FOR PUBLICATION

**UNITED STATES DISTRICT COURT**
**DISTRICT OF NEW JERSEY**

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| IN RE: FOSAMAX (ALENDRONATE SODIUM) PRODUCTS LIABILITY LITIGATION | |
| BERNADETTE GLYNN and RICHARD GLYNN, | Civil Action No. 11-5304, 08-08 |
| Plaintiffs, | OPINION |
| v. | |
| MERCK SHARP & DOHME CORP, | |
| Defendant. | |

PISANO, District Judge

Plaintiffs Bernadette Glynn and Richard Glynn ("Plaintiffs") brought this lawsuit against Defendant Merck, Sharp, & Dohme Corp. ("Defendant"), the manufacturer of Fosamax, which is a drug approved by the United States Food and Drug Administration ("FDA") for the treatment and prevention of osteoporosis. This matter is part of the multi-district litigation ("MDL") concerning Fosamax and involves allegations that Fosamax causes atypical femur fractures ("AFFs[1]"), it caused Plaintiff Mrs. Glynn's femur fracture, and Defendant failed to warn physicians about Fosamax and AFFs. Presently before the Court is Defendant's Motion for Summary Judgment based upon Federal Preemption [docket # 25], Motion for Judgment as a Matter of Law pursuant to Rule 50(a) [docket # 198], Renewed Motion for Judgment as a Matter of Law pursuant to Rule 50(a) [docket # 209], and Renewed Motion for Judgment as a Matter of

[1] The abbreviation of atypical femur fracture (singular) is "AFF."

Law pursuant to Rule 50(b) [docket # 216]. The issue in these Motions and before the Court is whether there is clear evidence that the FDA would not have approved a stronger warning to the Fosamax label, thereby warranting preemption of Plaintiffs' failure to warn claim. *See Wyeth v. Levine*, 555 U.S. 555 (2009). This Court heard oral argument on the federal preemption issue on March 8, 2013 and reserved decision until a trial record had been established. *See* Fed. R. Civ. P. 78. A jury trial took place from April 8, 2013 to April 29, 2013. On April 29, 2013, the jury returned a verdict for Defendant, finding that Plaintiff did not prove by a preponderance of the evidence that she experienced an AFF in April 2009. Because the record contains clear evidence that the FDA would not have approved a stronger warning to the Precautions section of the Fosamax label, this Court grants the Motions on federal preemption.

## I. BACKGROUND[2]

### A. Fosamax Approval & Mrs. Glynn's Fosamax Use

In September 1995, the FDA approved Fosamax for the treatment of osteoporosis in postmenopausal women, and in April 1997, the FDA approved Fosamax for the prevention of osteoporosis in postmenopausal women. Since this time, Fosamax has remained FDA approved for the treatment and prevention of postmenopausal osteoporosis.

In 2002, Dr. Murat Acemoglu first prescribed Fosamax to Mrs. Glynn after diagnosing her with "osteopenia – osteoporosis" [docket # 27, Confoy Dec., Ex. 27 & 28]. Mrs. Glynn took Fosamax until April 17, 2009, when she fractured her right femur. Final Pretrial Order ¶ 3.

[2] This Background section contains facts that pertain to the federal preemption issue. For a more complete discussion of the facts of this case, see this Court's Opinion dated April 11, 2013 [docket # 183].

