UNITED STATES OF AMERICA
BEFORE FEDERAL TRADE COMMISSION

DOCKET NO. 9267

In the Matter of

METAGENICS, INC.,
a corporation, doing business as
Ethical Nutrients,
and
JEFFREY KATKE,
individually and as an officer
of said corporation.

INITIAL DECISION

Lewis F. Parker
Administrative Law Judge

Dated: October 11, 1996

TABLE OF CONTENTS

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By: Lewis F. Parker, Administrative Law Judge

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I. INTRODUCTION

The Commission issued its complaint in this proceeding on August 16, 1994, charging Metagenics, Inc. ("Metagenics") and an officer, Jeffrey Katke, with violations of Sections 5(a) and 12 of the Federal Trade Commission Act by disseminating, or causing to be disseminated, false and misleading statements in advertisements and promotional materials for an orally-ingested product containing microcrystalline hydroxyapatite ("MCHC") under the name "Bone Builder."

The complaint charges that respondents have represented, directly or by implication, and without substantiation, that Bone Builder or MCHC:

1. builds bone or increases bone thickness;

2. restores lost bone;

3. halts or prevents bone loss or bone thinning;

4. restores bone strength;

5. halts, prevents or treats osteoporosis;

6. reduces or eliminates pain associated with bone ailments;

7. is superior to and/or more effective than other forms of calcium in the prevention or treatment of bone ailments; and

8. is more bioavailable, more absorbable, or more effectively utilized by the body than other forms of calcium.

The complaint also alleges that respondents have represented falsely that the claims for Bone Builder or MCHC are substantiated by scientific research, including clinical tests, scientific papers and/or scientific studies, and that by using the trade name "Bone Builder" respondents have made the unsubstantiated representation that the product builds, increases, or restores bone.

After extensive pretrial discovery, hearings were held in Boston, Massachusetts and Washington, D.C. from February 27, 1996 to April 17, 1996. The record was closed on April 30, 1996, and the parties filed their proposed findings of fact, conclusions of law and proposed orders on July 29, 1996. Replies were filed on August 29, 1996.

This decision is based on the transcript of testimony, the exhibits which I received in evidence, and the proposed findings of fact and conclusions of law, and answers thereto, filed by the parties. I have adopted several proposed findings verbatim. Others have been adopted in substance. All other findings are rejected either because they are not substantiated by the record or because they are irrelevant.

II. FINDINGS OF FACT

A. Metagenics' Business Activities

1. Metagenics, doing business as Ethical Nutrients, is a corporation organized, existing and doing business under and by virtue of the laws of the State of California with its principal office or place of business located at 971 Calle Negocio, San Clemente, California 92672. (Ans ¶1.)[1] The company, which began in 1983, is a formulator and distributor of nutritional and dietary supplements. (Tr. 1435; CX-9.2 p.9.)

2. Jeffrey Katke is an officer of Metagenics and its founder and Chief Executive Officer ("CEO"). His business address is 971 Calle Negocio, San Clemente, California 92672. Individually, or in

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[1]Abbreviations used in this decision are:

CX: Complaint counsel's exhibit.
RX: Respondents' exhibit.
Cplt: Complaint.
Ans: Answer.
CPF: Complaint counsel's proposed findings.
RPF: Respondents' proposed findings.

concert with others, he formulates, directs, and controls the acts and practices of Metagenics. (Tr. 1409; Ans ¶1.)

3. Respondents have manufactured, advertised, offered for sale, sold and distributed a dietary supplement containing microcrystalline hydroxyapatite ("MCHC") under various names such as "Bone Builder," "Cal Apatite," "Bone Mend," "EthiCal," and "Osseogenics." (Ans ¶2; Tr. 1536, 1538; CX-2-B1.) Respondents also offer for sale and sell MCHC to other parties who market the product under their own brand names. (Ans ¶2.) Bone Builder is a food and/or drug, as the terms "food" and "drug" are defined in Sections 12 and 15 of the Federal Trade Commission Act. (Cplt ¶2; Ans ¶2.)

4. The acts and practices of respondents challenged in the complaint have been and are in or affect commerce. (Ans ¶2.)

5. Metagenics sells approximately 400 dietary supplements (Tr. 1412, 1529, 1534-35; CX-9.1 - CX-9.5; CX-19; CX-20) and had annual sales in 1995 of $22 million. (Tr. 1529, 1439-40, 1480.)

B. The Dissemination Of Bone Builder Ads And Promotional Materials

6. From 1988 to the present, ads for Bone Builder have repeatedly appeared in national publications such as Let's Live, Better Nutrition, Delicious, Total Health, Mothering, and New Age Journal. (Tr. 1497-1500, 1508-21.) Product information and ads for Bone Builder have also appeared in Metagenics brochures. (See, e.g., CX-9.4, p. 6-7.) Examples of expenditures which Metagenics incurred advertising Bone Builder in 1993 include two full-page color ads in the national editions of New Age Journal that cost $4246 each (CX-16; CX-17), and a color ad in the fall issue of Mothering, costing $3000. (CX-18.)

7. The ads and promotional materials at issue were disseminated between 1988 and the time of the filing of the complaint against Metagenics in August 1994. (Tr. 1500; CX-2-A1 - CX-2-B13; CX-9.4, p. 6-7; CX-17; see also my Order Granting Complaint Counsel's Motion for Sanctions, Metagenics, Inc., et al., Dkt. 9267, April 28,

1995 (ruling that ads and promotional documents at issue are deemed to have been disseminated by respondents.))

8. Exhibit CX-2, entitled "Advertising and Promotional Material Extraction Chart," provides the specific language in the ads and promotional materials (CX-2-A1 - CX-2-B13) underlying each of the challenged claims in paragraphs 5 and 8 of the complaint and shows where and when this copy appeared in print. Additionally, CX-9.4, an Ethical Nutrients brochure, and CX-17, New Age Journal advertising invoices, show advertising and promotional copy that include claims challenged in the complaint. (CX-9.4, p. 6-7; CX-17.)

C. Bone Builder And MCHC

9. Bone Builder is an orally-ingested dietary calcium supplement made from ground cow bones containing microcrystalline hydroxyapatite concentrate ("MCHC"), an inorganic compound found in the matrix of bone, dicalcium orthophosphate, trace minerals, and protein. (Tr. 1416-18, 1422, 1425, 1463, 2738-39; Stipulations ¶3.)

D. The Marketing Of Bone Builder and MCHC

10. Between January 1989 and January 1995, Metagenics' wholesale sales of Bone Builder, which is sold at retail through health food stores, were over $3.16 million. (Ans ¶3; Tr. 1439-40; CX-14.) The suggested retail price of Bone Builder ranges from $9.95 for a 60-tablet jar to $32.95 for a 220-tablet jar. (CX-20; Tr. 1528.) When taken at the recommended dosage of 6 tablets per day a 60-tablet and 220-tablet bottle would cost $363 and $328 per year, respectively.

11. Since MCHC is calcium (Stipulations ¶5; Tr. 2436-38, 2447), Bone Builder competes with other calcium supplements such as Tums or Os-Cal, which contain calcium carbonate, one of the more widely used forms of calcium in the United States. (Tr. 2447-48, 2551-53.) These other brands typically sell for considerably less than Bone Builder. (See Exhibit 5, Motion In Limine Regarding Purported Substantiation Studies, Dkt. 9267, December 13, 1995.) Calcium

carbonate is often recommended because it is the least expensive form of calcium and is generally well absorbed. (See Tr. 99, 2551-53.)

E. The Role Of Calcium In Bone Health

12. Human bones serve two purposes: to provide the skeletal structure that protects internal organs and allows for muscular movement; and to provide a "storehouse" for three essential items: calcium, phosphorous and proteins. (Tr. 53.)

13. Bone health and strength is maintained throughout the life span by a process known as "remodeling"[2] or "turnover," in which bone cells are constantly being broken down (or "resorbed") and replaced. (Tr. 50, 93-94.) Remodeling is regulated by the thyroid and parathyroid hormones. (Tr. 93-94.)

14. Resorption is performed by "osteoclast" cells. "Osteoblast" cells build bone by filling in the holes created by the osteoclasts. When these processes are in equilibrium, an individual is said to be in "bone balance." If remodeling is imbalanced, either because of too much resorption or too little formation, bone is lost. (Tr. 93.) Overactive osteoclast activity can result in the removal of bone cells across the entire bone surface; when this occurs, the lost bone cannot be replaced. (Tr. 91-93.)

15. Beginning at conception, bones grow at a fairly steady rate. During puberty, bone mass, the amount of mineral per area of bone (Tr. 1308), increases rapidly; the outside, or cortical, bone grows larger, and the inside, spongy or trabecular, bone grows thicker and stronger. After puberty, bone continues to increase until a genetically-programmed "peak bone mass" is reached sometime between the ages of 18 to 30 or 35. (Tr. 61.) Peak bone mass cannot exceed each individual's genetically pre-determined level. (Tr. 658, 977-78.)

