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United States District Court,
S.D. New York.
PROCTER & GAMBLE PHARMACEUTICALS, INC. and Sanofi-Aventis U.S. LLC, Plaintiffs,
v.
HOFFMANN-LA ROCHE INC. and Glaxosmith-kline, Inc., Defendants.

No. 06 Civ. 0034(PAC).
Sept. 6, 2006.

DECISION

CROTTY, J.

***1** Having sought but failed on three prior occasions to obtain the intervention of the Food and Drug Administration ("FDA"), plaintiffs Proctor & Gamble Pharmaceuticals, Inc. and Sanofi-Aventis U.S. LLC ("P & G" or "Plaintiffs") invoked the Lanham Act § 43(a), 15 U.S.C. § 1125 and commenced this proceeding on January 4, 2006, alleging that defendants Hoffmann-La Roche Inc. and Glaxosmithkline, Inc. ("Roche" or Defendants") falsely advertised and improperly promoted their prescription drug, Boniva, for the prevention and treatment of osteoporosis in postmenopausal women. Shortly thereafter, P & G moved for a preliminary injunction enjoining Defendants' claim that Boniva has proven or demonstrated efficacy with regard to non-vertebral fractures. [FN1] The Court held a four-day evidentiary hearing on May 25, 26, 29 and 30, 2006 and heard oral argument on July 13, 2006. The Court has had the benefit of the parties' proposed findings of fact and conclusions of law.

> FN1. P & G seeks a preliminary injunction that, in addition to enjoining the allegedly false and misleading promotion and advertising of Boniva, also seeks the following relief: (1) that the proposed order be disseminated to Roche sales representatives; (2) that Roche implement a training program to ensure compliance by Roche sales representatives with the Court's decision and order; and (3) that Roche provide a corrective written statement to physicians, other healthcare providers, and healthcare customers visited by Roche sales representatives since April 1, 2005 regarding the Court's determinations. In a word, Defendants would be forced to tell the world their advertising claims were found to be false by a United States District Judge.

Notwithstanding this action, P & G continued to press its case with the FDA, seeking approval of an television ad which claimed that P & G's competitive product "Actonel" was superior to Boniva. On May 4, 2006, the FDA formally disapproved the proposed ad, asserting that Actonel's claim of superiority over Boniva was unproven. P & G did not produce this document until the hearing was half over. Granting P & G the relief it seeks in this action would be the same effectively as a finding that Boniva is inferior to Actonel.

In the briefest of summaries, the market for drugs for the prevention and treatment of osteoporosis in postmenopausal women consists of three dominant manufacturers. Merck makes Fosomax, which has a 50% share of the U.S. market. Plaintiffs' product, Actonel, is next with approximately 25%. Defendants' product, Boniva, is the last and newest entrant, starting in April 2005, and has less than 10% of the market today. Even before Defendants introduced Boniva, Plaintiffs recognized that Boniva's sales would likely come at Plaintiffs' expense, and not that of the established leader, Fosomax. Plaintiffs determined to protect its market share and to keep Defendants "in the starting blocks." (Ex. 143.)

As one might gather, these two sets of pharmaceutical behemoths are engaged in a marketing war over sales of FDA approved drug products. The market is both large and lucrative. The allegations, charges, counter charges and responses are but indications of the "money-big money-and the competition in the market for prescription drugs." *Rhone-Poulenc Rorer Pharms., Inc. v. Marion Merrell Dow*, 1994 U.S. Dist. LEXIS 20782, at * *1-2. The question before the Court is whether Defendants are making false claims in their promotion and advertising of Boniva in light of the scientific studies on which those claims rely, generally accepted principles of biostatistics, and

the state of scientific research related to osteoporosis. For the reasons which follow, the Court declines to intervene in the on-going marketing battle and denies the Plaintiffs' motion for a preliminary injunction.

FINDINGS OF FACT

I. The Parties

***2** Plaintiff Procter & Gamble Pharmaceuticals, Inc. ("P & G") is an Ohio corporation with its principal place of business in Mason, Ohio. P & G researches, develops, manufactures and markets pharmaceutical products. P & G is a wholly-owned subsidiary of The Procter & Gamble Company. Plaintiff sanofi-aventis U.S. LLC ("Aventis") is a Delaware limited liability company with its principal place of business in Bridgewater, New Jersey. Aventis researches, develops, manufactures and markets pharmaceutical products in the United States. Plaintiffs manufacture and market Actonel, a once-weekly medication for the prevention and treatment of osteoporosis in postmenopausal women, approved by the FDA for marketing and sale within the United States.

Actonel is P & G's largest selling pharmaceutical product and a "billion dollar brand." (Tr. 204 (Pratt).) [FN2] Prior to launch, P & G spent fifteen years developing the drug and spent approximately $800 million in its research and development. (Tr. 204 (Pratt).) P & G has spent $1 billion combined in marketing and sales expenses since launching Actonel. (Tr. 204-05 (Pratt).) The drug will generate between $930 and $940 million dollars in sales this fiscal year. (Tr. 205 (Pratt).) [FN3]

> FN2. Tr. ___" references the testimony at the evidentiary hearing, with the wintess' name in parenthesis. "Ex. __" references the parties' exhibits.
>
> FN3. P & G operates on a fiscal year running from July 1st through June 30th. (Tr. 228 (Pratt).)

Defendant Hoffmann-La Roche, Inc. ("Roche") is a New Jersey corporation with its principal place of business in Nutley, New Jersey. Roche researches, develops, manufactures, and markets pharmaceutical and diagnostic products. Defendant SmithKline Beecham Corporation d/b/a GlaxoSmithKline ("GSK") is a Pennsylvania corporation with business offices in Philadelphia, Pennsylvania and Research Triangle Park, North Carolina. GSK is a wholly-owned subsidiary of GlaxoSmithKline, a research-based pharmaceutical company headquartered in the United Kingdom. GSK researches, develops, manufactures, and markets pharmaceutical products.[FN4] Defendants manufacture and market Boniva, a once-monthly oral and once-quarterly injectable medication for the prevention and treatment of osteoporosis in postmenopausal women, approved by the FDA for marketing and sale within the United States.

> FN4. Defendants note that the Complaint actually names as a defendant GlaxoSmithKline, Inc., which is a Canadian company and apparently not the GSK entity Plaintiffs intended to name. That GSK entity is SmithKline Beecham Corp. d/b/a GlaxoSmithKline.

II. OSTEOPOROSIS AND BISPHOSPHONATES

A. Osteoporosis

The parties generally agree as to the basic scientific facts concerning osteoporosis. Osteoporosis, or porous bone, is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased risk of fractures. (Tr. 47-48 (Bilezikian); Tr. 551 (Chestnut).) The body has two types of bone that osteoporosis affects: cortical bone, which is the compact outer layer of the bone shaft, and trabecular (or cancellous) bone, which forms the sponge-like inner structure of bone. (Ex. 446.) Cortical and trabecular bone constitute distinct kinds of bone. (Tr. 44 (Bilezikian).) Individual sites contain both cortical and trabecular bone, although the proportion of each type of bone varies at particular skeletal sites. (Tr. 45-46 (Bilezikian); Tr. 552 (Chestnut); Ex. 446.) Cortical bone comprises 80% of the body's bone and is found in greater amounts in nonvertebral sites; trabecular bone makes up most of the vertebral system. (*Id.;* Tr. 44 (Bilezikian).) Thus, for example, the spine is 68% trabecular bone and 32% cortical bone; the hip is 50% trabecular bone and 50% cortical bone; and the forearm is between 80% and 95% cortical bone and the remainder trabecular (with increasing amounts of cortical bone found closer to the wrist). (Tr. 44-46 (Bilezikian); Tr.

552 (Chestnut); *see also* Ex. 94 at 8 .) [FN5]

> FN5. Dr. Chestnut testified that the vertebrae are comprised of 66% trabecular bone and 34% cortical bone. (Tr. 552 (Chestnut).) Dr. Chestnut also disagreed with the conclusion shown in Exhibit 446 that the femoral neck was comprised of 25% trabecular bone. (*Id.*). Dr. Chestnut contended that the makeup of bone at this site is closer to 30% to 35% trabecular and 65% to 70% cortical bone. (*Id.*)

***3** Bone remodels itself on a regular basis. (Tr. 46-47 (Bilezikian); Tr. 553 (Chestnut); Ex. 94 at 6-7.) Osteoclast cells remove bone in a process called "resorption," while osteoblast cells lay down new bone. (Tr. 553-54 (Chestnut); Ex. 384.) Osteoporosis develops over time when bone resorption (*i.e.*, bone loss) continually exceeds bone replacement. (Tr. 47-48 (Bilezikian).) The result is a decrease in bone mineral density ("BMD"), which is a measurement of bone quantity, as well as the structural deterioration of bone tissue, bone fragility, and increased risk of fractures.

In addition to being distributed differently throughout the body, cortical and trabecular bone also metabolize differently. (Tr. 45-47 (Bilezikian).) Trabecular bone is highly active metabolically such that it is continually being remodeled at a rate of 10% to 15% percent per year. (Tr. 46-47 (Bilezikian).) By contrast, cortical bone remodels at a much slower rate. (Tr. 46 (Bilezikian).) Trabecular bone is more vulnerable to osteoporosis because it has a higher bone turnover rate, leading to decreased BMD. (Tr. 557 (Chestnut).)

Osteoporosis can be diagnosed through a BMD test, which measures bone mass at various sites in the body with instruments called densitometers. (Tr. 49-50 (Bilezikian).) [FN6] Densitometers are x-ray based machines that are highly precise and accurate in measuring bone density of specific sites by grams of calcium per square centimeter. (Tr. 50 (Bilezikian).) Several important risk factors exist for osteoporosis and fracture beyond low BMD, including "[a]ge, history of fracture, existence of vertebral fracture, [and] mother's history of fractures." (Tr. 922 (Black).) Roughly ten million Americans have osteoporosis and roughly thirty-four million more have low bone mass, placing them at increased risk for the disease. (Compl.¶ 19.) Although osteoporosis affects both men and women and can occur at any age, the vast majority of those who develop the disease are postmenopausal women. (Tr. 48 (Bilezikian); Compl. ¶ 19.) The World Health Organization ("WHO") defines an individual as osteoporotic if that person's BMD T-score measures minus 2.5 or lower. (Tr. 52 (Bilezikian); Tr. 613 (Chestnut).)

> FN6. BMD levels are represented as a "T-score," which is the number of standard deviations below the bone density of a healthy twenty-to thirty-year old woman. (Tr. 52 (Bilezikian).) For example, the bone mineral density of a woman with a T-score of-1 is one standard deviation below the bone density of a normal, young woman. (Tr. 52 (Bilezikian).)

Osteoporotic fractures are commonly divided into two broad categories: vertebral fractures or fractures of the spine, and nonvertebral fractures or fractures of any other bones in the body. (Tr. 49 (Bilezikian).) In the United States, osteoporosis is responsible for about 1.5 million fractures each year, of which approximately half are vertebral fractures and half are nonvertebral fractures. (Tr. 49 (Bilezikian).) The major sites for nonvertebral fracture include the wrist, arm, clavicle (collarbone), rib, hip, pelvis, and leg. (Tr. 60-61 (Bilezikian).)

Hip fractures are the greatest cause of morbidity and mortality among fracture types, and are the most costly to treat. (Tr. 895-96 (Black); *see also* Tr. 49 (Bilezikian).) Plaintiffs' expert, Dr. John Bilezikian, testified that "hip fracture ... is the biggest because the economic toll of the hip fracture exceeds all the others combined." (Tr. 49 (Bilezikian).) In addition, hip fractures are also associated with high morbidity and mortality. (Ex. 94 at 5-6 (stating that approximately half of all patients who sustain a hip fracture fail to return to their previous activities of daily living and that mortality rates in the first year after the hip fracture can be as high as 20% in postmenopausal Caucasian women) (Bilezikian report).) Roche's clinician expert stated that "hip fracture is the major driving force ... behind the whole field," (Tr. 935 (Weinerman)), and that "the major public health issue is a reduction in hip fracture." (Tr. 936 (Weinerman).)

***4** BMD T-scores are a powerful predictor of fracture risk generally (Tr. 52, 63 (Bilezikian)), but

only partly predictive with regard to the location of fracture. (Tr. 53 (Bilezikian).) For example, Dr. Bilezikian testified that a T-score of-3 of the back and of-1 of the arm would signify that the back is at greater risk of fracture; however, the highest T-score reflects not only the highest risk of fracture for that particular site but also risk at other sites. (Tr. 53 (Bilezikian).) Patients' BMD T-scores can vary at various sites of the body and that the corresponding risk of fracture at those sites thus also varies. (Tr. 105 (Bilezikian); *see also* Tr. 117 (Bilezikian).)

B. Osteoporosis Drugs and Bisphosphonates

All osteoporosis drugs work principally by helping to build bone. Anti-resorptive medications slow the rate of bone resorption. (Tr. 53-55 (Bilezikian).) Although these drugs work systemically throughout the body (Tr. 557 (Chestnut)), the extent to which anti-resorptive drugs reduce turnover is a function of the metabolic rates of bone turnover at particular sites. (Tr. 47, 56 (Bilezikian) .) The primary effect of all three bisphosphonates is at trabecular sites where most remodeling occurs. (Tr. 556, 557 (Chestnut).)

The FDA has approved a number of anti-resorptive medications for the treatment of osteoporosis,[FN7] of which bisphosphonates are the most commonly-prescribed class. (Tr. 54 (Bilezikian); Tr. 940-41 (Weinerman).) In fact, bisphosphonates are considered the "gold standard" for treatment of osteoporosis and comprise in excess of eighty percent of total prescriptions in the osteoporosis market. (Tr. 205-06 (Pratt).) [FN8] The FDA has approved three bisphosphonates for the treatment and prevention of osteoporosis: alendronate (or Fosomax, manufactured and distributed by Merck); risedronate (or Actonel, manufactured and distributed by plaintiff P & G); and, ibandronate (or Boniva, manufactured and distributed by defendant Roche). (Tr. 54-55 (Bilezikian).) These three bisphosphonates share similar chemical qualities and all three inhibit osteoclasts, the cells that resorb bone. (Tr. 55 (Bilezikian); Ex. 98 at 2-3 (Chestnut Decl.).) Clinical trials have shown that bisphosphonates consistently reduce the risk of vertebral fracture, increase bone density and reduce the rates of bone remodeling. (Ex. 136 at 2 (Black report).) The results from these trials for nonvertebral fractures, including hip fractures, however, have been inconsistent. (*Id.*)

FN7. FDA-approved anti-resorptive medications fall into the following categories: (i) bisphosphonates, (ii) selective estrogen receptor modulators, (iii) calcitonin, a naturally occurring hormone involved in calcium regulation and bone metabolism, and (iv) estrogen/hormone replacement therapy (Tr. 53-55 (Bilezikian); Tr. 940 (Weinerman)).

FN8. P & G asserts that bisphosphonates are the gold standard and the "first-line" and "first choice" in drugs for osteoporosis treatments-over other non-bisphosphonate drugs such as Evista and Neocalcin-because bisphosphonates such as Actonel and Fosomax have shown nonvertebral fracture efficacy beyond the spine while the other non-bisphosphonate osteoporosis drugs have not (Tr. 214 (Pratt)).

Roche's clinician expert also testified that bisphosphonates are the first-line drug for many patients (Tr. 941 (Weinerman)). Advantages include that bisphosphonates are targeted drugs, focusing on improving bone quality, provide good tolerability, and are effective and potent (Tr. 940-41 (Weinerman)).

Although bisphosphonates have similar mechanisms of action pharmacologically, chemically they exhibit "subtle differences in their effects." (Tr. 904 (Black).) These effects may be due to "important pharmacokinetic differences" [FN9] with regard to their respective absorption uptake, distribution, and elimination. (Tr. 55 (Bilezikian).) When taken orally, the drugs differ in the extent to which they penetrate bone and in the time to penetrate bone. (Tr. 55 (Bilezikian).) In addition, the drugs differ in the extent to which each improves bone density (Tr. 56 (Bilezikian)), with Fomosax possibly being the most potent in improving bone density and reducing bone turnover. (Tr. 57 (Bilezikian).) As noted previously, individual sites comprised of varying proportions of trabecular and cortical bone turnover bone at differing rates. (Tr. 133 (Grauer).)

FN9. " 'Pharmacokinetics' involves the study of 'the action of drugs in the body over a period of time, including the processes of absorption, distribution, localization in tissues, biotransformation, and excretion.'' *Rhone-Poulenc Rorer Pharms. v. Merion*

> *Merrell Dow, Inc.*, No. 93-1044, 1994 U.S. Dist. LEXIS 20782, at *13 n. 5 (W.D.Mo. Sept. 30, 1994), *aff'd in part vacated in part by* 93 F.3d 511 (8th Cir.1996) (citing Dorland's Illustrated Medical Dictionary).