### B. History of Fosamax Label Change

On June 13, 2008, the FDA contacted Defendant and other bisphosphonate [3] manufacturers and requested any investigations they conducted "regarding the occurrence of atypical fractures with bisphosphonate use," any investigational plans, and "all hip and femoral fracture case reports" they received [docket # 26, Declaration of Karen A. Confoy in Support of the Motion for Summary Judgment and Motion for Summary Judgment Based Upon Federal Preemption ("Confoy Dec."), Ex. 5; docket # 27, Confoy Dec., Ex. 4]. The FDA also asked that Defendant and the other bisphosphonate manufacturers make an effort where possible "to clarify the fracture location and the duration of bisphosphonate exposure for all case reports." *Id.* The FDA explained that it was "aware of reports regarding the occurrence of subtrochanteric hip fractures in patients using bisphosphonates" and is "concerned about this developing safety signal." *Id.*

On July 18, 2008, Defendant responded to the FDA's request and included summary tables of clinical and post-marketing data, clinical Council for International Organizations of Medical Sciences ("CIOMS") reports, and post-marketing CIOMS reports [docket # 27, Confoy Dec., Ex. 6]. The FDA's review of this data as well as the data from other bisphosphonate manufacturers "did not show an increase in . . . [the risk of atypical subtrochanteric femur fractures] in women using these medications" [docket # 26, Confoy Dec., Ex. 7].

On September 15, 2008, Defendant submitted a Prior Approval Supplement ("PAS") to the FDA, proposing "to add language to both the Precaution[s] and Adverse Reactions/Post-Marketing Experience section[s] of the label to describe low-energy" subtrochanteric femoral

[3] Fosamax belongs to a class of drugs known as bisphosphonates.

fractures [docket # 27, Confoy Dec., Ex. 8]. Defendant explained that "[i]t is not possible with the present data to establish whether treatment with" Fosamax "increases the risk of [these] . . . low-energy subtrochanteric and/or proximal shaft fractures," but because there is a temporal association between these fractures and Fosamax, Defendant thought that it was "important to include an appropriate statement about them in the product label." *Id.* Defendant sought to add the following language to the Precautions section of the label:

> Low-Energy Femoral Shaft Fracture
>
> Low-energy fractures of the subtrochanteric and proximal femoral shaft have been reported in a small number of bisphosphonate-treated patients. Some were stress fractures (also known as insufficiency fractures) occurring in the absence of trauma. Some patients experienced prodromal pain in the affected area, often associated with imaging features of stress fracture, weeks to months before a complete fracture occurred. The number of reports of this condition is very low, and stress fractures with similar clinical features also have occurred in patients not treated with bisphosphonates. Patients with suspected stress fractures should be evaluated, including evaluation for known causes and risk factors (e.g., vitamin D deficiency, malabsorption, glucocorticoid use, previous stress fracture, lower extremity arthritis or fracture, extreme or increased exercise, diabetes mellitus, chronic alcohol abuse), and receive appropriate orthopaedic care. Interruption of bisphosphonate therapy in patients with stress fractures should be considered, pending evaluation of the patient, based on individual benefit/risk assessment.
>
> [*Id.*]

Additionally, Defendant proposed adding "low-energy femoral shaft fracture" to the Adverse Reactions/Post-Marketing Experience section of the label and the following statement to the Patient Package Insert: "Patients have experienced fracture in a specific part of the thigh bone. Call your doctor if you develop new or unusual pain in the hip or thigh." *Id.*

On April 15, 2009, an FDA representative e-mailed Defendant and stated that the proposed label change to the Adverse Reactions/Post-Marketing Experience section of the label would be approved but the label change to the Precautions section would not be approved [docket # 101, Cecchi Dec., Ex. 83; docket # 27, Confoy Dec., Ex. 10]. Two days later, Mrs. Glynn fractured her femur.

On May 22, 2009, one month after Mrs. Glynn's fracture, the FDA formally responded to Defendant's proposed label change, recommending that it add "low energy femoral shaft and subtrochanteric fractures" to the Adverse Reactions/Post-Marketing Experience section of the label; however, the FDA did not approve the label change to the Precautions section [docket # 27, Confoy Dec., Ex. 11]. Moreover, the FDA warned that Fosamax "may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if [it is] . . . marketed with" these label changes "before [FDA] approval . . . ." *Id.*

On July 2, 2009, Defendant submitted to the FDA a Changes Being Effected ("CBE") supplement to add information about femur fractures to the Adverse Reactions/Post-Marketing Experience section of the label because the FDA told Defendant that submitting a CBE supplement was the "quickest route to update the [Product Circular] PC" for Fosamax [docket # 27, Confoy Dec., Ex. 12]. On March 1, 2010, the FDA approved the CBE supplement [docket # 26, Confoy Dec., Ex. 9].