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[2]This and other relevant medical terms are defined in a glossary attached to complaint counsel's proposed findings.

16. After peak bone mass is achieved in their late 30s and early 40s, women begin to lose bone. This may lead to osteoporosis. Even before the menopause, as estrogen levels decrease, bone loss accelerates. After the menopause, estrogen levels drop markedly, resulting in a significant loss of bone mass. This loss is most rapid in the first few years after menopause, slowing down -- albeit continuing -- thereafter. (Tr. 61-63.)

17. Men, on the other hand, lose bone later in life than women and do so more slowly. By their late 60s and 70s, bone loss in Caucasian men causes fractures at a rate of one-third to one-half that of women. As men are living longer, fractures, particularly hip fracture, are no longer a problem limited to elderly women, but are becoming a significant event for elderly men as well. (Tr. 63.)

18. Physical activity, sex hormones, and calcium intake are the three most important factors that influence bone mass and density. (Tr. 2383-84.)

19. Some people have good bone mass even though they are physically inactive and have poor diets. (Tr. 136-37.) The current scientific assumption is that these individuals are genetically not predisposed to low bone mass or bone loss. (Tr. 66, 140.) On the other hand, some individuals develop severe osteoporosis even though they have a very good calcium intake and are not at risk for the disease. (Tr. 66.)

20. Calcium is an essential nutrient, a major component of bone, and plays a vital role in human physiology. (Stipulations ¶1.) About 99% of the body's calcium is contained in the skeleton, in the form of calcium hydroxyapatite, an inorganic compound in the matrix of bone. (Stipulations ¶2, ¶3; Tr. 206.) Calcium is necessary to mineralize the skeleton, giving it rigidity and strength.

21. Calcium is also essential for many other critical biochemical functions: clotting of blood; contraction and relaxation of the heart; as a vital link in nerve transmission and an aid in the passage of fluid through cell walls; as an essential element in enzyme regulation; and in the

stimulation of insulin secretion in adults. (Tr. 54-55; Stipulations ¶10.)

22. Digestion is required to release calcium into a soluble form that can be easily absorbed or assimilated. (Stipulations ¶6.) When the body does not receive adequate calcium through nutrition, it draws upon the supply of calcium in the skeleton to maintain an appropriate level in the blood. When calcium levels are supplemented, the parathyroid, which is responsible for bone resorption, reduces the secretion of parathyroid hormone, thus slowing bone resorption. (Tr. 147.)

23. Calcium intake during childhood, adolescence, and early adulthood greatly influences the development of peak bone mass by helping build bone and increasing bone density or thickness. (Stipulations ¶¶15, 19; Tr. 3180; Tr. 208.) Optimal calcium intake may be achieved through diet, calcium-fortified foods, calcium supplements, or various combinations of these. (Stipulations ¶20.) The preferred source of calcium is through calcium-rich foods such as dairy products. However, Dr. Heaney, one of respondents' experts, recognizes that ideally one should be getting calcium from natural sources, but "people can't do that, so there's a role for supplements." (Tr. 2524-25; see Tr. 215; CX-7-CAL-193, p. 1947.) In fact, since there is no test for calcium deficiency, the only way to assure that everybody is getting the calcium they need is to offer it to the whole population. (Tr. 2301-02; F. 295.)

24. Once bone is mature, ingesting additional amounts of calcium beyond the body's requirement is not only of no benefit to the skeleton, but can lead to the formation of kidney stones or "nephrocalcinosis."[3] (Tr. 55-56: Tr. 3180-81.) Too little calcium can cause soft bones, also known as "osteomalacia" or rickets. (See Tr. 42.)

25. If an individual is calcium deficient, bone loss can become accelerated. (Tr. 3183.)

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[3]This does not appear to be a serious problem for Dr. Raisz, one of complaint counsel's experts, testified that "for osteoporosis we just automatically increase the calcium intake on the basis that it could help, and it doesn't hurt." (Tr. 243.)

26. It is probably correct to assume that a high life-long intake of adequate calcium may diminish the later incidence of fractures; however, the data are not adequate to establish this as a scientific fact. (Tr. 161.)

27. Recognizing that "optimal calcium intake may vary according to a person's age, sex and ethnicity" and the influence of vitamin D, which is needed for calcium absorption, a recent consensus conference sponsored by the National Institutes of Health ("NIH") has recommended the following RDAs for calcium:

Children	
1-5 years	800 milligrams ("mg")
6-10 years	800 - 1200 mg
Adolescents/young adults	
11-24 years	1200 - 1500 mg
Men	
25-65 years	1000 mg
Over 65 years	1500 mg
Women	
25-50 years	1000 mg
Over 50 years (post-menopause)	
On estrogen	1000 mg
Not on estrogen	1500 mg
Over 65 years	1500 mg
Pregnant and nursing	1200 - 1500 mg

(CX-7-CAL-193, p. 1942-43).

28. The purpose of RDAs is to set the values high enough so that there is a "margin of safety," such that it accounts for a compliance level of less than 100%. (Tr. 143.) This margin also provides adequate calcium even for those whose intestinal absorption of calcium is low. (Tr. 161.)

29. Vitamin D is needed for calcium absorption in the small intestine. (Tr. 2188; Tr. 55-57, 141-42; Tr. 2519-20; see Tr. 1793.) Vitamin D is not a vitamin in the usual sense, but is a hormone that is synthesized through the skin and kidney, and transports calcium across the intestine via calcium-binding proteins. (Tr. 141-42; Stipulations ¶7.) The hormonal form of vitamin D, calcitriol, also is thought to be essential for the full differentiation and function of bone cells. (Tr. 141.)

30. Adequate vitamin D intake has been established at 400-800 "International Units" ("IU") per day. An inadequate intake of vitamin D results in a decline in the percentage of calcium absorbed. In general, a 1,000 mg intake of calcium in an average vitamin D-replete person results in an actual absorption of 300 mg of calcium. If a person is vitamin D deficient, calcium absorption can decrease to no more than 10 to 15% of dietary calcium, to the point of causing bone loss. (Tr. 55, 57; Stipulations ¶8.)

31. Estrogen is a female sex hormone whose production is deficient after menopause. (Tr. 48.) In the early post-menopausal years, estrogen loss results in a rapid increase in bone breakdown or resorption. This occurs for at least the first three years after menopause and probably the next three as well. This bone breakdown cannot be blocked by calcium; it can only be treated by estrogen, which has a direct effect on bone remodeling. After this initial period of rapid decrease, bone continues to be lost because of estrogen deficiency and estrogen treatment will slow bone breakdown during this phase as well. (Tr. 246-48.)

F. Osteoporosis

32. Osteoporosis is a condition in which bone mass decreases, causing bones to be more susceptible or predisposed to fracture. (Stipulations ¶11; Tr. 66; CX-7-CAL-193.)

33. Osteoporosis affects approximately 20-25 million people in the United States and is the major underlying cause of bone fractures in post-

menopausal women and the elderly. (Stipulation ¶17; Tr. 43-44.) It is a complex and multi-factorial disorder, with many risk factors, the most important being age-related and menopause-related bone loss. (Tr. 44.)

34. Osteoporosis is far more common in women than in men and in whites than blacks. (Stipulations ¶12.) Among Asian populations, the incidence of osteoporosis varies, with some having a higher incidence of osteoporosis and fractures than others. (Tr. 59-60.)

35. Other important factors bearing upon the occurrence of osteoporosis include genetics; childhood growth and development, i.e., attainment of peak bone mass; smoking; excessive alcohol consumption; calcium deficiency; lack of exercise; and the use of cortico-steroid medications, such as cortisone and prednisone (or "prednisolone"). (Tr. 43-44, 88-89; Stipulations ¶14; Tr. 2513-14; see Tr. 1675-76.)

36. Despite the identification of these risk factors, it is still unclear why some individuals suffer severe osteoporosis and others do not experience it. The difference seems to be unrelated to the treatments, risk factors, calcium intake, exercise or anything else that is known to scientists in the field. (Tr. 257.) It is assumed that these differences are genetically superimposed. (Tr. 60.)

37. Hip fracture, which almost always results from a fall, is the most serious result of osteoporosis. (Tr. 59.) However, because bone loss is not solely a function of calcium intake (Tr. 2514-16, 1518), there is no guarantee that by taking adequate calcium, a person will not develop osteoporosis. (Tr. 97.)

38. The U.S. population experiences more than 1.5 million fractures annually at a cost of approximately $6-10 billion per year to the health care system. (Stipulations ¶18.)