***5** While all three FDA-approved bisphosphonates increase bone density and reduce bone turnover (Tr. 62 (Bilezikian)), recent research shows that improvement in bone density-even though helpful-does not correlate very well with fracture prevention efficacy measures. (Tr. 64 (Bilezikian); Tr. 558 (Chestnut); Tr. 898 (Black); Ex. 141 at 5; *see also* Tr. 626 (Chestnut) (noting current academic debate regarding the correlation between bone mineral density, bone turnover, and fractures); Tr. 697 (Friend) (same); Tr. 965-66 (Weinerman) (same); *cf.* (Tr. 922 (Black) (noting that low BMD T-scores cannot be equated with being at "high risk" for osteoporosis).) Similarly, reduction in bone turnover while also related to fracture prevention efficacy is not as strongly linked to fracture prevention efficacy as previously thought. (Tr. 65 (Bilezikian); Tr. 558 (Chestnut).) Other factors may be at play in affecting fracture prevention efficacy, including bone's micro-architecture,[FN10] mineralization density, and the quality of collagen. [FN11] (Tr. 66-68 (Bilezikian).)

> FN10. Roche's medical expert, Dr. Chestnut, agreed that micro-architecture (along with BMD and bone turnover) present a "very important" component of bone quality. (Tr. 558 (Chestnut).) Dr. Chestnut opined, however, that the data do not show that Boniva affects micro-architecture differently from Fosomax or Actonel. (Tr. 559 (Chestnut).)

> FN11. Collagen is defined as the "major protein ... of the white fibers of connective tissue, cartilage, and bone." Stedman's Medical Dictionary 379 (27th ed.2000).

C. FDA Approval of Bisphosphonate Drugs for Osteoporosis

The FDA approves drugs for the treatment of osteoporosis, only after a drug demonstrates fracture efficacy in a large, randomized, placebo-controlled, double blind study in which a reduction in the risk of vertebral fractures is the primary endpoint. (Tr. 57, 58 (Bilezikian).) [FN12] Data showing improvement in bone density or reduction in bone turnover alone are insufficient for an indication of fracture reduction efficacy-*i.e.*, the FDA requires that clinical trials pre-specify reduction in fracture risk as a primary endpoint. (*Id.*) FDA approval, however, requires *vertebral* fracture efficacy only. (Tr. 57, 59 (Bilezikian); Tr. 563 (Chestnut); Ex. 94 at 4.) Fracture reduction efficacy at nonvertebral sites-of which there are six major areas (*i.e.*, the clavicle, arm, wrist, pelvis, hip, and leg)-is difficult to demonstrate. (Tr. 60-61, 97 (Bilezikian); Ex. 141 at 6.) [FN13] When researchers study nonvertebral fractures, they focus either on the hip or on a composite endpoint of a group of sites (Tr. 61 (Bilezikian)); but proven vertebral fracture efficacy does not equate to nonvertebral fracture efficacy. (Ex. 141 at 5; Tr. 70 (Bilezikian).) To demonstrate nonvertebral fracture prevention, the FDA requires that the clinical study on which a manufacturer bases its efficacy claim to have nonvertebral fractures as an endpoint. (Tr. 70 (Bilezikian).)

> FN12. Such a study involves a "controlled experiment," which is defined as follows:
>
> > An experiment where the investigators determine which subjects are put into the "treatment group" and which are put into the "control group." Subjects in the treatment group are exposed by the investigators to some influence-the "treatment"; those in the control group are not so exposed. For instance, in an experiment to evaluate a new drug, subjects in the treatment group are given the drug, subjects in the control group are given some other therapy; the outcomes in the two groups are compared to see whether the new drug works.
> >
> > "Randomization"-that is, randomly assigning subjects to each group-is usually the best way to assure that any observed difference between the two groups comes from the treatment rather than pre-existing differences.
> >
> > David H. Kaye and David A. Freedman, Reference Guide on Statistics, *in* Federal Judicial Center, *Reference Manual on Scientific Evidence* 162 (2d ed.2000). A double-blind experiment involves "human subjects in which neither the diagnosti-

> cians nor the subjects know who is in the treatment group or the control group. This is accomplished by giving a placebo treatment to patients in the control group." *Id.* at 163.
>
> In short, "[r]andomized clinical trials measure the efficacy of a treatment by comparing outcomes after therapy of patients randomized to one of at least two treatments." (Ex. 482 at 93.)

FN13. For example, Dr. Bilezikian testified that the wrist, with the highest proportion of cortical bone, has the lowest rate of turnover and that, for that reason, it is most difficult to show fracture reduction efficacy at that site. (Tr. 98 (Bilezikian).)

The FDA approved each of the three drugs-Fosomax, Actonel, and Boniva-initially, as indicated for the treatment and prevention of osteoporosis based on a daily dosage.[FN14] Subsequently, in order to obtain approval for weekly and monthly dosage, the makers of each of these drugs conducted one-year clinical trials called "bridging non-inferiority studies" to demonstrate equivalent efficacy at longer dosage intervals. (Tr. 68-69 (Bilezikian).) Unlike the pivotal clinical trials that established fracture prevention efficacy, bridging studies only examine rates of bone density and bone turnover and not of fractures. (Tr. 69 (Bilezikian) .)

FN14. The FDA approved Fosamax, a drug marketed by Merck & Co., as a daily drug in 1995 and for a weekly dosage in 2001. Plaintiffs received FDA approval for a daily formulation of Actonel in 2000, and subsequently as a weekly drug in 2002. (Tr. 203 (Pratt).) Boniva obtained approval for daily dosage in 2003. In 2005, the FDA approved Boniva for monthly dosage. Defendants started marketing Boniva immediately thereafter. In January 2006, the FDA approved Boniva as an intravenous drug for quarterly dosage.

D. The Clinical Trials and FDA Approvals

***6** The clinical trials associated with the FDA-approved bisphosphonates all established vertebral fracture efficacy (as the primary endpoint) and all sought to demonstrate nonvertebral fracture efficacy (as primary or secondary endpoints).[FN15] Merck's Fosomax involved several clinical trials (including FIT 1 and FIT 2). (Ex. 3 at 6; Tr. 70 (Bilezikian).) FIT 1 involved high-risk patients. (Tr. 70 (Bilezikian).) This trial was not powered [FN16] to show a reduction in nonvertebral fracture and nonvertebral fracture efficacy was not the primary endpoint; nevertheless, the data showed a statistically significant [FN17] reduction in spine and hip fracture. (Ex. 3 at 4-11; Tr. 70, 98 (Bilezikian).) [FN18] The "Indications and Usage" section of the FDA-approved label states that "Fosomax is indicated for the treatment and prevention of osteoporosis in postmenopausal women" and that "[f]or the treatment of osteoporosis, Fosomax increases bone mass and reduces the incidence of fractures, including those of the hip and the spine ." (Ex. 3 at 11.)

FN15. Dr. Bilezikian explained as follows:

> If a pivotal clinical trial that has not been powered to show efficacy at non-vertebral sites does not show efficacy at non-vertebral sites, one can only conclude that efficacy has not been proven. On the other hand, if a clinical trial shows non-vertebral fracture efficacy, even if the clinical trial was not powered to show this effect, one is entitled to reach the conclusion that the drug does reduce non-vertebral fracture. The FDA has held this view for many years.
>
> (Ex. 94 at 9.)

FN16. The statistical term "power" has been described as follows:

> The power of a study expresses the probability of finding a statistically significant association of a given magnitude (if it exists) in light of the sample sizes used in the study. The power of a study depends on several factors: the sample size; the level of ... statistical significance ... specified ...; and the specified relative risk that the researcher would like to detect. Power curves can be constructed that show the likelihood of finding any given relative risk in light of these factors. Often power curves are used in the design of a study to

determine what size the study populations should be.

Federal Judicial Center, Reference Manual on Scientific Evidence 362 (2d ed.2000); *see also* Tr. 174 (Marks) (explaining the term "powered" as meaning having enough study participants to have confidence in the data results); Tr. 876 (Black) ("From a statistical point of view, the issue of small sample sizes, is that you have low power, which is a low probability of finding an effect."); Ex. 99 at Bates number Roche _KF_0007296 ("Power is the ability of a study to detect a significant difference between treatment groups.... Power increases as sample size increases."); Ex. 482 at 94 ("The sample size of a well-designed randomized clinical is large enough to ensure a high probability, or *power* of detecting a clinically important *overall* difference between two treatment groups [and][a] large sample size gives assurance that if no effect in treatment is truly present, the probability ... of spuriously finding an effect is small.").

FN17. In most scientific work, the level of statistical significance required to obtain a statistically significant result is set conventionally at .05 or 5%. Federal Judicial Center, Reference Manual on Scientific Evidence 194 (2d 2000); *see also Smithkline Beecham Consumer Healthcare v. Johnson & Johnson-Merck Consumer Pharms. Co.,* 01 Civ. 2775, 2001 U.S. Dist. LEXIS 7061, at *7 n. 3 (S.D.N.Y. June 1, 2001) (statistical significance signifies the likelihood that the results could have occurred by chance); Tr. 880 (Black) (stating that "having a p-value below .05 makes the results more significant"). In order to assert that a drug is proven efficacious in a particular clinical trial, the data results must achieve statistical significance. (Tr. 127 (Grauer).) A statistical significance of .05 means that the researcher has 95% confidence in the conclusion reached and that in replicating the study that conclusion would be reached nineteen out of twenty times. (Tr. 169 (Marks); *see also* Tr. 197 (Marks) (describing statistical significance of .05.)

FN18. The FIT 2 trial was comprised of a lesser-risk study population and did not show statistically significant reduction in nonvertebral fractures, such as in the hip. (Tr. 99 (Bilezikian).)

P & G carried out two large, randomized, placebo-controlled, double-blind studies-the Multinational Study (VERT-MN), which was conducted primarily in Europe and Australia, and the North America study (VERT-NA). (Ex. 2 at 5.) P & G did not design these studies to be powered to show nonvertebral fracture risk reduction at composite endpoints, but the data in the VERT-NA trial did show statistically significant reduction of such fractures. (Tr. 73-74, 100 (Bilezikian).) [FN19] Moreover, while the VERT-NA showed statistically significant reduction in nonvertebral fractures at a composite group of six sites, it did not achieve statistical significance for any one of those individual six sites alone. (Tr. 100-01 (Bilezikian); Tr. 147 (Grauer).) The FDA label for Actonel states that "Actonel is indicated for the treatment and prevention of osteoporosis in postmenopausal women" and that "[i]n postmenopausal women with osteoporosis, Actonel increases BMD and reduces the incidence of vertebral fractures and a composite endpoint of nonvertebral osteoporosis-related fractures." (Ex. 2 at 14; *see also* Tr. 73 (Bilezikian).) There are limitations to Actonel's claims, however. The test data do not support "an Actonel non-spinal fracture claim for each/any skeletal site because they were not statistically ... 'proven' to have reduced the number of fractures in the Actonel group compared to the placebo. Rather ... Actonel failed to reduce fractures better than placebo at leg and hip and was in fact worse than placebo at collarbone." (FDA letter, p. 3, May 4, 2006.)

FN19. The data for the VERT-MN trial did not show statistically significant reduction in nonvertebral fractures, (Tr. 125 (Grauer))-either at individual sites or at a composite group of six sites. (Tr. 100 (Bilezikian).)

Roche conducted a three-year multicenter, double-blind, placebo-controlled, randomized study of the efficacy of Boniva, referred to as the BONE trial. (Ex. 5 at 32; Tr. 74 (Bilezikian).) Like the Fosomax FIT trials and the Actonel VERT-MN and VERT-NA trials, the primary endpoint of the BONE

trial was vertebral fracture reduction. (Tr. 74 (Bilezikian).) The BONE study pre-specified nonvertebral fractures as a secondary endpoint. (Tr. 74 (Bilezikian).) The BONE study showed statistically significant vertebral fracture efficacy for Boniva but not with regard to nonvertebral fracture efficacy. (Tr. 75 (Bilezikian).) [FN20] Significantly, the BONE study population was not as high-risk for hip fractures as other study populations in other comparable clinical trials. (Tr. 76-77 (Bilezikian); Tr. 128-29 (Grauer).) [FN21] The FDA-approved labeling for Boniva states that "Boniva is indicated for treatment and prevention of osteoporosis in postmenopausal women" and that "[i]n postmenopausal women with osteoporosis, Boniva increases BMD and reduces the incidence of vertebral fractures. Boniva may be considered in postmenopausal women who are at risk of developing osteoporosis and for whom the desired clinical outcome is to maintain bone mass and to reduce the risk of fractures." (Ex. 9 at 9.) This latter indication is not limited to vertebral sites. Boniva is the only bisphosphonate approved for once-monthly dosage. (Tr. 135 (Grauer).)

FN20. The published BONE study results indicated the following incidence rates for nonvertebral fractures: 8.2% in the placebo group; 9.1% in the daily Boniva group; and 8.9% in the "intermittent" or non-daily dosage Boniva group. (Ex. 4 at 1245.) This data showed that the results with regard to Boniva's nonvertebral fracture efficacy did not achieve statistical significance. (Tr. 170 (Marks).)

More specifically, the journal article states as follows:

The incidence of clinical nonvertebral fractures was low and similar between the placebo and active treatment groups.... The study population had a relatively high mean BMD at the proximal femur (total hip [mean T score = -1.73], femoral neck [mean T score = -2.03]) at baseline compared with other phase III clinical trials ... and therefore was at relatively low risk for new nonvertebral fractures.

(Ex. 4 at 1245.) As noted previously, a BMD T-score of -2.5 is considered osteoporotic. (Tr. 76 (Bilezikian).).

FN21. The T-score for the lumbar spine of study participants, however, was the same for both the BONE study and the Actonel trials (Tr. 80 (Bilezikian)).

***7** Thus, FDA-approved labeling states that Fosomax, Actonel, and Boniva are each indicated for the treatment and prevention of osteoporosis in postmenopausal women (Ex. 2 at 14; Ex. 3 at 11; Ex. 9 at 9; Tr. 101 (Bilezikian); Tr. 136-37 (Grauer)), and, while their labeling specifies distinctly what the pivotal trials showed for each drug with regard to nonvertebral fracture efficacy, usage is not limited to any specific site in the body. (Tr. 101 (Bilezikian).) In fact, the FDA in its Boniva approval letter noted that, while the BONE study failed to demonstrate nonvertebral fracture efficacy (Ex. 92 at 56), nevertheless the agency did not interpret these data "as a distinguishing therapeutic deficiency" of Boniva "due to the predominance of non-BMD related risk factors for [nonvertebral] fracture (*i.e.*, risk factors for falling)." (Ex. 100 at 2, Tr. 141 (Grauer).)

P & G concedes that the BONE trial does not prove that Boniva increases the risk for nonvertebral fractures. (Tr. 94, 104 (Bilezikian); *see also* Tr. 134 (Grauer) (same).) [FN22] Both Dr. Bilezikian and Dr. Grauer also concede that Boniva is neither ineffective nor dangerous, which of course the FDA has concluded as well. (Tr. 96 (Bilezikian); *see also* Tr. 134 (Grauer) (testifying that Boniva is safe to take).) In fact, Dr. Bilezikian prescribes Boniva to some of his patients, particularly patients who do not tolerate Fosomax or Actonel well. (Tr. 117 (Bilezikian).)

FN22. Dr. Bilezikian testified that in order for a drug to be *proven ineffective* for the treatment of a particular disease a study would need to be conducted that was powered for that endpoint (*i.e.*, that particular treatment) (Tr. 104 (Bilezikian)).

The differences in the claims allowed by the FDA for the three bisphosphonate drugs may very well be attributable to the differences in the testing populations, rather than in the drugs' comparative efficacies. Thus, if two drugs have comparable efficacies, it would be relatively easier to demonstrate effectiveness in a higher risk population than it would be in a

lower risk population. FIT 1 had a very high risk population while BONE had a relatively low risk population. The differences in the testing populations could also account for the differences in efficacy between FIT 1 and 2, and VERT NA and VERT MN, in which one test showed nonvertebral efficacy, but the companion test did not.