On March 10, 2010, the FDA issued a Drug Safety Communication, in which it stated that "[a]t this point, the data that FDA has reviewed have not shown a clear connection between bisphosphonate use and a risk of atypical subtrochanteric femur fractures" [docket # 26, Confoy Dec., Ex. 5]. The FDA did state, however, that it was "working closely with outside experts,

including members of the . . . American Society of Bone and Mineral Research Subtrochanteric Femoral Fracture Task Force, to gather additional information that may provide more insight into this issue." *Id.*

On September 14, 2010, the American Society for Bone and Mineral Research ("ASBMR") published an article entitled *Atypical Subtrochanteric and Diaphyseal Femoral Fractures: Report of a Task Force of the American Society for Bone and Mineral Research* [docket # 26, Confoy Dec., Ex. 13].[4] The report stated that although there is an association between long-term bisphosphonate use and AFFs, the association has "not been proven to be causal." *Id.* at 2269, 2287. The report concluded that although AFFs are rare, "they appear to be more common in patients who have been exposed to long-term BPs [("bisphosphonates")], usually for more than 3 years . . . ." *Id.* at 2287. The report further provided that although "BPs are important drugs for the prevention of common osteoporotic fractures," "atypical femoral fractures are of concern, and more information is urgently needed both to assist in identifying patients at particular risk and to guide decision making about duration of BP therapy. Physicians and patients should be made aware of the possibility of atypical femoral fractures and of the potential for bilaterality through a change in labeling of BPs." *Id.*

[4] In this report, the ASBMR defined AFF by listing its Major Features, which are required to satisfy the definition of AFF, and Minor Features, which may be associated with AFFs but are not required characteristics of them [docket # 26, Confoy Dec., Ex. 13]. The Major Features of an AFF are: (1) that it is "located anywhere along the femur from the distal to the lesser trochanter to just proximal to the supracondylar flare"; (2) "associated with no trauma or minimal trauma, as in a fall from a standing height or less"; (3) transverse or short oblique configuration; (4) noncomminuted; and (5) complete fractures extend through both cortices and may be associated with a medial spike, incomplete fractures involve only the lateral cortex. *Id.* The Minor Features of an AFF are: (1) localized periosteal reaction of the lateral cortex; (2) generalized increase in cortical thickness of the diaphysis; (3) prodromal symptoms such as dull or aching pain in the groin or thigh; (4) bilateral fractures and symptoms; (5) delayed healing; (6) comorbid conditions (e.g., vitamin D deficiency, rheumatoid arthritis, hyposphosphotasia); and (7) use of pharmaceutical agents (e.g., bisphosphonates, glucocorticoids, and proton pump inhibitors). *Id.*

The FDA responded to the report by issuing a Drug Safety Communication, in which it stated "[a]lthough it is not clear if bisphosphonates are the cause [of AFFs], these unusual femur fractures have been identified in patients taking these drugs" [docket # 26, Confoy Dec., Ex. 14]. Additionally, the FDA informed that the "optimal duration of bisphosphonate treatment for osteoporosis is unknown" but "clinical trial data . . . support[s] effectiveness for the reduction of common bone fractures for three to five years." *Id.* Regarding the ASBMR Task Force's recommendation of a label change, the FDA stated that it "has assembled and is thoroughly reviewing all long term data available on the products, as well as all safety reports, and *is considering* label revisions." *Id.* (emphasis added).