39. As a result of compression fractures of the vertebrae, many osteoporotics "shrink" or lose height, are bent over, and develop kyphosis, an arching spine that shortens them in the standing

position. Many patients "lose" from three to six inches of height in this manner. (Tr. 181.)

40. Osteoporosis is treated by a multiple approach which includes hormone replacement therapy, adequate calcium (through supplementation if necessary), vitamin D intake, and a good exercise program to maintain bone and muscle strength. (Tr. 665-68.) The literature for Bone Builder recognizes the desirability of this approach:

(a) It's certain that all of us will lose bone unless we practice prevention, and the best answer I know of is this program: take Bone Builder every day, get regular exercise that puts some stress on weight bearing bones, like legs, hips and pelvis and be moderate in the consumption of protein.

(CX-2/Exhibit A1.)

(b) Among the road signs which put women at risk [for bone loss] are: early removal of the ovaries; family history of osteoporosis; poor diet; lack of exercise; the heavy use of tobacco or alcohol; long term use of steroids in the treatment of other illnesses; poor digestion; small bones and slenderness as opposed to large bones and over-weight; chronic stress; a sedentary occupation; thin skin.

Obviously, any one or more of these risk factors in the individual's life should stimulate the introduction of a program of prevention to be continued for life, and this inevitably includes a nutritious diet, high in all necessary minerals, including calcium.

(CX-2/Exhibits A-11, B3; Tr. 182-84; Tr. 1802-03.)

(c) Risk Factors Contributing to Bone Loss:

1. Inherited predisposition (women or men; white women or black; small boned women or large).

2. Removal of ovaries at any age (oophorectomy).

3. Menopause.

4. Prolonged use of certain drugs such as members of the cortisone family, diuretics and antacids containing aluminum.

5. Zero pregnancies.

6. Digestive interference (stomach/intestinal resection, inadequate gastric juices).

7. Inadequate or inappropriate exercise.

8. Poor diet: low calcium foods, high phosphorous foods, (effervescent beverages, red meat, phytate laden cereals), calcium antagonists (alcohol, caffeine-containing beverages, tobacco).

9. Certain disease conditions: chronic liver disease, overactive endocrines (adrenals, thyroid, pancreas), kidney disease, prolonged immobilization.

10. Sedentary occupation, protracted bed rest, etc.

(CX-2/Exhibit A-11, B3; Raisz, Tr. 178-80; Lachance, Tr. 1803-05.)

(d) The management of osteoporosis includes primary prevention, in patients known to be at risk, secondary prevention of recurrences in patients who have already suffered osteoporotic fracture, and treatment of symptoms such as bone pain.

Risk factors include the menopause, enforce immobility, hypogonadism and oophorectomy, long term treatment with corticosteroids, cimetidine antibiotics, G.I. surgery, alcoholism, aluminum intake, excessive exercise, smoking,

excess caffeine consumption, and dietary insufficiency of Ca Mg2, Zn and Cu.

A variety of treatments are available for the management of osteoporosis (Woolf & Dixon 1984) perhaps reflecting the degree of uncertainty as to the Fluoride . . . Vitamin D . . . Sex Hormones . . . Salmon Calcitonin . . . Calcium supplements.

(CX-2/Exhibit B4.)

(e) THE PROBLEM: Osteoporosis. . .

THE SOLUTION: Regular exercise, a whole foods diet, smoking cessation, and adequate absorption of micro-nutrients will end the current rapid bone loss epidemic in the United States population.

(CX-2/Exhibit B5.)

(f) In osteoporosis, it appears other factors are at work, not just an absence of sufficient calcium in the diet.

(CX-2/Exhibit B6.)

(g) Risk factors associated with accelerated bone loss.

- Family history of osteoporosis.
- Lack of or inadequate exercise.
- Heavy use of tobacco or alcohol.
- Early removal of the ovaries (oophorectomy).
- Small boned and slenderness as opposed to large bones and overweight.

- Poor diet (low calcium foods, high phosphorus foods, calcium antagonists).

- Chronic use of certain drugs (steroid, diuretics and antacids containing aluminum).

- Certain disease conditions (chronic liver disease, cushings syndrome, hyperthyroid-ism).

- Menopause.

- Chronic stress.

- Poor digestion.

- A sedentary occupation.

(CX-2/Exhibit B10, B13.)

G. Respondents Agree That The Alleged Claims Were Made

41. During the trial of this proceeding, respondents offered no evidence contradicting complaint allegations regarding claims made in their ads. Respondents' proposed findings confirm that while their answer denied the allegations of Paragraphs 5 and 8 of the Complaint they did not, at trial, challenge the allegations of these paragraphs, and they concede that the representations set forth in ¶¶ Five and Eight of the Complaint were made. (RPF, pp. 2-3.)

42. Analysis of respondents' ads and promotional materials confirms that the alleged claims were made.

H. The Objective Product Claims Challenged In Complaint Paragraph 5 Were Made

1. Bone Builder Or MCHC Builds Bone Or Increases Bone Thickness

43. Respondents' ads and promotional materials represented that Bone Builder or MCHC builds bone or increases bone thickness. (See Complaint ¶5.1.) The following excerpts taken from the ads and promotional materials are typical of these claims:

Bone Builder is the best selling product in the marketplace for actually building bone. (CX-2-A1.)

You Can Do Something About Bone Loss - Fight Back With The World's Best Bone Builder! (CX-2-A4.)

The superior form of calcium proven to build bone (CX-2-A9; CX-2-A11; CX-2-B8; CX-9.4, p. 6.)

Bone Builder Builds Bone Like Nothing Else Can! (CX-2-B3.)

Bone Builder is the best. It builds bone - naturally, quickly and safely. (CX-2-B3.)

Bone Builder Builds Bone 400% Better than Calcium Gluconate (CX-2-B3.)

[M]icrocrystalline hydroxyapatite . . . increased bone thickness when taken in adequate amounts over long enough periods of time, a record no other form of calcium could achieve. (CX-2-B6.)

OUR BONE BUILDER BUILDS PROFITS AND BONE (CX-2-B9.)

The best Bone Builder for your customers. (CX-2-B9.)

Nothing can restore the spinal posture to normal in those whose spines have already shrunk because of osteoporosis. But there is now good evidence to suggest that microcrystalline hydroxyapatite has a significant effect in preventing the development of osteoporosis, its bone damaging consequences and can actually increase bone growth. (CX-2-B10.)

Increases cortical bone density (CX-2-B10; CX-2-B13.)

In those whose spines have already shrunk due to bone loss, there is now good evidence that MCHC can not only increase overall bone density, but also prevent further bone damage due to osteoporosis. (CX-2-B13.)

2. Bone Builder or MCHC Restores Lost Bone

44. Respondents' ads and promotional materials represented that Bone Builder or MCHC restores lost bone. (See Complaint ¶5.2.) The following excerpts taken from the ads and promotional materials are typical of these claims:

MCHC is proven to help restore lost bone, bone meal and calcium supplements are not! (CX-2-A2; CX-2-A5; CX-2-A7; CX-2-A8; CX-17.)

Bone Builder helps rebuild and restore lost bone. (CX-2-A4.)

BONE BUILDER can restore bone and has the clinical evidence to prove it! (CX-2-A9; CX-2-B8.)

BONE BUILDER can restore lost bone and has the clinical evidence to prove it! (CX-2-A11; CX-9.4, p. 6.)

Bone Builder contains Microcrystalline Hydroxyapatite, the only source of calcium proven to not only stop, but reverse bone loss. (CX-2-A12.)

The ONLY Form Of Calcium Proven To Restore Lost Bone. (CX-2-A12.)

The active ingredient [MCHC] in Ethical Nutrient's Bone Builder is a superior form of calcium that is proven to restore lost bone. (CX-2-B9.)

The Superior Form Of Calcium Proven To Restore Lost Bone. (CX-2-B9.)

MCHC has been proven not only to stop bone loss but to reverse it. MCHC can actually help restore lost bone. (CX-2-B11.)

3. Bone Builder or MCHC Halts or Prevents Bone Loss or Bone Thinning

45. Respondents' ads and promotional materials represented that Bone Builder or MCHC halts or prevents bone loss or bone thinning. (See Complaint ¶5.3.) The following excerpts taken from the ads and promotional materials are typical of these claims:

Bone Builder contains Microcrystalline Hydroxyapatite, the only source of calcium proven to not only stop, but reverse bone loss. (CX-2-A12.)

Where there is evidence that osteoporosis "runs in the family," and where there is evidence that calcium loss is already taking place, i.e., muscle spasms, receding gums, or loss of height, the ability of the microcrystalline hydroxyapati[t]e (bone) concentrate places prevention as a matter of the individual sufferer's choice. This safe, reliable, inexpensive, scientifically-tested preventative is his/hers to take as they choose and not dependent upon the whim of another. (CX-2-B2.)