E. The BONE Post-Hoc Sub-Group Analysis

Roche conducted a post-hoc, subgroup analysis of the BONE study data. (Tr. 83 (Bilezikian).) A post-hoc subgroup analysis examines data already collected and analyzed and is frequently used to gain "additional information, additional insights" and to devise new hypotheses for follow-up prospective trials. (Tr. 83 (Bilezikian); Tr. 170, 171 (Marks); Ex. 99 at Bates number Roche_KF_ 0007296.) A subgroup analysis can be conducted preplanned or post-hoc and examines the data of a subset or subsets of the study population. (Tr. 171 (Marks); Ex. 482 at 93.) Pre-specified subgroup analyses are accorded greater weight than post-hoc subgroup analyses. (Tr. 860 (Black).) Nonetheless, subgroup analyses are frequently conducted, particularly in connection with large clinical trials (Tr. 171, 186-87 (Marks); Tr. 859 (Black)),[FN23] and can provide useful information to the scientific, medical, and research community. (Tr. 187 (Marks); Ex. 482 at 93 ("Properly performed, analysis of subgroups can yield useful insights into therapy; unfortunately, many commonly used approaches are often uninformative or misleading.").) [FN24] Post-hoc, subgroup analyses may also be appropriate when other, similar trials (*e.g.*, FIT 1 and VERT-NA) report that a treatment effect appears to be concentrated in a particular subgroup of participants (*e.g.*, high risk). (Ex. 137 at 5 (citing Lawrence M. Friedman et al., Fundamentals of Clinical Trials 305 (3d ed.1998).) [FN25]

FN23. Subgroup analyses are not *per se* disfavored in the scientific community: "It is important that subgroups be examined [as][c]linical trials require considerable time and effort to conduct, and the resulting data deserve maximum evaluation." Friedman et al., at 304 (3d ed.1998).

FN24. In particular, subgroup analyses help researchers identify more precisely groups within the study population that might be benefitted or harmed by the treatment (Tr. 859 (Black)). Subgroup analyses are also undertaken to identify side effects in subsets of the study population (*id.*); *see also* Ex. 482 (Salim Yusef et al., *Analysis and Interpretation of Treatment Effects in Subgroups of Patients in Randomized Clinical Trials*, 266 JAMA 93 (July 3, 1991) ("[T]he chief aim of subgroup analysis should be to identify either consistency of, or large difference in, the magnitude of treatment effects among different categories of patients.").

FN25. Roche's expert, Dr. Black, urges that the BONE post-hoc subgroup is not "data dredging," but rather is permissible because the results of prior bisphosphonate trials showed nonvertebral fracture efficacy for women with low BMD T-scores (Ex. 137 at 1-6; *see also* Tr. 860, 869-72 (Black)). In particular, Black noted that the co-authors of *Fundamentals of Clinical Trials* identified this third category of subgroups-post-hoc, subgroup analyses based on prior studies-without criticism. (Tr. 863, 866-67 (Black).) Black testified that other factors may lend greater credibility to post-hoc subgroup analyses, including biological plausibility and whether the post-hoc subgroup results are consistent with previous research in the field. (Tr. 860, 872, 874 (Black).) Nonetheless, Dr. Black is sensitive to the risk of "data dredging." He requested that in subsequent analyses of the BONE study, subgroups should be identified in such a way so as to "retain[ ] some smattering of a priori" and to ensure that it is not "100 percent data based." (Tr. 695 (Friend).)

***8** As leading experts have noted,[FN26] "while subgroup analyses are important," "they must be ... interpreted cautiously." Friedman et al., Fundamentals of Clinical Trials at 306; *see also* Tr. 200 (Marks); Tr. 914 (Black); Ex. 482 at 97 ("encourag[ing] skepticism toward most reported subgroup effects") .[FN27] There are numerous reasons here for caution. Roche acknowledges that the BONE study post-hoc, sub-group results cannot be generalized beyond the subgroup with BMD T-scores of equal to and less than minus three. (Tr. 890 (Black).) Optimally, subgroup results should run in the same direction as those obtained for the overall population in the BONE test, but in this

analysis they run opposite. (Tr. 173-74 (Marks); Tr. 154-55, 163-64 (Grauer); *see also* Tr. 909 (Black).) Since subgroup analyses always involve smaller sample sizes than the complementary or overall population groups, they are accorded lower confidence levels. (Tr. 175 (Marks); *see also* Ex. 482 at 95 (subgroups often lack power).) While adjustments can be made for the multiplicity of runs conducted in post-hoc, subgroup analyses (Tr. 914 (Black)), data results from such analyses should be treated with caution and care. (Tr. 176 (Marks).

FN26. The parties are in agreement that Lawrence Friedman, Curt Furberg, and David DeMets are leading experts in the field of biostatistics and that their text, *Fundmentals of Clinical Trials*, is a recognized, authoritative treatise. (Tr. 190 (Marks); Tr. 861 (Black).)

FN27. "The FDA does not take into account post-hoc analyses in its review of applications for approval of drugs because this kind of analyses is fraught with potential biases." (Ex. 94 at 17 (Bilezikian report).)

Roche's post-hoc, subgroup analysis involved examining the BONE study data at multiple "cut points" in addition to analyzing the entire population: [FN28] *i.e.*, for patients with BMD T-scores of greater than -2; for patients with BMD T-scores of less than -2; for patients with BMD T-scores of less than -2.5; for patients with BMD T-scores of less than 3.0; and for patients with BMD T-scores of less than -3.5. (Ex. 32 at Slide 2; Tr. 177 (Marks).)

FN28. As noted previously, Roche deemed critical the fact that the overall BONE study population had a lower risk for fracture (*i.e.*, BMD T-score of -2 at the femoral neck) than the populations studied in the Actonel and Fosomax trials. (Tr. 571 (Chestnut).)

The BONE post-hoc, subgroup study article reported "a relative risk reduction of nonvertebral fractures ... in patients with a baseline femoral neck BMD T-score [of less than] 3.0." (Ex. 4 at 1245.) In this high risk population, Boniva reduced the incidence of nonvertebral fractures by 69%. (*Id.*) This post-hoc, subgroup comprised 13% of the entire BONE study population. (*Id.;* Tr. 85 (Bilezikian); Tr. 696 (Friend).) The complementary study population-the remaining 87% of the study population, who were at much lower risk-reached statistical significance in favor of placebo under one statistical test.

Medical experts for P & G and Roche agree that the BONE post-hoc, subgroup data is "relevant to the clinical setting," because in a high risk group, nonvertebral fractures were reduced. Nonetheless, the data must be "treated with caution." [FN29] Roche's expert, Dr. Chestnut, agreed with Dr. Bilezikian's view that the BONE study post-hoc, subgroup analysis showed that, in the high-risk group, Boniva was "associated" with a decrease in nonvertebral fractures. (Tr. 573 (Chestnut).) [FN30] All of Roche's experts, except Dr. Chestnut, agreed that the subgroup analysis did not prove or demonstrate that Boniva reduced the risk of nonvertebral fractures. [FN31] (Tr. 562-563 (Chestnut).) (Tr. 640, 674 (Friend); Tr. 868, 882, 886-87, 896 (Black); Tr. 962-63, 969 (Weinerman).) Dr. Black, for example, said that the BONE study "provides valid statistical evidence of an effect on nonvertebral fractures in the subgroup of women with low BMD." (Tr. 868 (Black); *see also* Tr. 883 (Black).) [FN32]

FN29. In the journal article which published the BONE study results, Dr. Chestnut and his co-authors stated:

> Although this is a retrospective analysis, and therefore its interpretation should be treated with caution, this study was well designed and conducted in a large number of patients. Consequently, it is likely that these findings will be relevant to the clinical setting.

(Ex. 4 at 1247; *see also* Tr. 589 (Chestnut) (same); Tr. 574 (Chestnut) (clinical importance of post-hoc, subgroup data).) Dr. Bilezikian testified using identical language to that in the article. Dr. Bilezikian stated that retrospective, post-hoc analyses should be "treated with caution" but that, since the BONE study was well designed and conducted with a large number of patients, the post-hoc subgroup "findings will be relevant to the clinical setting." (Tr. 85 (Bilezikian); *see also* Tr. 113 (Bilezikian) (same); Tr. 684 (Friend) (same).)

FN30. A statistical association is not the same as a statistically significant result. As a statistical term, "association" is defined as "[t]he degree of statistical dependence between two or more events or variables." Daniel L. Rubinfeld, *Reference Guide on Multiple Regression*, *in* Federal Judicial Center, *Reference Manual on Scientific Evidence* 222 (2d ed.2000). By contrast, "statistical significance" is defined as "[a] test to evaluate the degree of association between a dependent variable and one or more explanatory variables," such that "[i]f the calculated p-value is smaller than 5%, the result is said to be statistically significant (at the 5% level). *Id.* at 226. Dr. Chestnut agreed that an association is not the same thing as proof. (Tr. 588-89 (Chestnut).)

FN31. Dr. Chestnut testified that "proof" meant "shown in clinical trials" and "published" in scientific journals. (Tr. 587 (Chestnut).) Dr. Chestnut, however, conceded that in the four published articles concerning the BONE study, he has never stated that Boniva has been "proven" to reduce the risk of nonvertebral fractures either in the overall population or, significantly, in the subgroup. (Tr. 589 (Chestnut).)

FN32. Dr. Black provided the Court with helpful testimony regarding, in his expert opinion, the difference between "proof" and "valid statistical evidence." (Tr. 883 (Black).) Dr. Black commented favorably on the FDA's "concept of proof," which involves conducting a clinical trial, having generally a single primary endpoint, and if the endpoint can be demonstrated with statistically significant results, then the researcher can claim to have "proven" that the drug is effective for that endpoint. (Tr. 884 (Black).)

***9** The Court also notes the FDA's comment that "While the ... results are of academic interest, they come from post-hoc, subgroup analyses and are therefore inappropriate for inclusion in the labeling." (Ex. 92 at 26.) Accordingly, Boniva could not claim on its label efficacy with regard to nonvertebral fractures. (*Id.* at 14.) [FN33]

FN33. The FDA approval letter for Boniva, which was issued on April 29, 2003, stated as follows with regard to the nonvertebral fracture data:

> Of note, and distinct from studies for other approved bisphosphonates, study 4411 failed to demonstrate a treatment effect on non-vertebral fractures. This is not interpreted by the division review team as a distinguishing therapeutic deficiency of this particular bisphosphonate. Rather, treatment effects on non-vertebral osteoporotic fractures (most of which are traumatic in ultimate origin) have historically been difficult to demonstrate due to the predominance of non-BMD-related risk factors for such fractures (*i.e.*, risk factors for falling) that are not ameliorated by bisphosphonates.

(Ex. 100 at 2.) Roche concedes that the FDA does not deem data from retrospective analyses as "proof." (Tr. 685 (Friend).)

While the BONE study post-hoc, subgroup data does not prove or demonstrate nonvertebral fracture efficacy, that does not mean, however, that the data cannot be referred to or utilized, in the marketing of Boniva. It is relevant information, which when properly conveyed, can be of assistance to a physician. The question to be resolved is whether Defendants overstepped the appropriate boundaries for use of this data.

F. Bisphosphonate Class Efficacy

The Court heard conflicting testimony and evidence regarding the degree to which bisphosphonates can be ascribed as having a "class effect." [FN34] Roche admits that its sales force communicated a claim of bisphosphonate class efficacy. (Tr. 827-28 (Klein).) Further, Roche's initial sales aid stated "Once-monthly BONIVA-delivers bisphosphonate efficacy." (Ex. 15 at 2-3.) [FN35] Claims of bisphosphonate class effect-that is, that all bisphosphonates work the same and produce similar results-are of course made in the context of only three FDA-approved bisphosphonate drugs. P & G maintains that, since Roche has not proven nonvertebral efficacy for Boniva, to the extent the bis-

phosphonate class efficacy claim implicates nonvertebral fracture efficacy, such a claim is false and misleading.[FN36]

FN34. Dr. Bilezikian testified that a "class effect" refers to a family of drugs that all work the same. (Tr. 112 (Bilezikian).)

FN35. A sales aid or detail aid is a glossy promotional piece that sales representatives use during visits to physicians. (*See, e .g.*, Tr. 651 (Friend) (explaining physician sales aids).). "A physician sales aid is ... information about the safety, efficacy, [and] indication [of] the product which a sales representative would use in communicating with a doctor. It is ... a road map ... to make sure that [sales representatives] are giving appropriate, complete, and accurate information to a physician." (Tr. 651 (Friend).)

FN36. While the three drugs belong to the same class, that is not the same as having a class effect. "Head-to-head" clinical trials involving the three drugs would need to be conducted in order to demonstrate a "class effect" or how each was distinguished from the other. (Tr. 113 (Bilezikian).) A head-to-head study would need to be conducted comparing two or three bisphosphonates together to be able to compare them fairly and conclude whether a class effect exists. (*Id.; see also* Tr. 122, 142 (Grauer) (stating that comparisons of drugs require head-to-head studies).) Head-to-head trials have not been conducted comparing Fosomax, Actonel, or Boniva. (Tr. 122 (Grauer).)

At the hearing, Roche countered P & G's complaint with two arguments. First, Roche contends that, on the one hand, bisphosphonates should be viewed as having a class effect because these drugs have a similar chemical makeup and mechanism of action. (Tr. 555, 559-560 (Chestnut).) [FN37] Roche further notes that, because the FDA has approved these drugs for osteoporosis treatment and prevention without limitation to vertebral versus nonvertebral efficacy, the generalized bisphosphonate efficacy claim can be made. (Tr. 655-56 (Friend).) [FN38] Second, while Roche concedes that the BONE trial did not establish nonvertebral fracture efficacy for BONIVA, it contends that the nonvertebral fracture efficacy for all bisphosphonates has been inconsistent. (Tr. 546-47 (Chestnut); Tr. 864 (Black); Tr. 935 (Weinerman).

FN37. Dr. Chestnut explained a mechanism of action as involving in part the enzymatic pathways and chemical pathways. (Tr. 444 (Chestnut).)

FN38. The FDA, however, concluded that "the apparent correlation between vertebral BMD and vertebral fracture efficacy cannot be generalized to other skeletal sites" (Tr. 605 (Chestnut)), a conclusion with which Dr. Chestnut concurred. (*Id.*)

The FDA noted that Boniva's failure to demonstrate a treatment effect on nonvertebral fractures is "not interpreted ... as a distinguishing therapeutic deficiency of this particular bisphosphonate." (Ex. 100, p. 2.) More recently in May 2006, the FDA determined that Actonel's efficacy at a composite nonvertebral end point was not a scientific basis for Actonel's claim of superiority to Boniva. The FDA specifically noted that Actonel had failed to demonstrate efficacy at the leg, hip and collarbone. (FDA letter, May 4, 2006).) According to the FDA, Boniva is not inferior to other bisphosphonates by virtue of its lack of proven efficacy for nonvertebral fracture risk reduction; and similarly, Actonel is not superior to Boniva because of its efficacy at a composite nonvertebral end point. This leaves both products as effective for the prevention and treatment of osteoporosis in postmenopausal women, without limitation as to vertebral or nonvertebral sites.

***10** In making its claim of class efficacy, Roche emphasized its data related to vertebral fracture reduction, improvement in bone mineral density, and bone turnover reduction. (*See, e.g.*, Tr. 562-63 (Chestnut)). While all of this is so, and notwithstanding the FDA's determination that Boniva is not inferior to other bisphosphonates, and just recently that Actonel is not superior to Boniva, a class effect may be established only by head-to-head testing. Dr. Black, Roche's biostatistical expert, testified that "one cannot make a statement that there is a class effect of bisphosphonates with respect to nonvertebral fracture efficacy." (Tr. 918 (Black).) Dr. Chestnut (while arguing that class efficacy could be claimed, given statistically significant vertebral fracture reduction, im-

provement in bone mineral density, and bone turnover reduction) conceded that "[w]ithout a head-to-head study, *i.e.*, within the same trial, same populations, et cetera, it would be inappropriate to compare one drug to another." (Tr. 562 (Chestnut).)

The Court notes, however, that Defendants have not claimed bisphosphonate class effect in any sales aid or other published materials since October, 2005.

G. Clinical Diagnosis of Osteoporosis and Relevance of Clinical Trial Data

The Court also heard conflicting testimony regarding the clinical factors that physicians consider when prescribing osteoporosis medications. Dr. Bilezikian, P & G's expert, takes into account the BMD T-scores of patients at various sites when considering which medication to prescribe for osteoporosis. (Tr. 53, 117 (Bilezikian).). He also considers patients' tolerance for a drug, the dosage regime, and after testing and analysis has prescribed Boniva for his patients. He has no concern about Boniva's safety, but would not recommend Boniva to patients whose BMD T-scores are uniformly low. (Tr. 117 (Bilezikian).) By contrast, Dr. Chestnut testified that when considering whether to prescribe Actonel, Fosomax, or Boniva, he is "aware" of the efficacy data and also considers patients' tolerability, patient preference, and convenience. (Tr. 584-85 (Chestnut).) Dr. Chestnut indicated that he does not take into account differences in BMD T-scores at different sites. (Tr. 584 (Chestnut).) Dr. Weinerman, a practicing endocrinologist and clinician expert in osteoporosis, testified on behalf of Roche. He had a separate, well-founded approach to his use of bisphosphonates in treating his patients.