In October 2010, the FDA issued another Drug Safety Communication, informing that it would require all bisphosphonate manufacturers to add information on AFFs to the Precautions section of the drug labels and require a new Limitations of Use statement in the Indications and Usage section of the label because "these atypical fractures may be related to long-term . . . bisphosphonate use" [docket # 26, Confoy Dec., Ex. 15]. It reiterated that "[a]lthough it is not clear if bisphosphonates are the cause, these unusual femur fractures have been predominantly reported in patients taking bisphosphonates." *Id.* On January 11, 2011, Defendant submitted the agreed upon label changes to the FDA [docket # 27, Confoy Dec., Ex. 18]. Also in January 2011, the FDA issued an update on femur fractures and bisphosphonate use, stating "[a]lthough it is not clear that the drugs are a direct cause of these unusual fractures, they have mainly been reported in patients taking bisphosphonates" [docket # 26, Confoy Dec., Ex. 19].

Currently, the Fosamax label includes the following language: "Atypical, low-energy, or low trauma fractures of the femoral shaft have been reported in bisphosphonate-treated patients. . . . Causality has not been established as these fractures also occur in osteoporotic patients who

have not been treated with bisphosphonates. Atypical femur fractures most commonly occur with minimal or no trauma to the affected area" [docket # 26, Confoy Dec., Ex. 20].

### C. Procedural History

On September 15, 2011, Plaintiffs filed a Complaint in this Court against Defendant, alleging causes of action for: (1) failure to warn; (2) defective design; (3) negligence; (4) negligent misrepresentation; (5) breach of express warranty; (6) breach of implied warranty of fitness for a particular purpose; (7) breach of implied warranty of merchantability; (8) violation of the Consumer Fraud Act, N.J.S.A. 56:8-2 et seq.; (9) violations of the New York General Business Law, N.Y. Gen. Bus. Law §§ 349 et seq. and 350 et seq.; (10) unjust enrichment; (11) punitive damages pursuant to the New Jersey Product Liability Act, N.J.S.A. 2A:58C-1 et seq., and the New Jersey Punitive Damages Act, N.J.S.A. 2A:15-5.10, et seq.; and (12) loss of consortium on behalf of Plaintiff Richard Glynn [docket # 1].[5] Defendant moved for summary judgment based on federal preemption on January 15, 2013, arguing that Plaintiffs' claims, all of which ultimately concern a failure to warn, are preempted because the FDA rejected Defendant's proposed label change and this constitutes clear evidence that the FDA would not have approved a stronger warning to the Precautions section of the label [docket #25]. On March 8, 2013, the Court heard argument on the preemption issue and reserved decision on it [docket # 138]. On April 2, 2013, the Court reserved decision on the federal preemption motion until there was a complete trial record in the case [docket # 156].

[5] Subsequently, Plaintiffs decided to pursue only the following claims: (1) failure to warn; (2) breach of the implied warranty of fitness for a particular purpose; (3) violations of the New York General Business Law; and (4) punitive damages. The Court granted summary judgment on the New York General Business Law claims [docket # 183]. In addition, the Court granted a Motion for Judgment as a Matter of Law as to the breach of implied warranty of fitness for a particular purpose claim and punitive damages [docket # 198]. Trial Tr. 1896:2-17; 2586:20-22. Thus, the failure to warn claim is the only claim that remains. Trial Tr. 2586:11-12.