Most importantly, no other product in the United States is as effective at preventing bone loss. (CX-2-B5.)

[M]icrocrystalline hydroxyapatite halted bone loss...when taken in adequate amounts over long enough periods of time, a record no other form of calcium could achieve. (CX-2-B6.)

Microcrystalline hydroxyapatite [MCHC], therefore, provides the best bioavailable and effective means of preventing and reducing cortical bone thinning. (CX-2-B10; CX-2-B13.)

Arrests trabecular bone loss (CX-2-B10; CX-2-B13.)

MCHC has been proven not only to stop bone loss but to reverse it. (CX-2-B11.)

4. Bone Builder or MCHC Restores Bone Strength

46. Respondents' ads and promotional materials represented that Bone Builder or MCHC restores bone strength. (See Complaint ¶5.4.) The following excerpts taken from the ads and promotional materials are typical of these claims:

Although you can't stop the passage of time, you can help to keep your bones strong, and even regain bone strength that has already been lost. (CX-2-A4.)

Bone Builder: The Best Solution For Strong & Healthy Bones (CX-2-A4.)

STRONG BONES -- YOU NOW HAVE A CHOICE (CX-2-B2.)

5. Bone Builder or MCHC Halts, Prevents or Treats Osteoporosis

47. Respondents' ads and promotional materials represented that Bone Builder or MCHC halts, prevents or treats osteoporosis. (See Complaint ¶5.5.) The following excerpts taken from the ads and promotional materials are typical of these claims:

Where there is evidence that osteoporosis “runs in the family,” and where there is evidence that calcium loss is already taking place, i.e., muscle spasms, receding gums, or loss of height, the ability of the microcrystalline hydroxyapati[t]e (bone) concentrate places prevention as a matter of the individual sufferer's choice. This safe, reliable, inexpensive, scientifically-tested preventative is his/hers to take as they choose . . . . (CX-2-B2.)

Nothing can restore the spinal posture to normal in those whose spines have already shrunk because of osteoporosis. But there is now good evidence to suggest that microcrystalline hydroxyapatite has a significant effect in preventing the development of osteoporosis, its bone damaging consequences and can actually increase bone growth. (CX-2-B10.)

MICROCRYSTALLINE HYDROXYAPATITE[.] Prevention Against Osteoporosis! (CX-2-B13.)

In those whose spines have already shrunk due to bone loss, there is now good evidence that MCHC can not only increase overall bone density; but also prevent further bone damage due to osteoporosis. (CX-2-B13.)

6. Bone Builder or MCHC Reduces or Eliminates Pain Associated with Bone Ailments

48. Respondents' ads and promotional materials represented that Bone Builder or MCHC reduces or eliminates pain associated with bone ailments. (See Complaint ¶5.6.) The following excerpts taken from the ads and promotional materials are typical of these claims:

MCHC has been reported to improve fracture healing and relieve back pain in women with post menopausal bone loss. (CX-2-A2; CX-2-A5; CX-2-A7; CX-2-A8; CX-2-B11; CX-17.)

A significant statement recurs in a number of reports: MCHC either reduces or totally eliminated bone pain, which was not found true of any other substance. (CX-2-A11; CX-2-B3.)

[M]icrocrystalline hydroxyapatite...decreased pain and increased bone thickness when taken in adequate amounts over long enough periods of time, a record no calcium supplement could achieve. (CX-2-B6.)

7. Bone Builder or MCHC is Superior to and/or More Effective than Other Forms of Calcium in the Prevention and Treatment of Bone Ailments

49. Respondents' ads and promotional materials represented that Bone Builder or MCHC is superior to and/or more effective than other forms of calcium in the prevention and treatment of bone ailments. (See Complaint ¶5.7.) The following excerpts taken from the ads and promotional materials are typical of these claims:

Contains most absorbable form of calcium (CX-2-A1; CX-2-A6.)

Bone Builder is complete bone food. Vital amino acids, mucopolysaccarides [sic], magnesium, zinc, silica, manganese and other special trace minerals are bound together by nature with the most highly absorbable calcium. (CX-2-A1.)

MCHC is proven to help restore lost bone, bone meal and calcium supplements are not! (CX-2-A2; CX-2-A5; CX-2-A7; CX-2-A8; CX-17.)

Bone Builder helps rebuild and restore lost bone. And compared to other calcium supplements, Bone Builder is also the best absorbed form of calcium. (CX-2-A4.)

The superior form of calcium proven to build bone (CX-2-A9; CX-2-A11; CX-2-B8; CX-9.4, p. 6.)

Bone Builder contains Microcrystalline Hydroxyapatite, the only source of calcium proven to not only stop, but reverse bone loss. (CX-2-A12.)

The ONLY Form Of Calcium Proven To Restore Lost Bone. (CX-2-A12.

Contains most absorbable kind of calcium (CX-2-B3; CX-2-B5.)

Only MCHC provides calcium in an “extremely bioavailable form” and the studies on it have “also indicated the superiority of the substance over traditional soluble calcium supplements.” (CX-2-B3.)

BONE BUILDER is not merely another calcium supplement, although it happens to be the most highly absorbable form of calcium known. BONE BUILDER is hypoallergenic, palatable and cost-effective. Most importantly, no other product in the United States is as effective at preventing bone loss. (CX-2-B5.)

[M]icrocrystalline hydroxyapatite halted bone loss, decreased pain and increased bone thickness when taken in adequate amounts over long enough periods of time, a record no other form of calcium could achieve. (CX-2-B6.)

The superior form of calcium (CX-2-B7.)

WHAT IS THE BEST CALCIUM? Hydroxyapatite as found in BONE BUILDER, is the best absorbed and utilized form of calcium for people of all ages. (CX-2-B7.)

Microcrystalline Hydroxyapatite is a superior source of bio-available calcium. (CX-2-B7.)

The active ingredient [MCHC] in Ethical Nutrient's Bone Builder is a superior form of calcium that is proven to restore lost bone. Other forms of calcium cannot make this claim. (CX-2-B9.)

The Superior Form Of Calcium Proven To Restore Lost Bone. (CX-2-B9.)

No other form of calcium has been found to be as effective, as easily absorbed and as useful in all cases of calcium deficit as microcrystalline hydroxyapatite. (CX-2-B10.)

Other forms of calcium have been shown to slow bone loss, but not to stop it in most cases. That means that most people who

take calcium for their bones are still losing bone! MCHC has been proven not only to stop bone loss but to reverse it. MCHC can actually help restore lost bone. (CX-2-B11.)

8. Bone Builder or MCHC is More Bioavailable, More Absorbable, or More Effectively Utilized by the Body Than Other Forms of Calcium

50. Respondents' ads and promotional materials represented that Bone Builder or MCHC is more bioavailable, more absorbable, or more effectively utilized by the body than other forms of calcium. (See Complaint ¶5.8.) The following excerpts taken from the ads and promotional materials are typical of these claims:

Bone Builder is complete bone food. Vital amino acids, mucopolysaccarides [sic], magnesium, zinc, silica, manganese and other special trace minerals are bound together by nature with the most highly absorbable calcium. (CX-2-A1; CX-2-B3.)

Contains most absorbable form of calcium. (CX-2-A1; CX-2-A6.)

And compared to other calcium supplements, Bone Builder is also the best absorbed form of calcium. (CX-2-A4.)

Only MCHC provides calcium in an "extremely bioavailable form" and the studies on it have "also indicated the superiority of the substance over traditional soluble calcium supplements." (CX-2-B3.)

Bone Builder is concentrated microcrystalline hydroxyapatite - the form of bone nutrition best utilized by the body. (CX-2-B3.)

The calcium in MCHC is very well assimilated, in fact MCHC is among the best absorbed calcium sources. (CX-2-A10.)

Contains most absorbable kind of calcium. (CX-2-B3; CX-2-B5.)

BONE BUILDER is not merely another calcium supplement, although it happens to be the most highly absorbable form of calcium known. (CX-2-B5.)

Microcrystalline Hydroxyapatite is a superior source of bio-available calcium. (CX-2-B7.)

WHAT IS THE BEST CALCIUM? Hydroxyapatite as found in BONE BUILDER, is the best absorbed and utilized form of calcium for people of all ages. (CX-2-B7.)

There is speculation as to why an essentially insoluble calcium preparation should be more readily absorbed than soluble alternatives. This is probably the result of a number of factors. Calcium absorption is enhanced in the presence of protein or a [sic] organic matrix and the microcrystalline structure gives a large surface area from which the minerals may be released from the organic matrix into the intestines. CX-2-B10.)

No other form of calcium has been found to be as effective, as easily absorbed and as useful in all cases of calcium deficit as microcrystalline hydroxyapatite. (CX-2-B10.)