Given the range of possible diagnoses, and different methods for diagnosis and analysis, it appears that the sharing of relevant information, provided it is accurate, would be of assistance to physicians in devising the appropriate treatment for their patients with osteoporosis.

III. The Parties' Promotion and Marketing of Bisphosphonates

These pharmaceutical giants were well aware of their own products and their properties, their marketing strengths and weaknesses, and the impact that the success of one product might have on the other. P & G was concerned that Boniva's monthly dosage gave it a significant advantage over Actonel's weekly dosage requirement. P & G determined to stop Boniva in "the starting blocks." Roche at the same time understood that its dosage message could not come at the expense of efficacy. Thus, Roche decided to advertise bisphosphonate class efficacy. P & G attacked with a counter-detailing program in which it pointed to Boniva's lack of proven efficacy on nonvertebral fractures.[FN39] As previously indicated, P & G's chief concern is not public health and safety, but rather its market share. Its goal was to maintain market share, and to prevent Boniva from gaining share at Actonel's expense. Roche initially responded by distributing the BONE study. As P & G's counter detailing attacks on Boniva continued, in the Spring, 2006, Roche began to use the results of its post hoc, subgroup analyses in a sales aid for its marketing team. Of course, P & G's counter detailing does not justify Defendants making claims that are literally, or by implication, false and misleading; but the sequence of events is relevant to the analysis of the parties' assertions and defenses.

FN39. There is some evidence that P & G might have told physicians that Boniva had a "proven lack of efficacy." This statement is quite wrong. P & G now maintains that eventually a lingual "clarity" developed and its message was that Boniva had a "lack of proven" efficacy.

***11** The Court now turns to a review of how the parties' marketed their products and their competitive responses to one another.

A. Roche's Pre-Launch Analyses Concerning Boniva

Prior to launching Boniva, Roche believed that Boniva's nonvertebral data posed a serious issue. (Tr. 674 (Friend); Tr. 748, 750 (Heinig).) [FN40] Its market research confirmed that fracture efficacy had to be established, so that convenience of dosage message would be effective.[FN41] (Tr. 740-41 (Heinig).) Physician market research showed that doctors wanted both vertebral and nonvertebral fracture efficacy, with hip fracture efficacy being an important concern. (Tr. 743 (Heinig).)

FN40. *See also* Ex. 41 at Bates number Roche_FH_0008555 ("The BONE study was not powered to show non-vertebral fracture risk reduction, which leaves a data gap around non-vertebral fracture data ... [and] we must expect this facet of Boniva's effi-

cacy data to be the main point of attack by our competitors.").

FN41. With regard to efficacy, see for example: Ex. 33 at Bates number Roche_ZH_0030985 (2004 Advisory Boards for Boniva-Executive Summaries; discussing efforts to "help overcome lack of non-vertebral data") (December 12-13, 2003); *id.* at Bates number Roche_ZH_0030990 ("It was felt that the lack of an indication for non-vertebral fractures would be a major disadvantage in the crowded [bisphosphonate] marketplace, particularly for a late entry."); Ex. 40 at Bates number Roche_KP_0006762 ("The brand strategy requires that there is a perception of equal efficacy to Fosomax and Actonel."). *Id.* at 0006771 ("The Boniva Story and How to Stage It: Push class effect").

Roche's objective was to have doctors believe there was a bisphosphonate class effect in order to address fracture efficacy. (Tr. 745, 754, 756-7, 760 (Heinig).) [FN42] Based on its market research, Roche wanted to deliver dual messages. Its consumer advertising was based on the convenience of monthly dosage. (Tr. 768 (Heinig).) Its marketing and promotion to doctors emphasized class effect. (Tr. 766 (Heinig).)

FN42. There are numerous examples of Roche's intent to communicate these messages. *See, e.g.*, Ex. 39 at Bates number Roche_JL_0002441 ("Boniva Strategy Statement-... requires that we first establish the perception of equal, if not better efficacy."); *id.* at Bates number Roche_JL_0002443 ("Global Once-Monthly Boniva Positioning Platform"-"In osteoporosis, Boniva ... delivers superior real world effectiveness versus even weekly bisphosphonates ...."); *id.* at Bates number Roche_JL_0002448 ("2004 Goals and Objectives: Establish perception of efficacy equal to current [bisphosphonates]"); *id.* at Bates number Roche_JL_0002455 ("Opinion Leaders Objectives-Establish/reinforce perception of Boniva's equivalent efficacy"); Ex. 41 at Bates number Roche_FH_0008584 ("Key message platforms-the entry ticket ... the proven efficacy of the class").

The BONE post-hoc, subgroup analysis was not a part of the initial launch campaign. It is not mentioned in Plaintiffs' complaint of January 4, 2006, and the initial marketing documents (*i.e.*, those seen by the public-consumers and the medical community) do not refer or use any of the data. Use of the post-hoc, subgroup analysis was Roche's response to P & G's continuing counter detailing program.

B. Roche's Launch, Promotion, and Advertising of Boniva

One of the principal means of promoting prescription drugs involves sending out professional sales representatives to visit doctors in what the industry terms "detailing." (Tr. 206 (Pratt); Tr. 711 (Heinig); Tr. 797, 831 (Klein).) During such visits or "calls", sales representatives provide information to physicians about various drugs, including their indicated uses. (Tr. 206-07 (Pratt); Tr. 797-98 (Klein).) Pharmaceutical companies also advertise in medical and scientific journals, employ direct mail, and use the Internet to market and promote prescription drugs. (Tr. 207 (Pratt).) Direct-to-consumer promotion and advertising frequently entails television, print advertising, and direct mail and is intended to raise awareness among individuals of the existence of the disease and of the drug. (Tr. 207, 208 (Pratt).)

As is customary, prior to launch, Roche sent all launch materials (including the first sales aid, Web site text, and a promotional slide kit) to the FDA. (Tr. 641, 650, 652, 663, 666 (Friend).) The first sales aid required pre-clearance by the FDA (Tr. 666-67).[FN43] The FDA responded with comments, all of which were incorporated into the materials. (Tr. 641 (Friend).) When Roche revised the sales aids, it submitted those versions to the FDA for comment as well. (Tr. 641-42 (Friend).) With regard to television ads, the major networks require FDA pre-clearance. (Tr. 642 (Friend) .) [FN44] Roche submitted the ad story boards to the FDA, incorporated the agency's comments, and ultimately obtained pre-clearance. (Tr. 642 (Friend); Tr. 721 (Heinig).) Roche did not pre-clear the second TV ad because it was virtually the same as the first one. (Tr. 647 (Friend); Tr. 721 (Heinig).)

FN43. Subsequent sales aids did not require pre-clearance; Roche sent those to the FDA at deployment. (Tr. 729 (Heinig).)

FN44. The only substantive change that the FDA required Roche to make to the first ad was to delete a reference that Boniva was "easy" to take. (Tr. 645 (Friend).) The FDA noted that the drug was not easy to take because taking Boniva "involves strict adherence to dosing instructions." (Ex. 154 at Bates number Roche_0041225.)

1. April and October 2005 Boniva Detail Aids

***12** When Defendants launched Boniva in April 2005, they distributed a detail aid for sales representatives to use when visiting doctors. (Tr. 209 (Pratt).) Sales representatives visit doctors on a regular basis, sometimes as frequently as once weekly. (Tr. 933 (Weinerman).) A detail or sales aid is typically a large, glossy pamphlet that pharmaceutical companies provide to sales representatives. These pamphlets contain the company's authorized and approved messages that the company wants delivered to physicians during the course of visits. (Tr. 233 (Pratt).)

The front page of Roche's April 2005 sales aid stated: "Announcing the only once-monthly bisphosphonate" and the header across the next two pages stated "ONCE-monthly Boniva delivers bisphosphonate efficacy." (Comp. Ex. E, Ex. 15 at 2-3.) Roche believed that its overall message was that Boniva had once-monthly dosage and that it had bisphosphonate class efficacy. (Tr. 654 (Friend).) This sales aid did not contain any reference to nonvertebral fractures. (Tr. 656 (Friend).) On May 17, 2005, P & G wrote to both Roche (Ex. 118) and the FDA to complain about the sales aid, stating that the claim regarding bisphosphonate efficacy overstated Boniva's therapeutic efficacy. (Ex. 114 at 1; Tr. 209-10 (Pratt).) The FDA responded on May 20, 2005, noting that the issues P & G raised "appear to have some merit" and that the agency would "take this matter into further consideration" (Ex. 117); but eventually took no action.

Sales aids have an approximate six month shelf life and in October, 2005 Roche revised its original sales aid. (Ex. 342; Tr. 656 (Friend).) The second sales aid removed the term "bisphosphonate efficacy" and the reference to the drug being "new" and inserted a new header: "One tablet-once a month" which ran above a monthly calendar showing one pill per month. Immediately below the calendar, the text read: "BONIVA-proven fracture protection and the convenience of once monthly dosing." (Tr. 656 (Friend).) [FN45]

FN45. The FDA does not allow the claim "new" after six months and this claim had to be dropped. Roche sent the second sales aid to the FDA for review and comment at the time of deployment and not for pre-clearance (Tr. 657 (Friend)). It did not receive any FDA comments.

P & G filed two additional complaints to the FDA concerning Roche's October advertising. The FDA took no action on either letter. (Ex. 115, Ex. 116.)

2. July and August 2005 Television Commercials

Beginning in late July 2005, Roche began airing two 60-second television commercials for Boniva. (Exs.11-13.) The first, titled "Women In Restaurant," features four women of postmenopausal age, sitting in a restaurant discussing osteoporosis medications. (Exs.11-12.) One woman pulls a package of Boniva out of her bag and says: "Check this out." Her friends ask what the package is and she replies: "It's to strengthen my bones." As they pass the package around the table, one woman asks: "Let me see that. Once a month?" Another says: "Oh wow, that's great." The voiceover then states: "Introducing Boniva. A new once monthly prescription treatment for post menopausal osteoporosis. Clinically proven to build and maintain bone density." (*Id.*)

***13** The commercial then cuts to a full-screen image of a monthly desk calendar with four pills lined up next to each other-one for each week in the month-and shows a hand sweeping away all four pills and replacing them with a single one. The parties referred to this as the "sweep-and-replace" visual. (Tr. 744.) While the weekly pills are being swept away and replaced, the first woman responds: "Yeah, with Boniva you can." The voiceover then states: "And unlike treatments you take every week, you only need Boniva once a month." (Ex. 12.) The second commercial, which began airing in September 2005 and is titled "Women Talk Before Taking A Walk," contains similar statements and visuals. (Ex. 13.)

P & G alleges that both commercials convey the message that Boniva offers clinically proven efficacy comparable to that of the two weekly bisphosphonates. Roche contends that the ads convey the message that Boniva has a unique dosing option for patients

and that it is first osteoporosis drug to offer once-monthly convenience. (Tr. 644 (Friend).)

3. Boniva Web Site

Part of Roche's launch of Boniva included Internet promotion and a Web site. The Web page to which P & G objects states *en toto* as follows:

> It is estimated that osteoporosis causes approximately 1.5 million fractures (broken bones) every year in the U.S. Not only can these fractures be painful and disfiguring, they may reduce a person's ability to lead an active life. Osteoporosis affects every bone in the body, but the most common places where fractures occur are the back, hip, and wrists.
>
> Because osteoporosis thins bones, weakening them and making them more susceptible to fractures, it is essential that you talk to your healthcare provider about treatment options upon diagnosis. The disease is particularly serious because you don't see or feel your bones thinning, putting you at increased risk of experiencing a fracture from ordinary activities like bending and lifting or from a more traumatic event like falling. *Hip fractures can be especially traumatic and osteoporosis is responsible for approximately 300,000 of these fractures annually.*
>
> *Fortunately, there are medicines like once-monthly BONIVA available today.* BONIVA has been shown to prevent further bone loss and even increase bone density, lessening your risk of fractures. With BONIVA, you can continue to take care of yourself. As your healthcare provider about treatment and find out if BONIVA is right for you.
>
> (Ex. 14 (highlighting added).)

P & G contends that the last sentence of the second paragraph, taken together with the first sentence of the third paragraph, assert a claim of efficacy at the hip, (Tr. 219 (Pratt)) which Roche has never proved. Roche disagrees, arguing that the text makes two separate statements and that no claim of hip fracture efficacy is made. (Tr. 668 (Friend).)

P & G wrote to the FDA on October 19, 2005, amending its May, 2005 complaint about Roche's false and misleading claim, to include the Boniva Web site, as well as the updated sales aid. (Ex. 115; Tr. 219 (Pratt).) The FDA took no action on P & G's complaint.

4. Boniva Speaker Slide Program

***14** Roche developed a promotional slide kit for Boniva for use by doctors recruited to participate in a promotional speaker program. (Ex. 116 at 2.) The physicians are opinion leaders and Roche compensates them for their speaking. (Tr. 662 (Friend).) Approximately 500 doctors have participated in this speaker's bureau. (Tr. 665 (Friend). One of the slides in the kit refers to a post-hoc, subgroup analysis of patients with low femoral neck BMD. The data led to a discussion of nonvertebral fracture efficacy.

On October 27, 2005, P & G wrote to the FDA and added a new complaint concerning the physicians' promotional material on the ground the material "contain[ed] the false and misleading claim that Boniva has demonstrated efficacy against nonvertebral fracture." (Ex. 116 at 2; Tr. 220 (Pratt).) [FN46] Roche counters that the slides do not contain any claim that Boniva has been proven to reduce nonvertebral fractures. (Tr. 664 (Friend).) Again, the FDA took no action on P & G's complaint.

> FN46. P & G's Complaint cited the slide presentation kit as one of the allegedly offending promotional materials (Compl.¶ 51, Ex. F). P & G makes no mention of the promotional slide kit in its proposed findings of fact and conclusions of law. The Court treats this claim as abandoned, but recognizes that Plaintiffs make the same argument with regard to the sales aid that was introduced in the Spring, 2006 which also deals with the post-hoc, subgroup analysis.

5. Sales Representatives' Detailing

As noted earlier, "detailing" involves visits by company sales representatives to health care professionals. Roche has a sales force comprised of 706 representatives in its primary care division. (Tr. 797 (Klein).) These representatives promote four to five drugs at a time. (*Id.*) In the field, representatives average approximately eight calls a day, or forty calls a week (Tr. 798 (Klein), lasting approximately three to four minutes each. (Tr. 801 (Klein).) Sales representatives report to approximately seventy-five divisional sales managers, who in turn report to seven regional sales directors, who then report to the vice president of

sales. (Tr. 796-97.) Once or twice monthly, divisional managers observe sales representatives in the field at actual visits. (Tr. 711 (Heinig); Tr. 807 (Klein).) Sales representatives are paid, in part, on commission and have a financial incentive to have physicians write more prescriptions for the products they cover. (Tr. 844 (Klein).)

Sales representatives must comply with company regulations regarding how they use promotional materials. (Tr. 634 (Friend).) They are required to use materials as they are generated and cannot modify them, either physically or with regard to content. (Tr. 634-35 (Friend); Tr. 712 (Heinig).) Roche provides extensive training to sales representatives in connection with their promotion of company drugs. (Tr. 711 (Heinig); Tr. 799, 802-04 (Klein).) As part of the training, Roche makes available to sales representatives training "drive time" CD-Roms. (Tr. 799, 838 (Klein); Ex. 215.)

The Roche message, at launch, stressed once-monthly dosage convenience. (Tr. 800 (Klein).) Accordingly, Roche trained Boniva sales representatives to respond to questions, but not initiate discussion, regarding nonvertebral fracture efficacy. (Tr. 799 (Klein).) [FN47] Roche maintains that sales representatives were expressly instructed not to claim that Boniva has proven nonvertebral fracture efficacy (Tr. 804, 806 (Klein)), but rather to refer to the subset analysis results in the BONE article. (Tr. 804 (Klein).)

FN47. During this period, Roche instructed sales representatives, when asked questions about Boniva's nonvertebral fracture efficacy, to provide the physician with a reprint of the BONE article (Tr. 799 (Klein)).

***15** After launch, and as a result of P & G counter detailing, doctors frequently asked Roche sales representatives about Boniva's nonvertebral fracture efficacy. (Tr. 832 (Klein).) In time, Boniva sales began to fail to meet forecasts. (Tr. 832-33 (Klein).) There is no doubt that P & G's aggressive counter-detailing focused on nonvertebral fractures and that the conduct dampened Boniva's sales. (Tr. 833 (Klein).) [FN48] This was entirely consistent with P & G's stated goal of stopping Boniva in its "starting blocs." In September 2005, Roche retrained its sales force to proactively discuss nonvertebral fracture efficacy, but Roche did not put the material into a sales aid. (Tr. 834 (Klein).) [FN49]

FN48. Roche defined "counter-detailing" as speaking to doctors about the negative aspects of competitors' drugs as opposed to positive aspects of their own drugs. (Tr. 718 (Heinig).)