Trial began on April 8, 2013 and concluded on April 29, 2013. After the close of the Plaintiff's case, on April 20, 2013, Defendant filed a Motion for Judgment as a Matter of Law pursuant to Federal Rule of Civil Procedure 50(a) [docket # 198]. Defendant argued that although it submitted to the FDA all the information relevant to a label change and tried to change the Precautions section of the label to include low-energy femoral fractures, the FDA rejected the label change. On April 26, 2013, Defendant renewed its Motion for Judgment as a Matter of Law, again arguing that Plaintiffs' claims are preempted because Defendant proposed a change to the Precautions section of the Fosamax label and the FDA rejected it [docket # 209]. On April 29, 2013, the jury returned a verdict for Defendant, finding that Plaintiffs did not prove by a preponderance of the evidence that Mrs. Glynn experienced an AFF in April 2009. The following day, the Court held an in-person status conference to discuss the preemption issue as well as other MDL issues. The Court explained that it previously deferred decision on the preemption issue for "a complete record" and "the best way to do that was to try the" case. Hearing Tr., 6:10-14, April 30, 2013. Although Plaintiffs had several opportunities to present evidence on preemption, they requested additional time to present more evidence on the issue. The Court gave Plaintiffs twenty-one days to submit "proposed fact findings that are based upon the record in opposition to" the preemption motions. *Id.* at 19:24-20:1. Thereafter, on May 6, 2013, Defendant submitted a Renewed Motion for Judgment as a Matter of Law pursuant to Rule 50(b) [docket # 216]. Plaintiffs submitted an opposition brief and Defendant submitted a reply brief.

## II. DISCUSSION

### A. Standard

"If a court does not grant a motion for judgment as a matter of law made under Rule 50(a), the court is considered to have submitted the action to the jury subject to the court's later deciding the legal questions raised by the motion." Fed. R. Civ. P. 50(b). The movant may then file a renewed motion for judgment as a matter of law, and in "ruling on the renewed motion, the court may: (1) allow judgment on the verdict, if the jury returned a verdict; (2) order a new trial; or (3) direct the entry of judgment as a matter of law." *Id.*

### B. Plaintiffs' Claims Are Preempted

Defendant argues that Plaintiffs' claims are preempted under federal law because it proposed a label change to the Precautions section of the Fosamax label to include a warning about low-energy femur fractures, and the FDA rejected the label change after Mrs. Glynn's fracture. Defendant asserts that this constitutes clear evidence that the FDA would have rejected any warning about these fractures prior to Mrs. Glynn's femur fracture. Moreover, Defendant contends that Plaintiffs' claims are preempted for three additional reasons: (1) Plaintiffs did not present evidence that the FDA rejected the proposed label change for using the phrase "stress fracture" as opposed to AFF; (2) Plaintiffs did not show that the label change could have been successfully presented through a CBE supplement; and (3) Plaintiffs did not show that Defendant withheld any information from the FDA.

Plaintiffs, however, argue that Defendant has not shown clear evidence that the FDA would have rejected language about AFFs in the Precautions section of the Fosamax label prior to Mrs. Glynn's fracture. Plaintiffs assert that preemption is improper for the following reasons:

(1) the FDA rejected the PAS because Defendant used the phrase "stress fracture" instead of "atypical" fracture, and the FDA would have approved an appropriately worded warning; (2) Defendant could have changed the label through a CBE supplement; (3) Defendant did not provide all of the information it had on femur fractures and Fosamax to the FDA, and had it done so, the FDA would have approved a properly worded warning in 2008; and (4) Defendant failed to warn the FDA as soon as there was reasonable evidence of a causal association between Fosamax and AFFs.

Defendant submitted a reply brief, again arguing that preemption is proper because Defendant proposed a label change in 2008 and the FDA rejected it in 2009, after Mrs. Glynn's fracture. Defendant asserts that the FDA did not reject the label change because Defendant used the phrase "stress fracture" since references to "stress fractures" were included to aid in the early identification of low-energy femur fractures. Moreover, Defendant contends that it did not fail to submit information to the FDA. Lastly, Defendant points out that the evidence Plaintiffs presented in their brief was not introduced at trial and thus, is not properly before this Court on this Motion; even if it was properly before this Court, the evidence does not change the fact that clear evidence exists that the FDA would not have approved a stronger warning to the Fosamax label.