Microcrystalline hydroxyapatite [MCHC], therefore, provides the best bioavailable and effective means of preventing and reducing cortical bone thinning. (CX-2-B10; CX-2-B13.)

Best absorbed calcium source (CX-2-B10; CX-2-B13.)

There is speculation as to why an essentially insoluble calcium preparation should be more readily absorbed than soluble alternatives. This is probably the result of a number of factors, including the fact that MCHC is an organic protein calcium matrix from raw, young bone. Calcium absorption is enhanced in the presence of an organic protein matrix, since the microcrystalline structure offers a larger surface area from which the minerals may be released. (CX-2-B13.)

I. The Establishment Claims Alleged In Complaint Paragraph 8 Were Made

1. Scientific Research Proves that Bone Builder or MCHC Builds Bone or Increases Bone Thickness

51. Respondents' ads and promotional materials represented that scientific research proves that Bone Builder or MCHC builds bone or increases bone thickness. (See Complaint ¶8.1.) The following excerpts taken from the ads and promotional materials are typical of these claims:

Scientific studies have shown that a remarkable new substance called Microcrystalline Hydroxyapatite Concentrate (MCHC) can increase bone density even in cases of advanced bone loss. (CX-2-A1; CX-2-A2; CX-2-A5; CX-2-A7; CX-2-A8; CX-2-B11; CX-17.)

Researchers Confirm Superior Calcium *REVERSES BONE LOSS* (CX-2-A2; CX-2-A5; CX-2-A7; CX-2-A8; CX-2-B11; CX-17.)

Scientific studies have verified that oral consumption of this type of specially processed bone (MCHC) supplement can increase bone density even in cases of advanced bone loss! (CX-2-A2; CX-2-A5; CX-2-A7; CX-2-A8; CX-17.)

Research Shows New, Superior Form Of Calcium Increases Bone Density And Reverses Bone Loss. (CX-2-A3.)

Recent studies have shown that oral consumption of a remarkable new substance called Microcrystalline Hydroxyapatite Concentrate (MCHC) can increase bone density even in cases of advanced bone loss. (CX-2-A3.)

The superior form of calcium proven to build bone. (CX-2-A9; CX-2-A11; CX-2-B8; CX-9.4, p. 6.)

The latest research shows “microcrystalline hydroxy-apatite” is the superior form of calcium that can build bone. (CX-2-A9; CX-2-A11; CX-2-B8; CX-9.4, p. 6.)

Bone Builder contains Microcrystalline Hydroxyapatite, the only source of calcium proven to not only stop, but reverse bone loss. (CX-2-A12.)

Bone Mend consists of a number of components indicated by basic clinical research to promote increases in bone growth and density. (CX-2-B1.)

These are just a few of the controlled clinical trials to be found in the literature. The consensus of which is that microcrystalline hydroxyapatite halted bone loss, decreased pain and increased bone thickness when taken in adequate amounts over long enough periods of time, a record no calcium supplement could achieve. (CX-2-B6.)

Nothing can restore the spinal posture to normal in those whose spines have already shrunk because of osteoporosis. But there is now good evidence to suggest that microcrystalline hydroxyapatite has a significant effect in preventing the development of osteoporosis, its bone damaging consequences and can actually increase bone growth. (CX-2-B10.)

MCHC has been proven not only to stop bone loss but to reverse it. (CX-2-B11.)

Scientific studies have verified that oral consumption of a properly processed MCHC supplement can increase bone density even in cases of advanced bone loss! (CX-2-B11.)

In those whose spines have already shrunk due to bone loss, there is now good evidence that MCHC can not only increase overall bone density, but also prevent further bone damage due to osteoporosis. (CX-2-B13.)

In fact, in tests, MCHC as a bone food has been shown to actually produce a significant increase in bone mass, which has not been demonstrated in other form of calcium. (CX-9.4, p. 7.)

2. Scientific Research Proves that Bone Builder or MCHC Restores Lost Bone

52. Respondents' ads and promotional materials represented that scientific research proves that Bone Builder or MCHC restores lost bone. (See Complaint ¶8.2.) The following excerpts taken from the ads and promotional materials are typical of these claims:

Researchers Confirm Superior Calcium *REVERSES BONE LOSS* (CX-2-A2; CX-2-A5; CX-2-A7; CX-2-A8; CX-2-B11; CX-17.)

MCHC is proven to help restore lost bone; bone meal and calcium supplements are not! (CX-2-A2; CX-2-A5; CX-2-A7; CX-2-A8; CX-17.)

Research Shows New, Superior Form Of Calcium Increases Bone Density And Reverses Bone Loss (CX-2-A3.)

BONE BUILDER can restore bone and has clinical evidence to prove it! (CX-2-A9; CX-2-B8.)

Research has proven that MCHC effectively restores lost bone. (CX-2-A10.)

BONE BUILDER can restore lost bone and has the clinical evidence to prove it! (CX-2-A11; CX-9.4, p. 6.)

Bone Builder contains Microcrystalline Hydroxyapatite, the only source of calcium proven to not only stop, but reverse bone loss. (CX-2-A12.)

The ONLY Form Of Calcium Proven To Restore Lost Bone. (CX-2-A12.)

The active ingredient [MCHC] in Ethical Nutrient's Bone Builder is a superior form of calcium that is proven to restore lost bone. (CX-2-B9.)

The Superior Form of Calcium Proven To Restore Lost Bone (CX-2-B9.)

MCHC has been proven not only to stop bone loss but to reverse it. MCHC can actually help restore lost bone. (CX-2-B11.)

3. Scientific Research Proves that Bone Builder or MCHC Halts or Prevents Bone Loss or Bone Thinning

53. Respondents' ads and promotional materials represented that scientific research proves that Bone Builder or MCHC halts or prevents bone loss or bone thinning. (See Complaint ¶8.3.) The following excerpts taken from the ads and promotional materials are typical of these claims:

Researchers Confirm Superior Calcium *REVERSES BONE LOSS* (CX-2-A2; CX-2-A5; CX-2-A7; CX-2-A8; CX-2-B11; CX-17.)

Bone Builder contains Microcrystalline Hydroxyapatite, the only source of calcium proven to not only stop, but reverse bone loss. (CX-2-A12.)

Dixon's research of the many common forms of calcium used in the trials demonstrated effectively that only one form of calcium was capable of preventing bone thinning and actually restoring bone strength, and that was "whole bone extract (microcrystalline hydroxyapatite concentrate) (which) is well absorbed and does not have the disadvantages of the former preparations." (CX-2-B2.)

These are just a few of the controlled clinical trials to be found in the literature. The consensus of which is that

microcrystalline hydroxyapatite halted bone loss, decreased pain and increased bone thickness when taken in adequate amounts over long enough periods of time, a record no calcium supplement could achieve. (CX-2-B6.)

MCHC has been proven not only to stop bone loss but to reverse it. (CX-2-B11.)

4. Scientific Research Proves that Bone Builder or MCHC Restores Bone Strength

54. Respondents' ads and promotional materials represented that scientific research proves that Bone Builder or MCHC restores bone strength. (See Complaint ¶8.4.) The following excerpt, taken from a promotional material, typifies this claim:

Dixon's research of the many common forms of calcium used in the trials demonstrated effectively that only one form of calcium was capable of preventing bone thinning and actually restoring bone strength, and that was "whole bone extract (microcrystalline hydroxyapatite concentrate) (which) is well absorbed and does not have the disadvantages of the former preparations." (CX-2-B2.)

5. Scientific Research Proves that Bone Builder or MCHC Halts, Prevents or Treats Osteoporosis

55. Respondents' ads and promotional materials represented that scientific research proves that Bone Builder or MCHC halts, prevents or treats osteoporosis. (See Complaint ¶8.5.) The following excerpts taken from the ads and promotional materials are typical of these claims:

[R]esearch demonstrates that osteoporosis can safely and effectively be treated with a specially processed bone concentrate from young cattle. This remarkable new substance is called MCHC, and its introduction into mainstream American

health maintenance could mean longer, healthier lives for literally millions of people. (CX-2-A1.)

Important and exciting research demonstrates that osteoporosis can safely and effectively be treated with a specially processed bone concentrate from young cattle. This remarkable new substance called Microcrystalline Hydroxyapatite Concentrate (MCHC), could mean longer, healthier lives for literally millions of people. (CX-2-A2; CX-2-A5; CX-2-A7; CX-2-A8; CX-2-B11; CX-17.)

Of the substances used for experimentation to halt the progress of osteoporosis, only microcrystalline hydroxyapatite was considered to be totally free of "major potential hazard," which indicated its use for both "the treatment and prevention of osteoporosis." (CX-2-A11; CX-2-B3.)