FN49. (*See* Ex. 44 at Bates number Roche_AD_0001231 (noting "need to strengthen [Boniva's] efficacy message and that course correction is underway").)

Having caused a change in Roche's message of convenient dosage, P & G then complained about Roche's response. P & G contends that Roche representatives began to claim in sales calls that Boniva had proven nonvertebral efficacy in September, 2005. (Tr. 220 (Pratt).) Roche denies ever receiving reports of representatives conveying such allegedly unauthorized messages, either from managers or from physicians. (Tr. 807, 816 (Klein).)

P & G points to a CD dated January 10, 2006 as evidence that Roche trained its sales force to communicate a message of Boniva's proven nonvertebral fracture efficacy. In it, the CD instructs the sales force to on how to handle nonvertebral fracture-related concerns. (Ex. 215 at Bates number Roche_FH_0019731 to Roche_FH_0019736.) A scripted response-which goes through key points such as the fact that the study was post-hoc, involved a subgroup, showed no efficacy for the overall population-ends with the following statement: "Dr. does this data answer your questions regarding the proven efficacy of Boniva for nonvertebral fractures?" (Ex. 215 at Bates number Roche_ FH_0019732.) [FN50]

FN50. The training video also states "when you handle [the non-vertebral fracture] issue correctly you are going to find that at the end of the day that this question provides a huge opportunity for you to further establish the efficacy of Boniva and ultimately change customer's prescribing behavior" (Ex. 215 at Bates number Roche_FH_0019731.) Klein admitted that the statement referred to both vertebral and nonvertebral efficacy. (Tr. 821 (Klein).) Similarly, another training video dated August 8, 2005 ends with the question "Dr .... does this data effectively establish for

> you the efficacy of Boniva with non-vertebral fractures?" (Ex. 449 at Bates number Roche_AD_0001928.014).

Sales representatives typically jot down notes of their brief visits, which the industry terms "call notes." (Tr. 808 (Klein).) These notes are recorded on laptops and contain key points of the encounter. (Tr. 808 (Klein).) Call notes help representatives keep track of the content of previous visits. (Tr. 809-10 (Klein).) Most Roche representatives write call notes for the great majority of their calls. (Tr. 810 (Klein).) Roche argues that call notes are "abbreviations" and "shorthand version[s]" (Tr. 846 (Klein)) and that they do not reflect verbatim statements. (Tr. 809, 812, 848 (Klein).)

Of the approximately 25,000 call notes Roche produced in discovery, P & G identified 561 (approximately 2%) that it contends reflect claims of nonvertebral fracture efficacy. (Tr. 849.) Roche's Vice President for Sales, Thomas Klein, admitted that a few of the call notes stated that the representatives "did talk about proven efficacy in so many words of the nonvertebral data." (Tr. 813 (Klein).) Moreover, Klein testified that he followed up with thirteen representatives (again approximately 2% of the sales representatives), who accounted for the majority of calls, and reinforced to them that Roche's authorized message prohibited any claims of proven nonvertebral fracture efficacy. (Tr. 814-15 (Klein) .)

***16** Several sample call notes show what is typical of the 561 notes:

- "Scheduled Boniva lunch inservice with midwife-Maureen Chapmann-detailed Boniva proven reduction in fractures for nv and v [FN51] with 52% risk reduction at year 3-Bone study to further support fracture reduction and increased in BMD at 6 mths, and Mobile study with Bonvia [sic] increased BMD lumbar spine and total hip at year 1-discussed equal efficacy, safety and tolerability-similar GI AE with daily and monthly-reinforced that less frequent once monthly Boniva will adhere better compliance-discussed dosing restrictions and vouchers pt starts, coupons...." (Ex. 60.)

> FN51. "nv" is shorthand for nonvertebral and "v" indicates "vertebral" (Tr. 846 (Klein)).

- "Merck continues to harp on fx data. Used the BONE trial to prove Boniva's efficacy for prevent of hip fxs." (Ex. 61.)

- "Dr. B's birthday today ... going to play cards. Reviewed new pt voucher kits and reminded of convenience of Boniva with proven fracture protection at both vertebral and nonvertebral sites." (Ex. 63.)

Roche contends that its main message to physicians through sales representatives is "efficacy doctors want in a bisphosphonate with the tolerability patients desire in the convenience of a once-monthly tablet." (Tr. 713-14 (Heinig).) Klein, however, confirmed that Roche intended their sales representatives to communicate to doctors a message on nonvertebral fracture efficacy. (Tr. 830 (Klein; Tr. 850 (Klein) (stating "[w]e are drawing the conclusion that in the subset analysis we did show efficacy, yes")); *see also* Tr. 841 (Klein e-mail stating that "[t]he noise the competition is making provides a great opportunity to sell the efficacy of Boniva that is clearly demonstrated in the BONE study, including nonvertebral data"); Ex. 56 (same).)

The Court finds that the call notes support the conclusion that at least some Roche sales representatives made claims of nonvertebral fracture efficacy. But the percentage of such notes is small, and Roche adopted corrective measures with regard to sales representatives who were making these incorrect claims.

6. Current Boniva Sales Aid

In March 2006, Roche deployed a new sales aid, which is currently in use. (Ex. 343; Tr. 659 (Friend).) Roche sent this sales aid to the FDA prior to deployment; but the FDA did not comment. (Tr. 729 (Heinig).) This current sales aid makes no reference to "bisphosphonate efficacy." (Tr. 659 (Friend).) It picks up where the speaker slide kit of October, 2005 left off and refers to post-hoc, subgroup analysis of nonvertebral fractures. (Tr. 659-70 (Friend).) Roche used this material because P & G's continuous counter-detailing was having an impact. Doctors asked about Boniva's nonvertebral fracture data during Roche's detailing (Tr. 660 (Friend)); and Roche wanted to respond.

P & G renews here its earlier complaint to the FDA (*see* Ex. 116, P & G letter to FDA of October 27, 2005) that the sales aid makes literal and implied

claims of nonvertebral fracture efficacy in high-risk patients. (Tr. 222 (Pratt).) The currently-used, twelve-page Boniva sales aid contains the following statements:

***17** • "Boniva provides proven fracture protection and dosing that more patients prefer" (Ex. 343 at 1);

• "Boniva is proven to reduce fracture risk [header]: Significantly reduces vertebral fracture risk" (*id.* at 2); and

• "Only Boniva-demonstrated fracture risk reduction with an extended dosing interval in a pivotal fracture trial. (header) Significantly reduces vertebral fracture risk" (*id.* at 3).

• Boniva demonstrates fracture risk reduction in younger women. (Header) New vertebral fracture risk reduction for younger postmenopausal women. (*Id.* at 4).

On the fifth page of the sales aid, the following information appears:

Boniva provides nonvertebral fracture protection in high risk patients [FN52]

FN52. This statement is a header that is positioned at the top of the page in a larger font than the remainder of the page. Unlike the first four pages which use the words "proven" (p. 1 and 2) and "demonstrated" (p. 3 and 4), the fifth page uses a different word: "provides."

69% reduction in nonvertebral fracture risk (post hoc analysis) [FN53]

FN53. This statement is the header to a graph showing a placebo graph rising rapidly over time and a Boniva graph generally flat, leading to a large arrow pointing downwards with the statement 69% decrease.

Subpopulation [intent-to-treat] analysis of postmenopausal women with baseline femoral neck T-score <-3.0, Boniva 2.5 mg (n=123) vs placebo (n=124).

• In the overall BONE study population, the effect of Boniva on nonvertebral fractures was similar to that of placebo

• The mean baseline femoral neck BMD T-score was -2 for the overall study population, indicating lower risk for nonvertebral fractures

• In a post hoc analysis of 375 patients with baseline femoral neck BMD T-score <-3, indicating a higher risk for nonvertebral fracture, Boniva 2.5 mg daily significantly reduced the risk of nonvertebral fractures

(Ex. 343 at 5.) P & G's experts and lawyers concede that the bulleted information is literally true (*See e.g.*, Tr. 248-49 (Pratt)). Nonetheless, P & G asserts that the statement "Boniva provides nonvertebral fracture protection in high-risk patients" in conjunction with the chart makes a false efficacy claim regarding nonvertebral fracture protection that is inconsistent with the indications and usage section of Boniva's FDA-approved label. (Tr. 281 (Pratt).)

It is significant that the fifth page does not use the word "proven" or "demonstrated." Roche maintains that the sales aid does not claim anything is "proven" with regard to nonvertebral fractures. (*See* Tr. 661 (Friend). Dr. Friend testified that to be "shown" or "demonstrated" is not equivalent with being "proven" (Tr. 670 (Friend)), and that the sales aid merely states that it "provides" nonvertebral fracture protection to high-risk patients. (Tr. 671 (Friend)). Dr. Friend conceded, however, that the statement "Boniva provides proven fracture protection and dosing that more patients prefer" (Ex. 343 at 1) would be more accurate if it stated "proven vertebral fracture" instead. (Tr. 706 (Friend).)

C. P & G's Anticipation of and Response to Boniva's Launch

P & G anticipated that Boniva would present formidable competition for osteoporosis prescriptions in advance of Boniva's launch. (Tr. 257 (Pratt); Ex. 168 at Bates number P & G B0001453 (stating that "Boniva [would be] a serious threat for [Actonel's] business" and that P & G had to "keep them in the starting blocks").) [FN54] P & G company documents indicate that Actonel could lose up to a ten-point share within eighteen months of Boniva entering the market. (Ex. 168 at Bates number P & G B0001453.) During

the period prior to and concurrent with Boniva's launch, P & G company officials reasoned that distinguishing the nonvertebral efficacy of Boniva and Actonel would be critical to Actonel's retaining its market share in the market in light of Boniva's dosing advantage. (Tr. 258-60, 261-62 (Pratt); Ex. 145.).[FN55]

FN54. *See also* Ex. 146 at Bates number P & G B0000036 (mid-level P & G leadership team powerpoint presentation indicating "Boniva threat and the need for a crisis mentality'), P & G B0000037 ("US Actonel-Crisis Time!"), P & G B0000044 (noting approach necessary when in "crisis mode"); Ex. 147 at Bates number P & G A0001454 (noting new crisis focus and mentality).

FN55. *See also* Ex. 168 at Bates number P & G B0001454 (Actonel Plan of Action-April to September 2005, stating "[p]osition Actonel as a superior Bisphosphonate vs. Boniva: WE MUST WIN THE EFFICACY MESSAGE WITH NON-VERT DATA!!").

***18** During the latter part of 2005, P & G retained the survey firm of Compass to evaluate physician recall and perceptions. (Tr. 275 (Pratt).) Compass conducted a telephone survey, which indicated that physicians did not perceive fracture efficacy differences between Actonel and Boniva and did not perceive differences in the published data. (Ex. 181, p. 8-9, Tr. 285, 286 (Pratt).) In fact, the Compass study indicated that 52% of the physicians surveyed rated Boniva equal to or better than Actonel on nonvertebral fracture efficacy. (Tr. 286 (Pratt).)

The Compass survey confirmed what P & G already knew; and accordingly, P & G invigorated its campaign to convince physicians that Boniva had been not proven effective in nonvertebral fracture efficacy. In fact, P & G (such as planning presentations and sales-related training materials) alternately articulated the marketing message to be that "Boniva was proven ineffective," or that "Boniva was not proven effective." (*See e.g.*, (Ex. 147 at Bates number P & G A0001454).) [FN56] P & G now maintains-notwithstanding statements and comments contained in internal company documents generated during the planning phase-that P & G achieved lingual clarity, and never communicated any "proven ineffectiveness" claims regarding Boniva in professional or consumer promotional materials. (Tr. 245 (Pratt).)

FN56. *See, e.g.*, Ex. 147 at Bates number P & G A0001459 (October 11, 2005 company document stating that among P & G strategies would be to "[c]onvince professionals that Boniva is a third line therapy based on the proven lack of effect on non-vertebral efficacy")); Ex. 151 (January 6, 2006 internal P & G email from Pratt to Actonel Brand Manager, stating that overall defense message would remain "Boniva ... is an inappropriate first-line agent due to its proven lack of non-vertebral fracture efficacy"); Ex. 201 (November 1, 2001 P & G internal document indicating that the company's overall strategy would be to share data that "prove Boniva's ineffectiveness" related to nonvertebral fracture efficacy); Ex. 207 at Bates number P & G B0019211 (January 4, 2006 presentation by P & G public relations firm; referencing "Boniva has been proven to have no effect"); Ex. 210 (December 1, 2005 internal P & G e-mail; Actonel brand manger references "proven lack of non-vertebral fracture efficacy for Boniva"); Ex. 231 at Bates number P & G F0209509 (sales aid training video referencing Bonivas's proven lack of effect on non-vertebral fractures").

P & G contends that it delivered the following message that "Boniva is not proven to reduce the risk of non-vertebral fractures" and that "[i]n its 3-year clinical trial, Boniva *failed* to reduce the risk of non-vertebral fractures." (Ex. 201 at Bates number P & G B0002488 (stating key messages in P & G defense against Boniva).) This ad campaign was accompanied by a graphic of a skeleton which disintegrated, vividly demonstrating P & G's argument that there was nothing to Boniva's claim. At the hearing, P & G witnesses conceded that the BONE trial data does not prove Boniva is ineffective at reducing nonvertebral risks and any such statements would be false. (Tr. 102-105 (Bilezikian).) It is also clear that P & G's three letters of May and October 2005 are part of this campaign to keep Boniva in "the starting blocks." The same may be said of this litigation.

1. P & G Sales Aids

In mid to late November, 2005, P & G deployed new selling tool titled the BONE/VERT-NA Sales

Aid. (Tr. 230 (Pratt).) This sales aid stated: "Boniva is not proven to reduce the risk of nonvertebral fractures-In its pivotal 3-year clinical trial, Boniva failed to reduce the risk of nonvertebral fractures." (Ex. 229 at Bates numbers P & G A0004336, P & G A0004342; *see also* Tr. 231, 232 (Pratt).)

P & G also developed a training video to accompany the November 2005 sales aid. The video script contained the following negative comments on Boniva:

• "We will convince d.s. [sic] that Boniva is a suboptimal therapy based on the proven lack of effect on non-vertebral fractures" (Ex. 231 at Bates number P & G F0209509);

***19** • "Unlike Actonel, Boniva failed to reduce nonvertebral fractures. Actonel is clinically proven to prevent nonvertebral fractures" (*id.* & *id.* at Bates number P & G F0209510);

• "The back page of the sales aid shows simply put, Boniva failed to reduce the risk of nonvertebral fractures. In fact, Boniva was no different than placebo" (*id.* at Bates number P & G F0209510);

• "Bottom line, Boniva failed to reduce the risk of nonvertebral fractures" (*id.* at Bates number P & G F0209513); and,

• "Your primary selling message is 'nonvertebral' fracture protection. Convince physicians that Boniva is an inadequate therapy based on the proven lack of effect on non-vertebral fractures." (*Id.* at Bates number P & G F0209516.)

P & G deployed the training video to the sales force in November 2005. (Tr. 269 (Pratt).)

P & G implemented a new sales aid in April 2006. (Tr. 241 (Pratt); Ex. 232.) This promotional material states: "Boniva is not proven to reduce the risk of nonvertebral fractures-In its pivotal 3-year clinical trial, Boniva failed to reduce the risk of nonvertebral fractures." (Ex. 232 at Bates number P & G A0013093 & P & G A0013097.)

2. P & G Counter-Detailing

Roche argues that in November 2005, P & G instructed its sales force to tell physicians that Boniva has been proven not to reduce the risk of nonvertebral fractures. P & G denies this allegation (Tr. 243 (Pratt)). Roche further alleges that P & G instructed its sales force to tell physicians that Boniva causes fractures and that prescribing Boniva can lead to malpractice liability. P & G denies these allegations these as well. (Tr. 243-44 (Pratt).) Notwithstanding its denials, there may have been some basis to Roche's allegations. On May 11, 2006, P & G sent an e-mail to its sales force instructing representatives that, while they could state that "Boniva did not reduce the risk of nonvertebral fractures in its pivotal 3-year clinical trial" (Ex. 150), they could not state that "Boniva is *proven not to work* beyond the spine, or *proven not to work* against nonvertebral fracture." (Ex. 150.) The email further instructed the sales representatives that they could not claim that "Boniva *causes* fractures (nonvertebral or vertebral)" or that doctors might be liable for malpractice by prescribing Boniva. (Ex. 150.)