The Supremacy Clause provides that the "Constitution, and Laws of the United States . . . shall be the supreme Law of the Land . . . ." U.S. Const. art. VI, cl. 2. It "invalidates state laws that interfere with, or are contrary to, federal law." *Hillsborough County, Florida v. Automated Medical Laboratories, Inc.*, 471 U.S. 707, 712 (1985) (internal quotation omitted). Federal law preempts state law in three ways: (1) express preemption; (2) field preemption, and (3) conflict preemption. *Farina v. Nokia Inc.*, 625 F.3d 97, 115 (3d Cir. 2010), *cert. denied*, 132 S.Ct. 365

(2011); *Dobbs v. Wyeth Pharmaceuticals*, 797 F. Supp. 2d 1264, 1268 n.3 (W.D. Okla. 2011). Express preemption occurs when Congress states "in express terms" that it is preempting state law. *Hillsborough County, Florida*, 471 U.S. at 713. Field preemption occurs when Congress intends to preempt state law "in a particular area" or in other words "the scheme of federal regulation is sufficiently comprehensive . . . [so] Congress 'left no room' for supplementary state regulation." *Id.* Conflict preemption is when a "state law is in actual conflict with federal law"; this exists "where it is impossible for a private party to comply with both state and federal requirements . . . or where state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Sprietsma v. Mercury Marine, a Div. of Brunswick Corp.*, 537 U.S. 51, 64 (2002) (internal quotation omitted). This case concerns conflict preemption because Defendant argues that it was impossible to comply with the state law duty to warn and the FDA's regulations[6] since Plaintiffs argue that a warning about low-energy femur fractures should have been included in the Fosamax label but the FDA rejected a proposed warning.

Conflict preemption, however, "is a demanding defense." *Wyeth*, 555 U.S. at 573. As a result, generally, FDA approval or compliance with FDA labeling regulations is not a complete defense to a state failure to warn claim. *Id.* at 559. If, however, there is "clear evidence that the FDA would not have approved a change" to the prescription drug's label, then it is impossible to comply with both federal and state requirements[7] and the state failure to warn claim is

[6] Federal regulations "preempt state laws in the same fashion as congressional statutes." *Farina*, 625 F. 3d at 115 (citing *Fid. Fed. Sav. & Loan Ass'n v. de la Cuesta*, 458 U.S. 141, 153 (1982)).

[7] Federal regulations require that a drug's label "be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitely established." 21 C.F.R. § 201.57.

preempted. *Id.* at 571. *Wyeth* does not define "clear evidence," so "application of the clear evidence standard is necessarily fact specific." *Dobbs*, 797 F. Supp. 2d at 1270.

Here, preemption is warranted because there is clear evidence that the FDA would not have approved a change to the Precautions section of the Fosamax label prior to Mrs. Glynn's fracture. In September 2008, Defendant submitted a PAS to the FDA, seeking to add language about low-energy femur fractures to the Precautions and Adverse Reactions sections of the label. In May 2009, approximately one month after Mrs. Glynn's fracture, the FDA sent Defendant a letter approving the change to the Adverse Reactions section of the label but denying the change to the Precautions section of the label. The FDA's rejection constitutes clear evidence that the FDA would not have approved a label change to the Precautions section of the label prior to Mrs. Glynn's injury. *See Robinson v. McNeil Consumer Healthcare*, 615 F.3d 861, 873 (7th Cir. 2010) (finding clear evidence that the FDA would not have approved a label change because the FDA did not approve "a reference to SJS/TEN on the label of over-the-counter drugs containing ibuprofen, when it had been asked to do so in a submission"); *Dobbs*, 797 F. Supp. 2d at 1276-77 (finding clear evidence that the FDA would have rejected an expanded warning for Effexor after the FDA rejected the warning added by Defendant); *see also Wyeth*, 555 U.S. at 571-72 (holding that *Wyeth* "failed to demonstrate that it was impossible for [it] . . . to comply with both federal and state requirements" and reasoning that it "offered no such evidence" and never argued "that it attempted to give" a warning but "was prohibited from doing so by the FDA").

