimate effect of progestins on the development of human breast cancer is still unclear . . . ."[234] The Degge Group also determined that additional study was needed, and listed numerous case control studies and cohort studies that were on-going.[235] This report was published in 1992.[236] Plaintiff argued that Upjohn did nothing in response to the Degge Group's report.[237] By "Upjohn did nothing," Plaintiff's point is that Upjohn failed to do an "in-house" study.[238] Dr. Parisian was asked "did Upjohn ever do one thing . . . to find out the effect of MPA in combination with estrogen on breast cancer," and she responded "No."[239]

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[231]Doc. No. 651.

[232]Dr. Parisian testified that the first study that she could recall showing an increased risk of breast cancer when progestins and estrogens are used -- as opposed to estrogen alone -- was the Bergkvist Study, which was published in 1989. However, Dr. Parisian admitted that Bergkvist was not statistically significant. Feb. 13, 2008, Tr. at 1449.

[233]Feb. 15, 2008, Tr. at 1455; Feb. 19, 2008, Tr. at 2167.

[234]Plaintiff's Ex. 10116.

[235]Feb. 19, 2008, Tr. at 2168; Plaintiff's Ex. 10116.

[236]Feb. 19, 2008, Tr. at 2167-2168.

[237]Doc. Nos. 166, 651.

[238]March 3, 2008, Tr. at 2738-2740; March 5, 2008, Tr. at 2986-2987, 2993.

[239]March 3, 2008, Tr. at 2738.

Plaintiff's focus on the fact that Upjohn did not do its own breast cancer studies is of no consequence. This is argument, unsupported by the evidence -- there is no evidence that Upjohn was required to conduct its own "in-house" study. Additionally, Dr. Parisian did not reference any FDA regulations that require a pharmaceutical company to conduct an "in-house" study. In fact, as the agreed-to jury instruction points out, Upjohn's duty was "to test or otherwise discover risk about which a manufacturer should warn."[240] The unrebutted evidence was that pharmaceutical companies can monitor and rely on the research of independent investigators, rather than conduct their own studies.[241] So, Plaintiff's argument regarding Upjohn's own, in-house study falls well-short of creating a jury issue under the clear and convincing standard.

3. Summary of Evidence During Punitive Damages Stage

In Arkansas, a punitive damages claim "is properly submitted to the jury . . . where the claim is supported by 'substantial evidence.'"[242] Since this case lacked substantial evidence, I should not have submitted the punitive damages issue to go to the jury. Plaintiff presented evidence of what, at first blush, might be considered unsavory practices (*e.g.*, ghostwriting, advertising, countering negative press, *etc.*), but it falls short of establishing a submissible jury issue.

Plaintiff's burden was to show, by clear and convincing evidence, that Defendants knew or should have known of the consequences of their actions, and in the face of this knowledge continued a course with such abhorrent indifference to the consequences that malice can be inferred. But the evidence in this case establishes, at most, negligence. Defendants were aware of an association between estrogen and endometrial cancer in the late 1970s. Defendants knew that physicians were starting to prescribe progestin with estrogen in an effort to protect the

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[240]Doc. No. 554 (emphasis added).

[241]Feb. 19, 2008, Tr. at 2214.

[242]*Morris v. Union Pacific R.R.*, 373 F.3d 896, 903 (8th Cir. 2004).

endometrium. In the late 1970s and early 1980s, the scientific community believed that prescribing progestin to women on estrogen reduced the risk of endometrial hyperplasia.[243] By 1983, ACOG and OB-GYNs endorsed this idea, and the position was held steadfastly throughout the 1980s, 1990s, and today.[244] Additionally, the medical community believed, throughout the 1980s and into the mid-1990s,[245] that progestin protected women taking estrogen from breast cancer.[246]

Plaintiff conceded that the breast cancer risk associated with estrogen plus progestin had not been accepted when she ingested the drugs, but argued that this "has no bearing on [Defendants'] failure to study."[247] While it may have no bearing on a failure to study, it goes to the heart of the punitive damages issue -- did Defendants know or should they have known?

Plaintiff asserted that had Defendants done the "right" studies, they would have uncovered the breast cancer risk long ago.[248] Again, this is compensatory phase argument; punitive damages require much more -- clear and convincing evidence of reckless disregard is a heavier burden. Plaintiff's attacks on the inadequacies of the studies relied on by Defendants provide little support for punitive damages. There was no evidence that Defendants knew the

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[243]Feb. 19, 2008, Tr. at 2136.

[244]March 3, 2008, Tr. at 2789.

[245]See Feb. 13, 2008, Tr. at 1461 (Dr. Parisian agreed that up until 1995, "there was still an operating assumption and belief that progestins would reduce the risk of breast cancer posed by estrogen alone . . . .").