3. P & G Print Ads

On January 6, 2006, P & G ran a full-page advertisement in the *New York Times*, which the company titled the "Seven Reasons" ad. The ad states as follows:

> Actonel is clinically proven to help protect many bones where a woman is most vulnerable to fractures caused by osteoporosis: the spine and a combination of wrist, hip, collarbone, upper arm, leg and pelvis.
>
> What about the new osteoporosis medicine, Boniva? *Boniva is not proven to prevent fractures beyond the spine.*
>
> (Ex. 457.)

4. P & G's Proposed TV Ad and FDA's Rejection of the Ad

***20** On February 14, 2006, P & G submitted a proposed TV ad comparing Actonel to Boniva, entitled "One Good Reason," to the FDA for its review and comment. The proposed ad touted Actonel's efficacy "at a combination of leg, collarbone, pelvis, wrist, upper arm and hip." When asked about Boniva, the TV doctor replies: "Boniva has not been proven to prevent fractures beyond the spine." The TV postmenopausal osteoporotic woman exclaims: "Wow, I'll

stick with Actonel."

The FDA found the ad misleading. While the FDA acknowledged that Actonel was effective at a composite end point of wrist, humerus, hip, pelvis, leg and clavicle, it observed: "... none of the data from the individual fracture sites supports an Actonel non-spinal fracture claim for each/any skeletal site ... Rather ... Actonel failed to reduce fractures better than placebo at leg and hip and was in fact worse than placebo at collarbone."

As to the claims that Actonel was better than Boniva, the FDA stated "The proposed TV ad misleadingly suggests that Actonel is superior to Boniva, when such has not been demonstrated by substantial evidence. The totality of the comparative presentation suggests that Actonel will reduce the non-spinal fracture risk for the individual skeletal sites ... in comparison to (or better than) Boniva. However, the TV ads claim favoring Actonel's non-spinal fracture benefit versus Boniva is not adequately supported simply by comparing" Actonel's label (where there is an indication of efficacy at a composite non-vertebral site) with Boniva's label (where Boniva is effective only at a vertebral site). Actonel is not superior to Boniva and it is false and misleading for P & G to claim that it is.

The FDA sent this document to P & G on May 4, 2006, but P & G did not produce it until after the Memorial Day holiday break in the hearing. Furthermore, the document was withheld from two key witnesses for P & G, Pratt and Grauer, allowing them to testify without knowledge that the FDA had questioned, in effect, the entire basic premise of P & G's argument to the Court. The FDA's letter sheds new light on Roche's claim of class efficacy, and would appear to punch holes in P & G's argument that, given its indication of efficacy at a composite end point, it is somehow superior to Roche's Boniva. Significantly, given all of the testimony and arguments about hip fractures, the FDA stated that Actonel is no better at the hip than a placebo, according to P & G's own test data.

D. Actonel and Boniva Market Share

Since the launch of Boniva in April 2005, Actonel's overall share in the osteoporosis market has declined. (Tr. 206 (Pratt).) [FN57] P & G expected a decline in Actonel's market share following Boniva's launch, but the extent of the decline exceeded their expectations. (Tr. 224-28 (Pratt).) Currently, Actonel enjoys 25% of the overall osteoporosis market and 33% of the bisphosphonate market. (Tr. 206, 254 (Pratt).) In the bisphosphonate market, Fosomax commands the greatest market share (*i.e.*, 50%) (Ex. 168 at Bates number P & G B0001453), followed by Actonel, and then by Boniva. (Tr. 255 (Pratt) .) P & G estimates that Boniva's share the osteoporosis market to be less than 10% and in the range of 5% to 8% (Tr. 253 (Pratt)). Boniva's standing in the overall osteoporosis market is third or fourth. (Tr. 255 (Pratt).) With regard to Boniva's performance in the market, Boniva has been meeting or slightly exceeding expectations. (Tr. 717 (Heinig).) Roche considers Fosomax and Actonel to be Boniva's most direct competitors; since Fosomax was the first bisphosphonate to gain FDA-approval for sale and marketing but is becoming generic in 2008, Roche places Fosomax as the current leading competitor and Actonel as the long-term competitor. (Tr. 727, 739 (Heinig).)

> FN57. More particularly, following Boniva's launch, P & G experienced a decline in the growth of sales of Actonel and a steep drop in Actonel's new brand starts (from 31% prior to Boniva's introduction to 24.5% to 24% following the launch) (Tr. 224 (Pratt); Ex. 231 at Bates number P & G F0209507). With regard to P & G's forecast for Actonel, the brand is not meeting its forecast for the 2005-2006 fiscal year with regard to market share, prescriptions, or sales (Tr. 228 (Pratt)). While market share may have dropped, P & G studiously avoided presenting data on the entire size of the market, which may very well have expanded because of the combined advertising dollars expended by all of the drug companies more postmenopausal women may now be aware of the disease of osteoporosis, and the ready availability of possible drug treatment. While market share may have been lost, there is any evidence that there was a drop in revenue.

***21** None of this market share data is converted into annual revenues. No data is presented on overall market size. It may be that the market for osteoporotic drugs is expanding so that loss of share would not result in the loss of revenues. On this record, it is difficult to discern whether P & G has experienced

actual financial harm.

E. P & G's Consumer and Physician Surveys

P & G commissioned RL Associates, a market research and statistics firm, to conduct a survey of consumer perception of the two television ads Roche aired; and a survey of physician perception of Roches's sales aid. (Ex. 85; Tr. 288-340 (Rappeport).) RL Associates examined whether Roche's advertising and promotional materials conveyed to consumers and doctors, first, that Boniva had nonvertebral efficacy and, second, that clinical evidence supported that claim. (Tr. 292 (Rappeport).) Dr. Michael Rappeport, the managing partner and president of RL Associates and the principal involved in conducting the surveys, testified at the evidentiary hearing regarding the surveys. (Tr. 287-88.) The physician survey involved a telephone survey of sixty-three doctors. (Ex. 86 at 1.) In sum, Dr. Rappeport testified that the results of the two surveys showed "overwhelming evidence that Roche ... succeeded in persuading both consumers and ... physicians that [Boniva] is good for all kinds of fractures." (Tr. 349 (Rappeport, Ex. 85).) [FN58]

FN58. In particular, the RL Associates report concludes:

> We believe this data makes very clear that very large fractions of both the potential consuming public, and of potentially prescribing doctors, perceive the TV commercials and the primary sales aid to be saying that Boniva is efficacious for at least some non-vertebral fractures, and has been proven so by clinical tests.
>
> (Ex. 85 at 16.)

Roche attacked the reports as inadmissible because they are unscientific and unworthy of belief.

EVIDENTIARY ISSUES

I. Call Notes

Roche does not dispute that the call notes are admissible as business records pursuant to Federal Rule of Evidence. (July 13, 2006 Oral Argument Tr. at 87; *see also* Fed.R.Evid. 803(6).) The call notes are admissible evidence. *Zeneca Inc. v. Eli Lilly & Co.*, No. 99 Civ. 1452(JGK), 1999 WL 509471, at *2 (S.D.N.Y. July 19, 1999). The real question is the weight to be assigned to the offending call notes, given the very small percentage of incorrect claims, the concentration of incorrect claims among a small group of sales representatives, and the corrective counselling given by Roche to those sales personnel.

II. The Admissibility and Sufficiency of the Consumer and Physician Surveys

Consistent with Federal Rule of Evidence 703,[FN59] survey evidence may be admissible, when the survey is "properly designed, executed, and described." Shari Seidman Diamond, *Reference Guide on Survey Research, in* Federal Judicial Center, Reference Manual on Scientific America 231-32 (2d ed.2000) [hereinafter Diamond, *Reference Guide on Survey Research*]. In order for a survey to be admissible, it must be "conducted in accordance with generally accepted survey principles" and the "results [must be] used in a statistically correct way." *Id.* at 233-34. Thus, the "content and execution of a survey must be scrutinized." *Id.* at 237. For the reasons outlined below, the Court concludes that neither the consumer survey, nor the physician survey were conducted in accordance with generally accepted survey principles. In fact, both surveys suffer from a fatal combination of flaws that render them unreliable and inadmissible. *See Winning Ways, Inc. v. Holloway Sportswear, Inc.*, 913 F.Supp. 1454, 1470 (D.Kan.1996) (holding that, combined, the flaws rendered the surveys inadmissible).[FN60]

FN59. Federal Rule of Evidence 703 concerning "Bases of Opinion Testimony by Experts" states as follows:

> The facts or data in the particular case upon which an expert bases an opinion or inference may be those perceived by or made known to the expert at or before the hearing. If of a type reasonably relied upon by experts in the particular field in forming opinions or inferences upon the subject, the facts or data need not be admissible in evidence in order for the opinion or inference to be admitted....

FN60. The consumer survey and the physician survey each present a host of concerns that, in combination, render them inadmissi-

ble. Rather than address each and every one, the Court focuses on the most serious issues.

A. Consumer Surveys

***22** The consumer survey purported to examine consumer perception of Roche's two television ads. RL Associates retained an independent firm to collect data and this firm interviewed 416 individuals at sixteen malls throughout the United States. (Ex. 85 at 1, 5.) [FN61] All consumer interviews were conducted in December, 2005. (Tr. 380 (Rappeport); Ex. 85 at 5.) The consumer survey had several significant inadequacies.

FN61. RL Associates deemed the interviews conducted at one site unreliable and based the consumer survey results on interviews conducted at the remaining 15 sites. (Ex. 85 at 5.)

1. Closed-Ended Questions

The survey consisted of fourteen questions, and one follow up question for the interviewer. (Ex. 85, App. A at 2-3.) The first five questions were open-ended [FN62] and asked the following: (1) What is the main message or messages of this commercial? Please be as specific as possible. (2) Anything else? (3) As far as you can tell from the commercial, what is Boniva useful for? (4) Based on the commercial, what if any, are the advantages of Boniva? (5) Based on the commercial, what if any, are the disadvantages of Boniva? The opened-ended questions were followed by two closed-ended questions. The closed-ended questions came out of the blue, and raised the hypothesized questions which are at the heart of P & G's claim here:

FN62. Open-ended questions "require[ ] the respondent to formulate his or her own response." Diamond, *Reference Guide on Survey Research*, at 274.

6. If you recall, the commercial shows a calendar with four pills on it, one for each week. A hand removes the four pills and replaces them with one Boniva pill. Do you think the commercial says or implies that:

1. Compared to the four pills, Boniva reduces the risk of fractures in as many bones as the four pills?

2. Compared to the four pills, Boniva reduces the risk of fractures only in some of the bones and not in all of the bones where the four pills reduce the risk of fractures?

[If respondents answered that Boniva reduces the risks of fractures in as many types of bones, they were asked question 7.]

7. Based on the commercial, which of the following statements do you think is true?

1. There are clinical tests that have shown Boniva reduces the risk of fractures in as many types of bones as the four pills.

2. There are not clinical tests that have shown that Boniva reduces the risk of fractures in as many types of bones as the four pills.

The responses to open-ended questions indicated that the main messages of the Roche ads were once-a-month convenience, the prevention of bone loss, and that people should consult their doctors. (Ex. 89 at 17.) These open-ended questions did not generate any responses related to the implied messages hypothesized by P & G regarding nonvertebral fractures or class effect. (Ex. 89 at 10.) RL Associates did not bother analyzing the responses to the open-ended questions. (Ex. 89 at 9; Tr. 433 (Wind).) Instead, it relied exclusively on the responses to the closed-ended questions to formulate its conclusion.

The open-ended format is well suited to surveys focusing on a simple and/or primary claims made in ads. *In re Stouffer Foods Corp.*, 118 F.T.C. at 808. "On the other hand, open-ended questions are likely to understate secondary claims, particularly where ... those claims are also rather complex by virtue of being both compound and comparative." *Id.* n. 28 Thus, it was not inappropriate for RL Associates to formulate proper, closed-ended questions in order to assess whether Roche's TV ads communicated the messages P & G complains of, *i.e.*, messages that concern secondary, complex, and implicitly comparative claims.

2. Order Bias

***23** But closed-ended questions, however helpful,[FN63] can be leading and suggestive and require

incorporation of several well-established mechanisms to minimize bias. *Id.* at 806. For example, the questions ought to be rotated. *In re Stouffer Foods Corp.*, 118 F .T.C. at *806; *see also* Tr. 433, 468 (Wind). RL Associates failed to rotate the subparts in closed-ended questions 6 and 7, and that very likely contributed to biased and unreliable responses.[FN64] *Rust Env't & Infrastructure, Inc. v. Teunissen*, 131 F.3d 1210, 1218 (7th Cir.1997) (affirming district court rejection of a survey that failed to incorporate random rotation of questionnaire options).

FN63. For example, Roche's expert on market research, Dr. Wind, testified that he uses closed-ended questions but incorporates them into questionnaires with great care. (Tr. 479 (Wind).)

FN64. Dr. Rappeport conceded that some authorities instruct that questions should be rotated to reduce "order bias" and that he believes in some circumstances that rotation should be incorporated, particularly with questionnaires involving six or seven categories. (Tr. 383 (Rappeport).) Nevertheless, Dr. Rappeport contended that handing a respondent a card with two potential answers mitigates against order bias. (Tr. 342 (Rappeport).) Dr. Rappeport further claimed not to be acquainted with the term "primacy effect." (Tr. 385 (Rappeport).) Given the wide usage of this term, *see* Diamond, *Reference Manual on Scientific Evidence*, at 274 (defining "primacy effect" as "[a] tendency of respondents to choose early items from a list of choices" and the "opposite of a recency effect"), the Court finds Dr. Rappeport's answer not credible.

3. Lack of Funneling or Control Questions

Other forms of bias involving closed-ended questions include "yea saying," "which is the tendency to give the answer the participant believes the interviewer is seeking." *In re Stouffer Foods Corp.*, 118 F.T.C. at 806. The questions here are very suggestive of the desired answers. This effect can be mitigated through the use of a control question. *Id.* at 808 ("The [Federal Trade] Commission has long recognized that a control of some kind is necessary for closed-ended questions and that ... there is a potential for yea-saying inherent in the closed-ended question format."). Control questions offer a "don't know" or "no opinion" type of option, as part of a set of response alternatives to a closed-ended question. Diamond, *Reference Guide on Survey Research*, at 275. Such questions screen out respondents who may truly not have an opinion on the issue under investigation and minimizes guessing. *Id.* RL Associates neglected to include any "funnel," "full-filter" questions, [FN65] or "quasi-filter questions."

FN65. A filter question screens out those respondents who do not have an opinion on the issue under investigation before asking the question proper. Diamond, *Reference Guide on Survey Research*, at 273. In addition, funnel questions usually follow open-ended questions and precede closed-ended questions. (Tr. 432 (Wind).)

4. Leading / Suggestive Closed-Ended Questions

"A survey is not credible if it relies on leading questions which are 'inherently suggestive and invite guessing by those who did not get any clear message at all." *Johnson & Johnson-Merck Consumer Pharms. Co. v. Rhone-Poulenc Rorer Pharms., Inc.*, 19 F.3d 125, 134 (1994) (citation omitted). What the women surveyed in the malls knew about fracture reduction and clinical testing is, in all likelihood, limited. Certainly, the challenged TV ads said nothing about either topic. Accordingly, the survey should have provided respondents with all possible options to any question (including the options of "neither" or "don't know"). (Tr. 432, 471 (Wind).) The reliability of the answers elicited by the closed-ended questions is undermined by the survey failure to inform respondents that they could also respond in this way. *See Coors Brewing Co. v. Anheuser-Busch Cos.*, 802 F.Supp. at 972 (citing *Home Box Office v. Showtime/The Movie Channel*, 665 F.Supp. 1079, 1084 (S.D .N.Y.), *aff'd in part and vac'd in part*, 832 F.2d 1311 (2d Cir.1987)).[FN66]

FN66. The *Reference Guide on Survey Research* states:

> Closed-ended questions have some additional potential weaknesses that arise if the choices are not constructed properly. If the respondent is asked to choose one response among several choices, the response chosen will be meaningful only if the list of choices is exhaustive, that is, if the choices

> cover all possible answers a respondent might give to the question. If the list of possible choices is incomplete, a respondent may be forced to choose one that does not express his or her opinion. Moreover, if respondents are told explicitly that they are not limited to the choices presented, most respondents nevertheless will select an answer from among the listed ones.
>
> Diamond, *Reference Guide on Survey Research*, at 253; *see also id.* at 250 (providing additional explanation of the importance of including "no opinion" and/or "don't know" options).

There is no doubt that the closed-ended questions were leading and suggestive, (Tr. 429 (Wind).), and the RL survey gave the respondents no options whatsoever.