Indeed, the evidence presented at trial establishes that the FDA would not have approved a label change to the Precautions section of the Fosamax label prior to Mrs. Glynn's injury. In fact, Dr. Cheryl Blume ("Dr. Blume"), one of Plaintiffs' experts who was "central" to Plaintiffs' preemption analysis, testified that the FDA "rejected" Defendant's PAS. Hearing Tr., 12:24-

13:13, April 2, 2013; Trial Tr., 661:10-14. Moreover, Dr. Lisa Rarick ("Dr. Rarick"), one of Defendant's experts who worked for the FDA for fifteen years, testified that the FDA "rejected a precaution" to the Fosamax label in their May 22, 2009 letter to Defendant. Trial Tr., 2436:22-24; 2501:7-9. Dr. Rarick further testified that although the FDA had the authority to ask Defendant to submit "alternative precautionary language" if it was "still contemplating [that] they might accept a precaution," the FDA did not do so, thereby indicating that it would not accept a label change to the Precautions section of the Fosamax label at that time. *Id.* at 2501:10-2502:1. Furthermore, Dr. Rarick testified that the FDA had the authority to request that Defendant "make a label change to include reports of low-energy spontaneous subtrochanteric or atypical femur fractures," but they never made such a request. *Id.* at 2485:4-8; 2578:2-12. Thus, clear evidence exists that the FDA would not have approved a label change to the Precautions section of the Fosamax label prior to Mrs. Glynn's fracture because Defendant submitted a label change and the FDA rejected it, and the FDA never required Defendant to submit new language or change the label, which demonstrates that the FDA did not think that the label should have been changed at that time.

Plaintiffs did not present any evidence at trial to refute preemption. First, Plaintiffs did not offer any evidence that Defendant's PAS was rejected due to language, specifically the use of "stress fracture" instead of "AFF," or that the FDA would have approved a properly worded label change. Instead, it would have been improper for Defendant to use the term "AFF" in 2008 when they submitted the PAS because, as Dr. Blume testified, the phrase "atypical femur fractures . . . wasn't even contrived until 2010 or 2011." *Id.* at 725:22-24. In addition, Dr. Cornell, the Clinical Director of Orthopaedic Surgery at the Hospital for Special Surgery and one of Plaintiffs' experts, explained that Fosamax "can lead to . . . subsequent stress fracture

formation," and when he wrote about these fractures, he was "talking about atypical femur fractures." *Id.* at 1264:20-1265:8. Moreover, Dr. Rarick testified that in rejecting Defendant's PAS, the FDA did not conclude that the label was "confusing to doctors" or that "stress fractures didn't look as severe and significant as . . . atypical femur fractures"; instead, Dr. Rarick stated that the FDA rejected the PAS because the "data didn't support the precaution language." *Id.* at 2512:10-18. This testimony demonstrates that the FDA did not reject the PAS due to Defendant's use of the phrase "stress fracture." Not only was the phrase AFF not coined in 2008, but some doctors used "stress fracture" as a term to refer to low-energy subtrochanteric fractures.

Second, Plaintiffs did not offer any evidence that Defendant could have submitted a CBE supplement to change the Precautions section of the Fosamax label. A CBE supplement gives a "manufacturer . . . the ability to change the label without FDA approval." *Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 392 (7th Cir. 2010); *Dobbs*, 797 F. Supp. 2d at 1271 (citing 21 C.F.R. § 314.70(c)(6)(iii)) (stating it is "an exception to the requirement of advance approval for label changes under certain circumstances"). A CBE supplement "allows a pre-approval label change by the manufacturer where the change is needed to add or strengthen a contraindication, warning, precaution or information about an adverse reaction." *Dobbs*, 797 F. Supp. 2d at 1271 (citing 21 C.F.R. § 314.70(c)(6)(iii)(A)). Like a PAS, the "proposed change must be based on 'reasonable evidence of' an association between a hazard and the drug at issue; however, a causal relationship need not have been definitely established." *Id.* (citing C.F.R. § 201.57(c)(6)(i)). After the label change has been affected, the "FDA has the opportunity to consider whether or not it will accept the change." *Mason*, 586 F.3d at 392. Drs. Blume and Rarick testified that if the FDA rejects a CBE label change, the manufacturer must change the