Where there is evidence that osteoporosis "runs in the family," and where there is evidence that calcium loss is already taking place, i.e., muscle spasms, receding gums, or loss of height, the ability of the microcrystalline hydroxyapati[t]e (bone) concentrate places prevention as a matter of the individual sufferer's choice. This safe, reliable, inexpensive, scientifically-tested preventive is his/hers to take as they choose and not dependent upon the whim of another. (CX-2-B2.)

The only positive reports on halting the devastation and crippling of osteoporosis have come through the medical administration of small, carefully monitored quantities of estrogen along with calcium, or through the administration of a product little known in the United States, but widely used in Europe and England: microcrystalline hydroxyapatite. (CX-2-B6.)

Nothing can restore the spinal posture to normal in those whose spines have already shrunk because of osteoporosis. But there is now good evidence to suggest that microcrystalline hydroxyapatite has a significant effect in preventing the

development of osteoporosis, its bone damaging consequences and can actually increase bone growth. (CX-2-B10.)

In those whose spines have already shrunk due to bone loss, there is now good evidence that MCHC can not only increase overall bone density, but also prevent further bone damage due to osteoporosis. (CX-2-B13.)

6. Scientific Research Proves that Bone Builder or MCHC Reduces or Eliminates Pain Associated with Bone Ailments

56. Respondents' ads and promotional materials represented that scientific research proves that Bone Builder or MCHC reduces or eliminates pain associated with bone ailments. (See Complaint ¶8.6.) The following excerpts taken from the ads and promotional materials are typical of these claims:

MCHC has been reported to improve fracture healing and relieve back pain in women with post menopausal bone loss. (CX-2-A1; CX-2-A5; CX-2-A7; CX-2-A8; CX-2-B11; CX-17.)

In the intervening decade many other controlled tests have been conducted in English hospitals. A significant statement recurs in a number of reports: MCHC either reduced or totally eliminated bone pain, which was not found true of any other substance. (CX-2-A11; CX-2-B3.)

These are just a few of the controlled clinical trials to be found in the literature. The consensus of which is that microcrystalline hydroxyapatite halted bone loss, decreased pain and increased bone thickness when taken in adequate amounts over long enough periods of time, a record no calcium supplement could achieve. (CX-2-B6.)

7. Scientific Research Proves that Bone Builder or MCHC is Superior to and/or More Effective Than Other Forms of

Calcium in the Prevention or Treatment
of Bone Ailments

57. Respondents' ads and promotional materials represented that scientific research proves that Bone Builder or MCHC is superior to and/or more effective than other forms of calcium in the prevention or treatment of bone ailments. (See Complaint ¶8.7.) The following excerpts taken from the ads and promotional materials are typical of these claims:

Researchers Confirm Superior Calcium *REVERSES BONE LOSS* (CX-2-A2; CX-2-A5; CX-2-A7; CX-2-A8; CX-2-B11; CX-17.)

MCHC is proven to help restore lost bone; bone meal and calcium supplements are not! (CX-2-A2; CX-2-A5; CX-2-A7; CX-2-A8; CX-17.)

Research shows new, superior form of calcium increases bone density and reverses bone loss. (CX-2-A3.)

The superior form of calcium proven to build bone (CX-2-A9; CX-2-A11; CX-2-B8; CX-9.4, p. 6.)

The latest research shows "microcrystalline hydroxy-apatite" is the superior form of calcium that can build bone. (CX-2-A9; CX-2-A11; CX-2-B8; CX-9.4, p. 6.)

Some calcium supplements can be worse than not taking anything at all. At best, others may slow bone loss, occasionally stopping it. But, BONE BUILDER can restore bone and has clinical evidence to prove it! (CX-2-A9; CX-2-B8.)

Only MCHC provides calcium in an "extremely bioavailable form" and the studies on it have "also indicated the superiority of the substance over traditional soluble calcium supplements." Of the substances used for experimentation to halt the progress of osteoporosis, only microcrystalline hydroxyapatite was considered to be totally free of "major potential hazard," which

indicated its use for both “the treatment and prevention of osteoporosis.” (CX-2-A11; CX-2-B3.)

Some calcium supplements can be worse than not taking anything at all. At best, others may slow bone loss, occasionally stopping it. But, BONE BUILDER can restore lost bone and has clinical evidence to prove it! (CX-2-A11; CX-9.4, p. 6.)

Bone Builder contains Microcrystalline Hydroxyapatite, the only source of calcium proven to not only stop, but reverse bone loss. (CX-2-A12.)

The ONLY Form Of Calcium Proven To Restore Lost Bone. (CX-2-A12.)

Dixon's research of the many common forms of calcium used in the trials demonstrated effectively that only one form of calcium was capable of preventing bone thinning and actually restoring bone strength, and that was “whole bone extract (microcrystalline hydroxyapatite concentrate) (which) is well absorbed and does not have the disadvantages of the former preparations.” (CX-2-B2.)

BONE BUILDER is a pure microcrystalline hydroxyapatite compound (MCHC), a substance which has been scientifically demonstrated to be the most effectively utilized source of calcium known. This highly useful substance is distinguished by its unusual ability to be absorbed into the bloodstream. For example, studies have shown it to be absorbed at twice the rate of calcium gluconate. (CX-2-B5.)

These are just a few of the controlled clinical trials to be found in the literature. The consensus of which is that microcrystalline hydroxyapatite halted bone loss, decreased pain and increased bone thickness when taken in adequate amounts over long enough periods of time, a record no calcium supplement could achieve. (CX-2-B6.)

The active ingredient in Ethical Nutrient's Bone Builder is a superior form of calcium that is proven to restore lost bone. Other forms of calcium cannot make this claim. (CX-2-B9.)

The Superior Form of Calcium Proven To Restore Lost Bone (CX-2-B9.)

Microcrystalline hydroxyapatite (MCHC) is a comprehensive supplement which appears to provide calcium in an extremely bioavailable form. This has been demonstrated in a number of calcium balance and calcium absorption studies, many of which have indicated the superiority of MCHC over traditional soluble calcium supplements. (CX-2-B10.)

No other form of calcium has been found to be as effective, as easily absorbed and as useful in all cases of calcium deficit as microcrystalline hydroxyapatite [MCHC]. (CX-2-B10; CX-2-B13.)

Other forms of calcium have been shown to slow bone loss, but not to stop it in most cases. That means that most people who take calcium for their bones are still losing bone! MCHC has been proven not only to stop bone loss but to reverse it. MCHC can actually help restore lost bone. (CX-2-B11.)

In fact, a number of calcium balance and absorption studies have proven MCHC to be superior over traditional soluble calcium supplements. MCHC also contains fluoride, which is incorporated into the skeleton as *fluorapatite* and this may reduce the resorption of bone. . . . MCHC, therefore, provides the best bioavailable and effective means of preventing and reducing cortical bone thinning. (CX-2-B13.)

8. Scientific Research Proves that Bone Builder or MCHC is More Effectively

Utilized by the Body Than Other Forms of Calcium[4]

58. Respondents' ads and promotional materials represented that scientific research proves that Bone Builder or MCHC is more effectively utilized by the body than other forms of calcium. (See Complaint ¶8.8.) The following excerpts taken from the ads and promotional materials are typical of these claims:

> Only MCHC provides calcium in an "extremely bioavailable form" and the studies on it have "also indicated the superiority of the substance over traditional soluble calcium supplements." (CX-2-B3.)
>
> BONE BUILDER is a pure microcrystalline hydroxyapatite compound (MCHC), a substance which has been scientifically demonstrated to be the most effectively utilized source of calcium known. This highly useful substance is distinguished by its unusual ability to be absorbed into the bloodstream. For example, studies have shown it to be absorbed at twice the rate of calcium gluconate. (CX-2-B5.)
>
> Microcrystalline hydroxyapatite (MCHC) is a comprehensive supplement which appears to provide calcium in an extremely bioavailable form. This has been demonstrated in a number of calcium balance and calcium absorption studies, many of which have indicated the superiority of MCHC over traditional soluble calcium supplements. (CX-2-B10.)
>
> No other form of calcium has been found to be as effective, as easily absorbed and as useful in all cases of calcium deficit as microcrystalline hydroxyapatite [MCHC]. (CX-2-B10; CX-2-B13.)

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[4]Although establishment claim ¶8.8 is worded slightly differently from the corresponding objective product claim ¶5.8, the phrases "more bioavailable" and "more absorbable" as used in ¶5.8 are virtually synonymous with "more effectively utilized by the body" and are, therefore, included in this claim.

Best absorbed calcium source * * * Proven by scientific studies on humans (CX-2-B10; CX-2-B13.)

Microcrystalline hydroxyapatite (MCHC) is a comprehensive bone supplement which has been demonstrated to provide calcium in an extremely bioavailable form. * * * In fact, a number of calcium balance and absorption studies have proven MCHC to be superior over traditional soluble calcium supplements. (CX-2-B13.)