5. Inappropriate Control

***24** A survey's control attempts to address in part the possible biasing effect of the questioning and a respondent's prior beliefs. (Tr. 434 (Wind).) [FN67] In Lanham Act cases, courts accept as a measure of the message conveyed the difference between the results obtained in the test and the control. (Tr. 461 (Wind).) The control may simply purge the allegedly deceptive material from the ad. Diamond, *Reference Guide on Survey Research*, at 257; *see also* Exs. 365, 366, 376. Rather than eliminating the questionable material from the ads, a method P & G's expert conceded would be appropriate, RL Associates chose a prominent disclaimer at the beginning of the ads as its control. [FN68] The disclaimer was suggestive and implanted responses to closed-ended questions, which Dr. Rappeport conceded as a possibility. (Tr. 399 (Rappeport).). Defendants' expert, Dr. Wind, called the disclaimer "very powerful." (Tr. 437 (Wind).)

> FN67. Controls for surveys in Lanham Act cases are described as follows:
>
> > By adding an appropriate control group, the survey expert can test directly the influence of the stimulus [or complained of message]. In the simplest version of a survey experiment, respondents are assigned randomly to one of two conditions. For example, respondents assigned to the experimental condition view an allegedly deceptive commercial, and respondents assigned to the control condition either view a commercial that does not contain the allegedly deceptive material or do not view any commercial. Respondents in both the experimental and control groups answer the same set of questions. The effect of the allegedly deceptive message is evaluated by comparing the responses made by the experimental group members with those of the control group members....Both preexisting beliefs and other background noise should have produced similar response levels in the experimental and control groups.
> >
> > Diamond, *Reference Guide on Survey Research*, at 257.
>
> FN68. The control groups in the RL Associate study were shown the test commercial with an additional statement at the beginning of the commercial, which appeared on the screen and was read by the announcer. The statement said: "Unlike other osteoporosis drugs, the advertised drug you are about to see in this commercial has only been shown to reduce fractures of the spine and has not been shown to reduce fractures of other bones such as the hip or wrist." (Ex. 89 at 11.) Obviously, RL Associates did not know that Actonel was not effective at the hip either.

6. Inadequate Data Collection

In addition to these structural and design inadequacies, the RL Associates surveys had serious data collection flaws. These failures include (among other concerns): the failure to collect nonresponse information in accordance with generally accepted market survey principles (Tr. 357 (Rappeport); Tr. 422 (Wind)); [FN69] the destruction of signed interviewer instruction sheets and pages of the original interview forms (Tr. 421-22 (Wind)); flawed interviewer and screening instructions, including the omission of appropriate and inappropriate topics while escorting respondents to the interviewing site (Tr. 422 (Wind)); the failure to comply with a myriad of instructions provided to site supervisors (Tr. 366-69 (Wind)); the failure to address differences in handwriting (Tr. 421

(Wind) (problems included the same handwriting under different interviewers' names and different handwriting under the same interviewer's name)); and, the inclusion of unqualified interviewers. (Tr. 457 (Wind) (three to four of the interviewers were fifteen to seventeen years of age).) [FN70]

FN69. The *Reference Manual on Scientific Evidence* states that a survey report should provide in detail: "a description of the results of sample implementation, including (a) the number of potential respondents contacted, (b) the number not reached, (c) the number of refusals, (d) the number of incomplete interviews or terminations, (e) the number of noneligibles, and (f) the number of completed interviews." Diamond, *Reference Guide on Survey Research*, at 270; *see also* Ex. 187 (Council of American Survey Research Organizations, Code of Standards and Ethics for Survey Research 11 (1997-2004) (same)).

FN70. The Court did not conclude that a criminal background rendered an interviewer *per se* unqualified. Both Dr. Rappeport and Dr. Wind testified that, prior to this case, in their experience, litigants had never raised the criminal background history of interviewers as a concern. (Tr. 381 (Rappeport); Tr. 358, 456, 459 (Wind).)

These flaws in combination with the earlier described methodological deficiencies are fatal to the admissibility of the consumer survey.

B. Physician Survey

RL Associates also conducted a telephone survey of physicians' perceptions to the sales aid; and reported the results in January 2006. (Ex. 85.) To date, Roche has deployed three Boniva sales aids: the first in April 2005 in connection with Boniva's commercial launch, the second in October 2005 (Ex. 342), and the third in March 2006. (Ex. 343.) As noted previously, Roche is currently using the March 2006 revised sales aid. (Ex. 343; Tr. 659 (Friend).) Thus, the survey does not study the sales aid currently in use. As a result, the physician survey, which focused an earlier version of the sales aid, is completely irrelevant to the sales aid currently in use, as P & G's expert conceded. (Tr. 353 (Rappeport).) [FN71] *See* *American Home Prods. v. Proctor & Gamble Co.*, 871 F.Supp. 739, 750 (D.N.J.1994) (consumer surveys must test precisely the contested promotional materials). This is far from the only shortcoming with the survey.

FN71. Dr. Rappeport testified that so long as a sales aid had been "changed in some respect" the physician survey would have no applicability whatsoever. (Tr. 353 (Rappeport).)

1. No Control

***25** First, the physician survey lacked any control. Dr. Rappeport maintained that a control group is unnecessary for sophisticated respondents like doctors, who are unlikely to "guess" (Tr. 346, 404 (Rappeport)). This is a marked departure from generally accepted market research practices. (Tr. 447 (Wind).) *ConAgra, Inc. v. George A. Hormel & Co.*, 784 F.Supp. 700, 728 (D.Neb.1992) ("Since no control was used, the ... study, standing alone, must be significantly discounted."), *aff'd*, 990 F.2d 368 (8th Cir.1993).

2. Probing

Second, the physician telephone survey suffered from extensive and inappropriate probing. (Ex. 218.) [FN72] The Court accepts Dr. Wind's testimony that the verbatim responses from the physicians indicate improper probing in forty-two out of sixty-three cases. (Tr. 441 (Wind).) Wind further maintains that the probing indicates a suggestive implanting with regard to fractures. (Tr. 487 (Wind).) The Court examined the verbatim responses from the sixty-three respondents (Ex. 218) and found numerous instances of probable probing.[FN73] Obvious examples of probing included the following:

FN72. With regard to probing the *Reference Guide on Survey Research* states as follows:

> When questions allow respondents to express their opinions in their own words, some of the respondents may give ambiguous or incomplete answers. In such instances, interviewers may be instructed to record any answer that the respondent gives and move on to the next question, or they maybe instructed to probe to obtain a more complete response or clarify the meaning of the ambiguous response. In

> either situation, interviewers should record verbatim both what the respondent says and what the interviewer says in the attempt to get clarification. Failure to record every part of the exchange in the order in which it occurs raises questions about the reliability of the survey, because neither the court nor the opposing party can evaluate whether the probe affected the views expressed by the respondent.
>
> Diamond, *Reference Guide on Survey Research*, at 253.

FN73. The Court finds that the following examples suggest probing: Ex. 218 at Bates number P0001258 (11-Q5 ("Fractures are directly related in post menopausal women to trauma and osteoporosis. No, I don't recall anything else."); 31-Q5 ("There's a bullet point that says that higher BMD at all skeletal sites. Nothing else."); Bates number P001266 (99999-Q3 ("Spinal, I don't remember if it's anything about hips. But it is for vertebral fractures. It reduces the fractures of the neck and the lumbar spine. No, nothing else.").

• "Vertebral. I can't remember." (Ex. 218 at Bates number P0001263 (565-Q3)); and

• "More of the compression fractures of the vertebrae and hip fractures. Nothing." (Ex. 218 at Bates number P0001266 (1024-Q3).

The unauthorized probing calls into the question the reliability of the responses generated in the physician telephone survey.

3. Sample Size

The sample size of the telephone physician survey involved only sixty-three respondents. Dr. Rappeport said the primary reason for the small sample size was economic. (Tr. 347 (Rappeport)). This claim of economy is completely out of character with P & G's spending to beat Boniva in the marketplace, to say nothing of the costs of this litigation. In any event, the sample size here is too small to be reliable. (Ex. 89 at 21.)

These reasons, plus others, are more than sufficient to determine that the physician survey results are inadmissible.[FN74]

FN74. Additional grounds for deeming the telephone survey results of physician perceptions inadmissible include: relying on suggestive and leading questions; failing to ask open-ended questions; biased context; inappropriate sample selection; and misleading analysis. (Ex. 89 at 6.)

CONCLUSIONS OF LAW

I. Preliminary Injunction Standard

In a Lanham Act action:

> The burden is upon the party seeking preliminary relief from the district court to show not only that it is likely to suffer irreparable injury if relief is denied but also that there is either (1) a likelihood of success on the merits or (2) sufficiently serious questions going to the merits to make them a fair ground for litigation, with a balance of hardships tipping decidedly in the plaintiff's favor.

Procter & Gamble Co. v. Chesebrough-Pond's Inc., 747 F.2d 114, 118 (2d Cir.1984) (citing *Coca-Cola v. Tropicana Prods., Inc.*, 690 F.2d 312, 315 (2d Cir.1982).

II. Overview of Lanham Act

"Section 43(a) of the Lanham Act proscribes ... false or misleading descriptions of fact in connection with any goods in commerce that are likely to cause confusion or that misrepresent the nature, characteristics, qualities, or geographic origin of the goods." *S.C. Johnson & Son, Inc. v. Clorox Co.*, 241 F.3d 232, 238 (2d Cir.2001) (citation omitted).[FN75FN76] "To obtain permanent injunctive relief against a false or misleading advertising claim pursuant to section 43(a), a plaintiff must demonstrate by a preponderance of the evidence that an advertisement is either literally false or that the advertisement, though literally true, is likely to mislead and confuse consumers." *McNeil-P.C.C., Inc. v. Bristol-Myers Squibb Co.*, 938 F.2d 1544, 1548-49 (2d Cir.1991) (citation omitted); *see also* *S.C. Johnson & Son, Inc. v. Clorox Co.*, 241 F.3d at 238 (same). Section 43(a) requires a showing of materiality-that is, "the plaintiff must also show that

the defendants misrepresented an inherent quality or characteristic of the product." *S.C. Johnson & Son, Inc. v. Clorox Co.*, 241 F.3d at 238 (citation omitted). Several additional principles are applicable.

> FN75. Section 43(a) of the Lanham Act states:
>
> > (1) Any person who, on or in connection with any goods or services, or any container for goods, uses in commerce any word, term, name, symbol, or device, or any combination thereof, or any false designation of origin, false or misleading description of fact, or false or misleading representation of fact, which-
> >
> > (A) is likely to cause confusion, or to cause mistake, or to deceive as to the affiliation, connection, or association of such person with another person, or as to the origin, sponsorship, or approval of his or her goods, services, or commercial activities by another person, or
> >
> > (B) in commercial advertising or promotion, misrepresents the nature, characteristics, qualities, or geographic origin of his or her or another person's goods, services, or commercial activities, shall be liable in a civil action by any person who believes that he or she is or is likely to be damaged by such act.
>
> 15 U.S.C. § 1125(a).
>
> FN76. P & G also asserts a claim of unfair competition under the common law of the State of New York. Unfair competition claims under the Lanham Act and the common law are evaluated according to the same principles. *SOP, Inc. v. Sirrom Sales, Inc.*, 130 F.Supp.2d 364, 365 (N.D.N.Y.2001) (citing *American Footwear Corp. v. General Footwear Co.*, 609 F.2d 655, 664 (2d Cir.1979)).

***26** First, "[w]here the advertising claim is shown to be literally false, the court may enjoin the use of the claim without reference to the advertisement's impact on the buying public." *McNeil-P.C.C ., Inc. v. Bristol-Myers Squibb Co.*, 938 F.2d at 1549 (citation and internal quotation marks omitted). Second, "[w]here a plaintiff's theory of recovery is premised upon a claim of implied falsehood, a plaintiff must demonstrate, by extrinsic evidence, that the challenged commercials tend to mislead or confuse consumers." *Johnson & Johnson * Merck Consumer Pharms. Co. v. Smithkline Beecham Corp.*, 960 F.2d 294, 297 (2d Cir.1992) (citations omitted). "It is not for the judge to determine, based solely upon his or her own intuitive reaction, whether the advertisement is deceptive ... [since] the question in such cases is-what does the person to whom the advertisement is addressed find to be the message?" *Id.* (citation omitted). "[T]he success of a plaintiff's implied falsity claim usually turns on the persuasiveness of a consumer survey." *Id.* at 298 (citation omitted).

III. The Lanham Act Claims

P & G asserts both literally false and impliedly false claims on the following bases: (1) that Roche's two television ads make impliedly false claims of product parity; (2) that Roche's Internet Web page makes a literally false claim of hip fracture prevention efficacy; (3) that Roche's detail aids make an impliedly false claim of product parity; (4) that Roche's detail aids make an implied establishment claim of product parity; and (5) that Roche's sales force engaged in literally false claims of product parity.

A. Television Ads

P & G challenges two virtually identical Boniva television commercials that began airing in July 2005, several months after product launch. In the Complaint, P & G plead literal and implied claims with regard to the television ad, asserting that both commercials conveyed the message "that Boniva has been proven to be a more convenient substitute for the weekly osteoporosis drugs" (Compl.¶ 43). More particularly, P & G objects to one part of the commercials in which four unidentified pills on a calendar are swept away and replaced by a single pill-*i.e.*, the "sweep-and-replace" visual-during which time the announcer states that "unlike treatments you take once a week, you only need Boniva once a month." (Tr. 217 (Pratt).)

1. Literally False Claim

The parties agree that the commercials do not reference, directly or indirectly, nonvertebral fracture

efficacy or data. (Tr. 648-49.) Nor do these commercials expressly state that Boniva is as effective as other osteoporosis drugs and thus is substitutable *and* it provides the convenience of once-monthly dosage. All the ad states, when the "sweep-and-replace" visual is shown, is "And unlike treatments you take week [sic], you only need Boniva once a month" (Ex. 12)-which is a literally true statement. P & G does not assert a literally false claim.

2. Impliedly False Claim-Standard Analysis

***27** P & G contends that Roche conveys an impliedly false message in two television ads for Boniva. To test this message P & G commissioned RL Associates to conduct a consumer survey. (Ex. 85; Tr. 287-88, 292 (Rappeport).) The admissibility and "probative value of a consumer survey is a highly fact-specific determination and a court may place such weight on survey evidence as it deems appropriate." *Johnson & Johnson-Merck Consumer Pharms. Co. v. Rhone-Poulenc Rorer Pharms.*, 19 F.3d at 134 (citation omitted). As noted previously, the Court found that the consumer survey was marred by serious deficiencies and was not conducted in accordance with generally accepted principles of market research. *See* Diamond, *Reference Guide on Survey Research,* at 233-34; *Coors Brewing Co. v. Anheuser-Bush Co.*, 802 F.Supp. at 972 (stating that the evidentiary value of a survey's results rests upon the underlying objectivity of the survey itself); *Gilbert/Robinson, Inc. v. Carrie Beverage-Missouri, Inc.*, 758 F.Supp. 512, 524 (E.D.Mo.1991) ("A survey is considered to be properly conducted if the survey was fairly and scientifically conducted by qualified experts and impartial interviewers ..., if the questions upon which the results relied do not appear to be misleading or biased, and if the recordation of responses was handled in a completely unbiased manner ." (citation omitted)). P & G's consumer survey is so riddled with fundamental structural and implementation flaws that it is unreliable and, hence, inadmissible. *L & F Prods. v. Procter & Gamble Co.*, 45 F.3d at 712.

Accordingly, P & G's motion for injunctive relief with regard to the two Boniva television commercials is DENIED.

B. Literally False Claim-Internet Web Site

P & G asserts that the Boniva Web site asserts a literally false claim. [FN77] (P & G did not assert impliedly false claims based on the Web site.) More specifically, P & G argues that the literal meaning and necessary implication of this page, when read in its entirety, is that Boniva has been proven to "lessen the risk" of hip fractures.

> FN77. The text of the full website is set forth at pg. 28-29. P & G points to the last sentence of the second paragraph: "Hip fractures can be especially traumatic and osteoporosis is responsible for approximately 300,000 of these fractures annually"; and the first sentence of the third paragraph: "Fortunately, there are medicines like once-monthly BONIVA available today." P & G then reads the two sentences together as a false claim by Boniva of efficacy at the hip.