label, otherwise it will be misbranded. Trial Tr. 733:16-734:9; 2502:8-16. Thus, since the FDA rejected Defendant's PAS, it would not have approved a CBE seeking to add the same language to the label that it just rejected in the PAS, and any changes Defendant made using the CBE supplement would cause the drug to be misbranded. In addition, Dr. Rarick testified that the FDA could have requested that Defendant submit the label change using the CBE instead of the PAS method, but the FDA did not do so. *Id.* at 2489:19-22. Moreover, Dr. Rarick opined that the CBE method was not "the appropriate method to submit" a label change regarding low-energy subtrochanteric femur fractures because this "topic . . . was under FDA's review . . . ." *Id.* at 2493:11-22. As a result, the evidence does not show that Defendant could have changed the Precautions section of the Fosamax label using a CBE supplement.

Third, Plaintiffs did not show that Defendant failed to provide all the information it had on femur fractures to the FDA and that Defendant failed to warn the FDA as soon as there was reasonable evidence of a causal association between Fosamax and AFFs. Instead, Dr. Blume and Dr. Santora, Defendant's employee who is responsible for Fosamax, testified that Defendant supplied the Odvina report, Goh report, Adverse Event Reports, and data it obtained from physicians; Defendant also submitted information when the FDA requested it in 2008. *Id.* at 729:5-730:21; 2175:16-21; 2176:4-10; 2254:15-19; 2261:13-2262:8. Regarding the timing of Defendant's proposed label change, there is no evidence that Defendant failed to submit the label change when it had reasonable evidence of a causal association between Fosamax and femur fractures. Defendant submitted the PAS three months after the FDA requested information from bisphosphonate manufacturers, and as late as March 2010, the FDA did not see a "clear connection between bisphosphonate use and a risk of atypical subtrochanteric femur fractures" [docket # 26, Confoy Dec., Ex. 5].

Not only did Plaintiffs fail to offer any evidence at trial to refute preemption but the exhibits Plaintiffs cited in their opposition brief were not presented at trial [docket # 218]. This is inappropriate on a Motion for Judgment as a Matter of Law where "the court is limited to the trial record and nothing else." *Laymon v. Lobby House, Inc.*, 613 F. Supp. 2d 504, 510 (D. Del. 2009). Even if the evidence Plaintiffs cited were part of the trial record, this Court is not persuaded that it would change the fact that there is clear evidence that the FDA would not have approved a stronger warning prior to Mrs. Glynn's fracture.

Therefore, preemption is warranted in this case. Defendant submitted a PAS in 2008 seeking to change the Precautions section of the Fosamax label to include information on low-energy subtrochanteric femur fractures, but the FDA rejected the PAS in May 2009, one month after Mrs. Glynn's fracture. This constitutes clear evidence that the FDA would not have approved a stronger warning prior to Mrs. Glynn's fracture. Although Plaintiffs have had several opportunities to introduce evidence in opposition to preemption, they have not refuted the fact that clear evidence exists. Consequently, based on the record before the Court, Plaintiffs' failure to warn claim is preempted.

## III. CONCLUSION

For the reasons outlined above, this Court grants Defendant's Motion for Summary Judgment based upon Federal Preemption [docket # 25], Motion for Judgment as a Matter of Law [docket # 198], second Motion for Judgment as a Matter of Law [docket # 209], and Renewed Motion for Judgment as a Matter of Law [docket # 216] and enters judgment in favor of Defendant. An appropriate Order accompanies this Opinion.

Dated: June 27, 2013

/s/ Joel A. Pisano
JOEL A. PISANO, U.S.D.J.