J. The Representation Made By Use Of The Trade Name "Bone Builder"

59. Through the use of the trade name "Bone Builder," respondents represented that the product builds bone or increases bone thickness. They did not represent that it restores lost bone. (See Complaint ¶10 - ¶12.) The following excerpts taken from the ads and promotional materials are typical of these claims:

Bone Builder is the best selling product in the marketplace for actually building bone. (CX-2-A1.)

WORLD'S BEST BONE BUILDER (CX-2-A1; CX-2-B2; CX-2-B5.)

You Can Do Something About Bone Loss - Fight Back With The World's Best Bone Builder! (CX-2-A4.)

THE ONE AND ONLY BONE BUILDER (CX-2-A6.)

Bone Builder Builds Bone Like Nothing Else Can! (CX-2-B3.)

Bone Builder is the best. It builds bone - naturally, quickly and safely. (CX-2-B3.)

OUR BONE BUILDER BUILDS PROFITS AND BONE (CX-2-B9.)

The best Bone Builder for your customers. (CX-2-B9.)

K. The Parties' Expert Witnesses

1. Complaint Counsel's Expert Witnesses

(a) Dr. Lawrence G. Raisz

60. Dr. Raisz is a graduate of Harvard Medical School and is currently a professor of medicine and head of the Division of Endocrinology and Metabolism at the University of Connecticut Health Center. He is also the program director for its general clinical research center.

61. Dr. Raisz has, for forty years, been interested in bone metabolism, is one of the founders of the American Society of Bone and Mineral Research, and is on the editorial boards of most of the journals involved with bone research. (Tr. 39.) He is a member of the scientific advisory board of the National Osteoporosis Foundation, and chairs its education committee. (Tr. 39-40.)

62. Dr. Raisz is an expert in bone biology and bone cells, and in his opinion has more knowledge in that area than Dr. Heaney, one of respondents' experts; on the other hand, Dr. Heaney's knowledge of calcium supplementation and calcium absorption is greater than Dr. Raisz'. (Tr. 109.)

(b) Dr. Michael F. Holick

63. In 1971, Dr. Holick received a Ph.D. in biochemistry from the University of Wisconsin. In 1976, he received his M.D. degree from the same school. He was an intern and resident at Harvard Medical School.

64. Dr. Holick is a professor of dermatology, endocrinology and physiology at the Boston University Medical Center. He is director of the general clinical research center, the osteoporosis clinic, and the Vitamin D skin and bone research laboratory at the University. (Tr. 286-88.)

65. Dr. Holick's laboratory conducts research into Vitamin D, calcium metabolism and bone health, and the osteoporosis clinic treats patients with that disease. (Tr. 288-89.)

66. Dr. Holick has written several articles dealing with calcium metabolism and bone health. (Tr. 290.) He also gives 20-25 lectures a year on osteoporosis to general practitioners and conducts grand rounds at the medical schools and other institutions dealing with osteoporosis. (Tr. 292-93.)

67. Dr. Holick serves on the board of several learned journals and is a member of the American Association of Physicians, a prestigious organization whose members are invited and elected, as well as many other societies. (294-95.)

68. Respondents challenge Dr. Holick's credibility, bias, and ethics. (RPF 107-118.) While I disagree with Dr. Holick's testimony in many respects, I reject respondents' claims. Dr. Holick testified at great length with respect to complicated issues and I have no reason to believe that he was biased, lacked credibility or acted unethically.

2. Respondents' Expert Witnesses

(a) Dr. Paul A. Lachance

69. Dr. Lachance is the Chairman of the Food Science Department at Rutgers University and is a professor of food science and nutrition. (Tr. 1593.) Food Science is the study of the biology, chemistry and physics involved in the processing of food. The science of nutrition studies the biological and physiological process involved in the growth, maintenance and repair of an organism and its organs. (Tr. 1594.) Dr. Lachance specializes in the interface between these two disciplines. (Tr. 1595.) He is a member of several learned societies. (Tr. 1596-98.)

70. Dr. Lachance has been involved with the United States astronaut program for several years (Tr. 1599-1600), particularly with respect to the effects of weightlessness on the metabolism of bones,

muscles, and the heart. At one time, Dr. Lachance was in charge of NASA's research into bone loss in astronauts. (Tr. 1603)

71. Dr. Lachance is on the board of the Journal of the American College of Nutrition and is editor of a monthly newsletter, Food, Nutrition and Health. (Tr. 1613.) He has also served on several peer review panels of scholarly journals. (Tr. 1615-18) One particular area of his expertise is calcium as it relates to bone metabolism. (Tr. 1621.) He has also lectured on osteoporosis. (Tr. 1622-23.)

(b) Dr. Robert P. Heaney

72. Dr. Heaney is a graduate of the Creighton University School of Medicine. After obtaining his medical degree, Dr. Heaney was trained in clinical research at the Oklahoma Medical Research Foundation and at the NIH, Bethesda, MD. (Tr. 2282-83.)

73. Dr. Heaney became chairman of Creighton's Department of Internal Medicine in 1961 and was, simultaneously, head of its Department of Endocrinology and Metabolism. Two years later he became the chancellor for all the health programs at Creighton. For the past twelve years, he has done pure research. (Tr. 2283.)

74. Dr. Heaney is a fellow of several learned societies and has twenty-one scientific committee memberships. (Tr. 2284-88.)

75. Dr. Heaney, a world-recognized authority on calcium (Tr. 1297), who was described by Dr. Lachance as a giant in his field (Tr. 1675, 1778-79, is a member of the board of the National Osteoporosis Foundation and serves on its scientific advisory board. (Tr. 2288-89.) He is or has been on the editorial boards of nine scientific publications, including the Journal of Bone and Mineral Research and serves as a peer reviewer for several publications. (Tr. 2292-93.)

76. Dr. Heaney has had eighty-one abstracts and ninety-one scientific papers published. (Tr. 2296-97.) He is a member of Creighton's osteoporosis research center. (Tr. 2298.)

(c) Dr. Linda G. Strause

77. Dr. Strause obtained her doctorate in developmental neurophysiology at the University of California, Santa Barbara. She is an adjunct professor at the University and has done clinical research in trace mineral metabolism, the biochemistry of trace minerals, and bone metabolism and nutrition. (Tr. 2680-81.)

78. Dr. Strause is an adjunct visiting professor at the University of California, San Diego, where she teaches an introduction to human nutrition, including the role of calcium in the body. (Tr. 2682-83.) Dr. Strause is conducting a clinical trial on a new therapy for osteoporosis for Quintiles, Inc. (Tr. 2684) and has been involved in other trials. (Tr. 2685-94.) She is a member of several learned societies (Tr. 2695-96) and she had 46 scientific papers published. (Tr. 2696-97.) She considers herself an expert in trace minerals and bone metabolism. (Tr. 2690.)

L. Standards of Substantiation Required By Experts

79. Experts testifying for the parties agree that to establish the efficacy of particular treatments for bone ailments, the ideal, or "gold standard" (Tr. 1258-62) should be a prospective intervention trial or study which is randomized, double-blind, and placebo-controlled, and which observes the effects of changes in a single variable, such as calcium intake, over a period of one to three years. (Tr. 862-64, 985-89, 3168, 70-72, 78; see Tr. 589-90, 738, 786, 925, 928, 965, 1027; see also Tr. 2493, 2582, 1655, 1693, 1746-47.)

80. The results of such a trial must be statistically significant, and where a new treatment is involved, it is preferable to have confirming studies. (See, however, Heaney, Tr. 2661 (ignoring suggestions raised by data because the differences are not statistically significant is a mindless application of a standard).) While epidemiologic and retrospective studies can provide useful information, the population may not provide the accuracy offered by studying a randomized population. (Tr. 76, 77-78, 985.)

81. An example of an ideal study to determine the efficacy of a treatment for osteoporosis is provided by one recently accepted by the U.S. Food and Drug Administration ("FDA"). This study involved approximately 1,000 patients with low bone density and osteoporosis. Patients were given either calcium with a placebo or calcium and the drug being tested. They were followed for three years and bone density and fracture incidence were recorded. The drug-treated population experienced a 30% reduction in vertebral fractures, and the FDA considered this sufficient grounds to approve the drug. (Tr. 68.)

82. No studies have been performed using Bone Builder and no long-term randomized prospective studies or trials have been conducted with MCHC. (Tr. 73.) However, since calcium is calcium (F. 357), studies of other forms of calcium are relevant. Such studies, including randomized clinical trials, have been conducted:

> If you would give us your opinion of what would constitute competent and reliable scientific evidence to prove both -- each of those claims. [3 and 5]
>
> A. If we talk about bone loss, which is both 3 and 5, because bone mass is one of the measures of osteoporosis and may be the way the diagnosis is made, then a competent investigation would be a randomized controlled trial in which one group was given calcium and the other one wasn't. And in which the rate of change of bone mass over time was measured. And in which it was found that the rate of change on calcium was less negative or maybe even positive or zero in comparison with the rate of change on --
>
> Those studies have been done over and over again and we referred to them at great length yesterday. (Heaney, Tr. 2582.)