Every single sentence of the text on the website is literally true. P & G must demonstrate that the website is literally false by necessary implication. "A representation is conveyed by necessary implication when, considering the advertisement at issue in its entirety, the audience would recognize the claim as readily as if it had been explicitly stated." *John Wiley & Sons. Inc. v. Palisade Corp.*, No. 04 Civ. 3359, 2005 U.S. Dist. LEXIS 24631, at *18 (S.D.N.Y. Oct. 21, 2005) (citations and internal quotation marks omitted). "To be found false by necessary implication-a variant of literal falsity-the challenged advertisement must be susceptible to no more than one interpretation." *Id.* (citation and internal quotation marks omitted); *see also Johnson & Johnson-Merck Consumer Pharms. v. Procter & Gamble Co.*, 285 F.Supp.2d 389, 391 (S.D.N.Y.2003) (citing cases). The doctrine of necessary implication, however, does not convert all messages implied by an advertisement into supportable claims of literal falsity. *Clorox Co. P.R. v. Procter & Gamble Co.*, 228 F.3d 24, 35 (1st Cir.2000). As the First Circuit explained:

> ***28** The greater the degree to which a message relies upon the viewer or consumer to integrate its components and draw the apparent conclusion, however, the less likely it is that a finding of literal falsity will be supported. Commercial claims that are implicit, attenuated, or merely suggestive usually cannot fairly be characterized as literally false.

Id. at 35 (citing *United Ind. Corp. v. Clorox Co.*, 140 F.3d 1175, 1181 (8th Cir.1998)). Notably, the

Second Circuit has yet to adopt this doctrine, although district courts in the Circuit apply it. *Smithkline Beecham Consumer Healthcare, L.P. v. Johnson & Johnson-Merck Consumer Pharms. Co.*, 19 Fed. Appx. 17, 20 (2d Cir.2001); *see also S.C. Johnson & Son. Inc. v. Clorox Co.*, 241 F.3d 232, 237 (2d Cir.2001) (same).

P & G's argument requires the reader to read the hip fracture sentence together with the next sentence (in a separate paragraph) and come to the single, inescapable conclusion that Boniva is effective in preventing hip fractures, even though that is not what it says. The Court finds that the text is susceptible to more than one interpretation. While one reader might infer that Boniva prevents hip fractures; a more careful, closer reader would conclude otherwise-*i.e.*, that the Web site does not affirmatively make this assertion. To enjoin the Web site, at trial, P & G will need to present extrinsic evidence that consumers are mislead or confused by the Web site. The doctrine of necessary implication does not apply in this instance.

Accordingly, P & G's motion for preliminary injunctive relief related to the Boniva Web site is DENIED.

C. Impliedly False Claim of Product Parity-Sales Aid

To prevail on its impliedly false claim regarding the sales aid, P & G must demonstrate by extrinsic evidence that the challenged advertisement tends to mislead or confuse consumers. *Johnson & Johnson * Merck Consumer Pharms. Co. v. Smithkline Beecham Corp.*, 960 F.2d at 297. RL Associates' survey of physician perceptions focused on a sales aid no longer in use in the field. Thus, the telephone survey results are not probative of physician perceptions of the sales aid currently in use. *See American Home Prods. v. Procter & Gamble Co.*, 871 F. Sup. 739, 750 (D.N.J.1994) (concluding that a consumer survey of one ad would have no relevance to another ad). But even if the survey focused on the current sales aid, the survey results are not reliable, as previously found; and are inadmissible. *Ortho Pharm. Corp. v. Cosprophar, Inc.*, 32 F.3d 690, 695-96 (2d Cir.1994) (affirming inadmissibility ruling of improperly conducted market surveys). Alternately, even if admissible, the Court rejects them. *L & F Prods. v. Procter & Gamble Co.*, 45 F.3d 709, 712 (2d Cir.1995).

P & G argues that an exception to the requirement of extrinsic evidence applies in this case. It claims that Roche has intentionally set out to deceive the public and done so in an egregious manner. In these circumstances, P & G argues it has satisfied its burden. *Johnson & Johnson * Merck Consumer Pharms. Co. v. Smithkline Beecham Corp.*, 960 F.2d at 298-99 (citations and internal quotation marks omitted). There is no doubt that Roche intended to convey to physicians that Boniva was a bisphosphonate, that there was a class effect, and that there was fracture efficacy. It also intended to convey that, in a post-hoc analysis of a limited subgroup, Boniva reduced hip fracture, pointing out all the data from which the conclusion had been drawn. [FN78] *See* Ex. 495 at 18-19, 26-27 (Heinig March 30, 2006 deposition). The issue is whether Roche's conduct is of an egregious nature.[FN79]

FN78. P & G's chief complaint concerning the current sales aid focuses on the claims and chart on page 5 (*See* p. 34-36 *supra*.) Thus the Court focuses its analysis on post-hoc, subgroup claim only.

FN79. The Court will follow the two-prong test set out by the Second Circuit in *Johnson & Johnson.*

***29** The use of post-hoc subgroup data is not in itself egregious. P & G concedes that the information can be useful to the public, if communicated properly. Indeed, Plaintiffs' expert, Dr. Bilezikian, referred to the post-hoc data in a doctors' tutorial he filmed for Roche and Boniva. The Court notes that P & G also has relied on post-hoc analyses for promotional purposes. (Tr. 154-64 (Grauer).) In fact, in an e-mail reacting to Roche's use of post-hoc subgroup data for promotional purposes, Dr. Grauer wrote: “we are living very comfortably on post hoc analyses (HIP, 6 months vert, 6 months non vert, osteopenia, Heany, etc) and so does the competition.” (Ex. 197 at Bates number P & G F0171724.) Further, the FDA has found that Boniva's lack of proven efficacy at non-vertebral sites is “not a therapeutic deficiency” in comparison to other bisphosphonates. Accordingly, the FDA allows Boniva to be utilized for the prevention and treatment of osteoporosis in postmenopausal women at both vertebral and nonvertebral sites. As recently as May 4, 2006, the FDA found that P & G could not claim that Actonel was superior to Boniva, simply because of its efficacy at a composite end

point. Indeed, the FDA noted that Actonel could not claim nonvertebral fracture efficacy for "each/any skeletal site"; Actonel is no better than a placebo at leg, hip and worse than placebo at the collarbone.

In these circumstances, the Court cannot say that Defendants have engaged in "egregious" conduct in connection with their advertising and promotion of Boniva.[FN80] Here, the parties are engaged in a marketing battle about their competitive drug products. The FDA has not found that Defendants' ads are false and misleading, despite P & G's repeated requests that it do so. Instead, the FDA found P & G's proposed TV ad claiming superiority over Boniva false and misleading. While the claims and counter charges may be heated, they do not appear to be atypical of conduct in a competitive marketplace. *See Johnson v. Johnson-Merck Consumer Pharms. Co. v. Rhone-Poulenc Rorer Pharms., Inc.* 19 F.3d 125 (3d Cir.1994) (conduct of a kind common in the industry cannot be egregious).

> FN80. "Egregious" is defined as "extraordinary in some bad way; glaring; flagrant" and is synonymous with "outrageous" and "notorious." Webster's New Universal Unabridged Dictionary 624 (1996).

P & G's motion for preliminary injunctive relief on this theory of liability is thus DENIED.

D. Implied Establishment Claim-Sales Aid

P & G asserts that Roche's current sales aid makes an implied establishment claim of nonvertebral fracture efficacy. While not mentioned in the complaint, and not the subject of a consumer or physician survey, it is now the critical focus of P & G's arguments for preliminary injunction relief.

The fifth page of the current sales aid states "BONIVA provides nonvertebral fracture protection in high-risk patients." (Ex. 343 at 5.) Underneath the prominent header in smaller text, the aid reads: "69% reduction in nonvertebral fracture risk (post hoc analysis)" which is footnoted. A graph is shown and below the graph, the aid provides information about the BONE post-hoc subgroup study. P & G bases liability, in part, on assertion of both express and implied "establishment claims"-that is, that Roche is either expressly or impliedly relying on tests or studies to support its efficacy and product equivalence claims. But P & G does not question that the data presented can be utilized, and Roche's statements in the sales aid accurately reflect the post-hoc, subgroup data (Oral Argument, July 13, 2006, pg. 8-9).

***30** As the Second Circuit has explained:

> A plaintiff's burden in proving literal falsity ... varies depending on the nature of the challenged advertisement. Where the defendant's advertisement claims that its product is superior plaintiff must affirmatively prove defendant's product equal or inferior. Where ... defendant's ad explicitly or implicitly represents that tests or studies prove its product superior, plaintiff satisfies its burden by showing that the tests did not establish the proposition for which they were cited.

Castrol, Inc. v. Quaker State Corp., 977 F.2d at 63. These types of claims are termed "establishment claims." [FN81] Importantly, the Second Circuit has stated that "even [where] the tests [are] not directly referred to in connection with [a] claim," a plaintiff can still rely on and analyze data generated by the defendant as scientific support that the challenged advertisement is false. *McNeil-P.C.C., Inc. v. Bristol-Myers Squibb Co.*, 938 F.2d at 1549.

> FN81. An implicit establishment claim involves an ad that relies on scientific studies by making an implicit superiority or parity claim by showing a graph or diagram. *Zeneca Inc. v. Eli Lilly & Co.*, No. 99 Civ. 1452, 1999 U.S. Dist. LEXIS 10852, at *89 (S.D.N.Y. July 15, 1999). An express establishment claim involves an ad that explicitly states, for example, "that studies show." *Id.*

Both parties agree that the BONE post-hoc, subgroup data do not scientifically prove or establish that Boniva provides nonvertebral fracture protection-either to the overall population or to the high-risk subgroup. Contrary to what P & G argues, however, the sales aid at issue does not expressly make that claim. The data from the post-hoc, subgroup analysis is not in itself inaccurate or unreliable. P & G contends that its arrangement, association and headers used in the sales aid make a claim of nonvertebral efficacy. Since the various panels of the sales aid have to be read together to support P & G's argument, however, that very process negates a finding that there is an

express claim. *See SmithKline Beechham*, 2001 U.S. Dist. LEXIS 7061 at *27 (S.D.N.Y. June 21, 2001). ("The greater the degree to which a message relies upon the viewer or consumer to integrate its components and draw the apparent conclusion, however, the less likely it is that a finding of literal falsity will be supported.") Whether an implied claim is made depends on the graphs, diagrams, other visuals, as well as the text.

The fifth panel does not use the word "proven" or "demonstrated." P & G asks that "proven," which is used on the first and second pages and the word "demonstrated" used on pages 3 and 4 concerning vertebral fractures, be read into the fifth page. But the deliberate use of a different word: "provide," as opposed to "proven" or "demonstrated," is significant. Clearly, "provide" does not mean "proven" or "demonstrated." It is critical that this aid is not targeted to the general public, which generally receives the convenience of monthly dosage message. The word "provides" alerts the sophisticated reader-the prescribing physician-that there is a difference. That difference is elaborated on in the charts, graphs and text which in combination clearly state what is being "provided."

As the data presented from the post-hoc, subgroup analysis is not inaccurate or unreliable, the Court rejects P & G's argument that the aid is false and finds the header on page five, plus the information supplied below the header, when read together, provides the reader with accurate clinical information. (*See, e.g., Avis Rent-A-Car*, 782 F.2d at 385 (refusing to enjoining an advertisement because the challenged heading was followed by a picture and text that explained it). *Quaker State Corp. v. Castrol, Inc.*, 92 Civ. 2332, 1992 U.S. Dist. LEXIS 4880 at *11 (S.D.N.Y. April 13, 1992 (denying a motion for a preliminary injunction because the "text flushes out the bones of the headline" and "reading the text of [the] advertisement together with the headline, as *Avis* explicitly commands, results in a statement which is factually correct").

***31** There is no evidence that physicians were misled or deceived in any way by the fifth page of the sales aid. Further, Roche's experts have testified that there is nothing false or misleading about the data itself which appears on page five. In reaching this conclusion, the Court gives weight to several additional factors. First, the sophistication of the target audience is one that is fully capable of discerning the difference between "proven," "demonstrated" and "provides." The audience is also fully capable of discerning that it was being presented with a "post-hoc" analysis of a subgroup. The subgroup data is fully disclosed and the results in that subgroup are compared with the results achieved-or not achieved-in the entire test population.

Dr. Bilezikian, Plaintiffs' expert at the hearing, also appeared in an ad for Defendants in which he discussed the post-hoc data. He testified that Boniva's post-hoc subgroup data was useful and was associated with a significant reduction of nonvertebral fractures. (Tr. 114 (Bilezikian).) Second, notwithstanding P & G's best efforts concerning an earlier version of this sales aid (*See* October 29, 2005 letter to FDA, Ex. 116), the FDA has taken no action. Finally, granting an injunction here at best would only change the word "provides" in the header to something like "associated with" or "valid statistical evidence." The equitable powers of the Court cannot be invoked for such minor wordsmithing. Certainly, there is no basis on this record for P & G's draconian relief that Defendants be forced to visit every doctor called upon over the last 16 months and provide a corrective written statement that Boniva's claims were false and misleading.

The Court finds that Plaintiffs did not establish a likelihood of success that the sales aid currently in use makes an establishment claim of proven or demonstrated nonvertebral fracture efficacy. Accordingly, P & G's motion for injunctive relief under this theory of liability with regard to the sales aid is DENIED.

E. Literally False Claim-Sales Force Detailing

"Courts have consistently held that oral statements by a company's sales representatives concerning a product constitute 'commercial advertising or promotion' under the Lanham Act." *Zeneca, Inc. v. Eli Lilly and Co.*, 1999 U.S. Dist. LEXIS 10852, at *88 (citing cases). Both sides agree that sales representatives are trained to tell doctors only what is previously authorized. In other words, sales calls are not spontaneous, but are carefully scripted presentations. Thus, there is no surprise that sales representatives talked about Boniva's bisphosphonate class efficacy, as well as data relating to Boniva's nonvertebral efficacy.

Roche officials admitted that the company

wanted to communicate the message of bisphosphonate class efficacy. (Tr. 754, 756-57, 760, 766 (Heinig); Tr. 827-28 (Klein).) P & G urges that Boniva's claims of class efficacy was misleading because it implied that Boniva had the same nonvertebral efficacy as Actonel. When the FDA approved Boniva for market, it stated that Boniva was not inferior as a bisphosphonate because it had not demonstrated nonvertebral efficacy. And on May 4, 2006, the FDA stated that Actonel was not superior to Boniva simply because Actonel had efficacy at a composite nonvertebral end point. It would be difficult on this record to find that Defendants' claim was false and misleading. In any event, Roche's claim of bisphosphonate class effect was dropped from Roche's promotional materials some ten months ago.

***32** Roche officials agree that they wished to communicate its data on nonvertebral fracture efficacy to physicians as well. (Tr. 773-74 (Heinig); Tr. 850 (Klein).) The evidence suggests that the sales representatives were "not instructed to say there was proven efficacy.... No, we were very careful not to have the representatives present this as proven information." (Tr. 804, 806 (Klein).) Fewer than 600 Roche call notes support P & G's argument. This is only two percent of the total number of call notes produced. Further analysis by Defendants demonstrated that these call notes were made by a very small percentage of the overall sales force. These representatives were spoken to and the appropriate messaging was reconfirmed. (Tr. 814 (Klein.)) The Court has already determined that the message with regard to nonvertebral efficacy based on the post-hoc subgroup analysis was not false and misleading. So long as the representatives were staying with the post-hoc data, there can be no misconduct.

Given the vigor with which P & G attempted to preserve its market share by denigrating Boniva, Roche was clearly entitled to respond with its own data, provided that the data was truthfully and accurately presented. Further, the Court finds that Roche made a good faith effort to educate its work force concerning the data from the post-hoc, subgroup analysis, and what could and could not be fairly said about it. Since P & G picked this fight in order to preserve its market share and profits, it would not be equitable to permit P & G to dictate or limit Defendants' response, so long as it is not false and misleading.

Since the sales force messaging is not false and misleading, it cannot serve as the basis for preliminary injunctive relief and, accordingly, it is DENIED.

CONCLUSION

In light of the disposition of the motion for preliminary injunction, it is unnecessary to consider Roche's arguments about P & G's unclean hands or laches. Similarly, it is unnecessary to consider the public health exception to the unclean hands doctrine. With regard to public health, however, there is no doubt that Boniva is a safe and effective drug which the FDA has approved for the treatment and prevention of osteoporosis in postmenopausal women, without limitation as to vertebral and nonvertebral sites. According to the FDA, Boniva is not inferior to other bisphosphonates, nor is Actonel superior to Boniva by virtue of Actonel's efficacy at a composite nonvertebral end point.

In sum, the Court finds that P & G has not demonstrated that the TV advertising, websites, sales aids and sales force detailing are false and misleading. Accordingly, the motion for preliminary injunction is DENIED in all respects.

SO ORDERED

S.D.N.Y.,2006.
Procter & Gamble Pharmaceuticals, Inc. v. Hoffmann-LaRoche Inc.
Not Reported in F.Supp.2d, 2006 WL 2588002 (S.D.N.Y.), 2006-2 Trade Cases P 75,465

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