[246]Feb. 19, 2008, Tr. at 2165, 2230. Dr. Gambrell published an article in 1983 that suggested a reduced risk of breast cancer in women who were on the combination of estrogen and progestins. Feb. 19, 2008, Tr. at 2210. Also, Dr. Dey testified that Wyeth conducted internal research, that it shared with the FDA, that "found that some of the components in Premarin protected against breast cancer." March 5, 2008, Tr. at 2896. This testimony was unimpeached.

[247]Doc. No. 651.

[248]*Id.*

studies they conducted or relied upon were inadequate to support their position on the breast cancer issue; and sufficient evidence of reckless disregard is missing.

Upjohn repeatedly attempted to get advertisements approved that suggested indications that had not been approved for Provera. Upjohn submitted the ads, the FDA reviewed the ads, and the FDA rejected them; this appears to be how the process works between the FDA and pharmaceutical companies. Evidence that the FDA scolded Upjohn four or five times, over 20 years, because its proposed advertisements were overly broad, does not establish reckless indifference -- this might be different had Upjohn acted contrary to the FDA's criticisms.

Wyeth used advertising to promote estrogen and progestin products. Wyeth also considered suggestion from a public relations firm on how to respond to studies that reflected poorly on its products and present the media with balanced report of the facts. These actions, standing alone or when considered with the other evidence in this case, do not establish reckless disregard.

Once again, to warrant punitive damages, Plaintiff's burden was to prove, by clear and convincing evidence, that: (1) Defendants knew or should have known, in light of the circumstances at the time, that not testing and warning would naturally and probably result in injury; and (2) Defendants continued to not test and warn with reckless disregard for the consequences from which malice can be inferred.[249] Plaintiff's evidence established neither.

CONCLUSION

Based on the findings of fact and conclusions of law above, Defendants' Motions to Strike Dr. Parisian's testimony from the punitive damages phase is GRANTED in PART, and

[249] *D'Arbonne Const. Co., Inc. v. Foster*, 123 S.W.3d 894 (Ark. 2003).

her testimony is STRUCK, as outlined above. Absent the improperly admitted testimony, there is insufficient evidence for a punitive damages award.

Because Plaintiff failed to present clear and convincing evidence warranting punitive damages, Defendants' Motions for Judgment as a Matter of Law (Doc. Nos. 637, 642) are GRANTED as to punitive damages, and the punitive damages awards are VACATED.

If Defendants' Motion for Judgment as a Matter of Law had not been granted, they, at least, would be entitled to a new trial on punitive damages. Accordingly, in the alternative, Defendants' Motion for New Trial is GRANTED.

Plaintiff's Motions for Taxation of Costs (Doc. No. 631) is DENIED without prejudice. The motion should forthwith be modified in consideration of this Order as well as the concessions Plaintiff made in her May 5, 2008 reply.[250]

Since I have a deep and abiding faith in randomly selected juries, I am always reluctant to set aside a jury finding. This jury was very attentive throughout. I admitted much evidence that should not have been admitted. The fault is mine alone.

IT IS SO ORDERED this 8th day of July, 2008.

/s/ Wm. R. Wilson, Jr.
UNITED STATES DISTRICT JUDGE

[250]Doc. No. 653.

ADDENDUM NO. 5

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF ARKANSAS
WESTERN DIVISION

In re:	:	**MDL Docket No. 4:03CV1507-WRW**
	:	**4:04CV01169**
PREMPRO PRODUCTS LIABILITY LITIGATION	:	
	:	
DONNA SCROGGIN	:	**PLAINTIFF**
v.	:	
WYETH, et. al.	:	**DEFENDANTS**

SECOND AMENDED JUDGMENT[1]

This action came on for jury trial Monday, February 4, 2008, the Honorable William R. Wilson, Jr., United States District Judge, presiding.

The issues having been duly tried, the jury rendered a verdict in the liability / compensatory damages phase on Monday, February 25, 2008.[2]

Now, therefore, pursuant to the liability / compensatory damages verdict:

Judgment is entered in favor of the Plaintiff Donna Scroggin and against Defendants Wyeth, Wyeth Pharmaceuticals Inc., and Pharmacia & Upjohn Company LLC, jointly and severally, in the sum of $2,750,000.00, with post-judgment interest at the rate of 1.35% per annum.[3]

Additionally, Plaintiff's costs are taxed against Defendants, joint and severally, in the sum of $24,287.72.

IT IS SO ORDERED this 30th day of July, 2008.

/s/ Wm. R. Wilson, Jr.
UNITED STATES DISTRICT JUDGE

[1]This Second Amended Judgment effectively GRANTS Plaintiff's Amended Motion for Taxation of Costs (Doc. No. 661) and Defendants' Motion to Amend Judgment (Doc. No. 664).

[2]Although the jury found Defendants liable for punitive damages, this finding was vacated by a July 8, 2008 Order.

[3]This was the interest rate on the date the original Judgment was entered -- March 26, 2008.