M. Respondents' Substantiation

1. Mr. Katke's Qualifications To Judge Whether Metagenics' Claims Were Supported By Scientific Evidence

83. Mr. Katke, Metagenics' CEO, searched for and reviewed the scientific literature on MCHC before deciding to market Bone Builder. (Tr. 1440-43, 1448-54.)

84. According to Mr. Katke, his review of the scientific literature substantiates the claims challenged in the complaint. (Tr. 1422-28, 1507.) He decided the content of Metagenics' ads for Bone Builder. (Tr. 1473-74.)

85. Prior to advertising Bone Builder, Mr. Katke did not ask either his consultants, Dr. Jeffrey Bland and Dr. Jerry Meduski, or his trial experts, Dr. Heaney, Dr. Lachance, and Dr. Strause, to read any of the scientific articles on MCHC. (Tr. 1448-49, 1459-60, 1474, 2484, 2486, 1696-97; see 2709, 2726.)

86. Mr. Katke is neither a physician nor a scientist and he is not qualified to judge whether the substantiation proffered by Metagenics substantiates the claims made in the challenged ads. (Tr. 1432, 1430, 1409, 1429, 1410-14.)

2. The Substantiation Documents Offered By Metagenics

87. The documents offered as substantiation by Metagenics (RPF 132 et. seq.) were rejected by complaint counsel's experts as not supporting its claims. Several reasons were given by their experts:

(a) Review Articles

88. Reviews are not original; they are, rather, a summary of other studies, and they are not evidence which can substantiate scientific conclusions. (Tr. 206-07, 250-52, 338, 445, 781-82.)

(b) Editorials

89. An editorial is an expression of personal opinion and does not provide a solid basis for a scientific conclusion. (Tr. 338, 577, 743-44.)

(c) Book Chapters

90. Book chapters are not scientific studies. (Tr. 551, 637-84, 774-75.)

(d) Abstracts

91. As a general rule, scientists do not rely on abstracts because they are preliminary reports which are usually not peer reviewed. (Tr. 655.)

(e) Studies In Which Subjects Received Vitamin D

92. Because Vitamin D is essential for calcium absorption in the intestine (Tr. 55), it may be that any benefits demonstrated by a test group supplemented with Vitamin D are due to its effects rather than to the calcium. (Tr. 43, 55, 334, 347, 2190-92, 228-29.)

(f) Animal Studies

93. Scientific tests involving animal models do not provide substantiation for claims involving human bone health. (Tr. 324-25.)

(g) Other Bone Diseases And Unusual Forms Of Osteoporosis

94. It is not appropriate to extrapolate from studies involving unusual bone diseases to the claims at issue here. (Tr. 75-76, 334, 51-52, 801-03, 477, 352-54, 93-94, 518-19, 728, 827, 919, 347-50, 873.)

(h) Bed Rest

95. Bone loss associated with bed rest is unique and conclusions from studies involving bed rest cannot be extrapolated to other patterns of bone loss. (Tr. 560-62, 798-99, 953.)

(i) Formative Years

96. To the extent that calcium contributes to bone-building during the formative years, articles that address this period of life cannot be extrapolated to adults. (Tr. 755-57, 967, 977-78.)

N. Analysis of Scientific Papers Offered By Respondents As Substantiation For The Claims Which Were Made

97. Respondents have offered clinical tests, scientific papers and scientific studies as substantiation for claims 1 through 8 in Paragraphs 5 and 8. Each scientific paper, etc., is described and analyzed with respect to each claim or claims which they allegedly substantiate.

98. My analysis of these scientific papers keeps in mind the rigorous scientific standards discussed by Dr. Raisz and Dr. Holick. See, e.g., Tr. 3188:

Q. Dr. Holick.... Is it your testimony that a scientific paper which reports the results of prior well-conducted clinical trials is not reporting scientific fact.

A. That's correct.

However, I have considered these studies in light of other considerations such as the professional qualifications of the researchers (Dr. Lachance: if a review is by Dr. Heaney, "it's okay," Tr. 1725) (but see Dr. Holick Tr. 567-69) and whether the paper is peer-reviewed (Heaney, Tr. 2334: "Review articles are peer reviewed. Even editorials are peer reviewed. These journals generally have very high standards").

99. Dr. Heaney also stated that while review articles are not evidence (Tr. 2534) and that he would not, in general, rely on one as substantiation (Tr. 2534):

since review articles are peer reviewed . . . if one makes a statement in a review article or summarizes the literature and says: "Here is what it shows," that's not -- to begin with that's not just opinion. That's simply a restatement of the facts. (Tr. 2535.) (But see Dr. Holick, Tr. 3170-71.)

Dr. Heaney also testified that if he were a manufacturer trying to make a new product for the elderly, "I'd start with reviews." This is particularly appropriate:

> when a consensus is achieved as was true in the case for increased calcium intake, then I would think that I could rely upon [review articles] without having to go further. . . . (Tr. 2327, 2535.)

100. Furthermore, the complaint does not allege that only gold standard studies are acceptable as substantiation. See ¶8 which defines "scientific research" as "including clinical tests, scientific papers and/or scientific studies. . . ."

101. My analysis of respondents' substantiation documents gives little weight to those which respondents' experts did not discuss at trial as well as those whose merits are not discussed in their proposed findings (that is, those articles which are merely described by their experts as being written and published by reputable authors and publishers). (See, for example, CX-7-CAL-64 (F. 131).)

102. Finally, while each document is, by necessity, categorized as substantiating, or not substantiating, a particular claim, it should be understood that none of them have been considered in isolation. Rather, they contribute to a body of evidence, including expert testimony, from which one can determine whether a particular claim is or is not substantiated.

1. Claim 1: Bone Builder or MCHC Builds Bone or Increases Bone Thickness

103. CX-7-MCHC-1: The Influence of Ossein-Hydroxyapatite Compound ("Ossopan")[5] on the Healing of a Bone Defect, by M. Annefeld, et al., in The Journal of Current Medical Research and Opinion (1986).

This is an animal study which examined the effects of different calcium preparations in healing defects made in the bones of rabbits. I agree with Dr. Holick that this article does not substantiate a finding that calcium or MCHC builds bone or increases bone thickness in humans. (Tr. 324, 870-71.)

104. CX-7-MCHC-8: Extracts of Bone Contain a Potent Regulator of Bone Formation by R.H. Drivdahl, G.A. Howard and D.J. Baylink, in Biochimica et Biophysica Acta. (1982).

This study is irrelevant since it was designed to determine how protein is made in rat bones. This article did not study the effect of calcium or MCHC on bone building and does not substantiate claim 1. (Tr. 339-40, 472, 872-73, 2113-14.)

105. CX-7-MCHC-10: Vitamin D. Hydroxyapatite and Calcium Gluconate in Treatment of Cortical Bone Thinning in Postmenopausal Women With Primary Biliary Cirrhosis by Owen Epstein, Sheila Sherlock, et al., in The American Journal of Clinical Nutrition (1982).

This study concluded that calcium plus vitamin D "prevents or retards" cortical bone thinning in patients with primary biliary cirrhosis. This result does not substantiate claim 1 since it was not statistically significant. (Tr. 873.)

106. CX-7-MCHC-13: The Use of a Whole Bone Extract in the Treatment of Fractures by T.J. Mills, et al., in Manitoba Medical Review (1965).

Dr. Heaney testified that this study could be construed as substantiating claim 1 if fracture healing is considered to be building bone. (Tr. 2470.) Since he did not give a firm opinion, I find that it does not substantiate claim 1. (Tr. 874-75.)

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[5]Ossopan is essentially the same as MCHC. (Tr. 205-06.)

107. CX-7-MCHC-15: Clinical Trial of Microcrystalline Hydroxyapatite Compound ('Ossopan') in the Prevention of Osteoporosis Due to Corticosteroid Therapy by A. Pines, et al., in Current Medical Research and Opinion (1984).

This study is rejected as substantiation for claim 1 because no statistical difference was reported between the two groups involved. (Tr. 919-20.) The merits of this study were not discussed by respondents' experts.

108. CX-7-MCHC-17 Examination of New Bone Growth on Aluminum Oxide Implant Contact Surfaces After Oral Administration of Ossein-Hydroxyapatite Compound to Rats by K.H. Schmidt, et al., in Current Medical Research and Opinion (1988).

Although stating that results from rat studies may be applicable to humans (Tr. 2212), Dr. Holick testified that this study using rats provides no insight into the impact of MCHC or calcium on bone thickness or bone building. (Tr. 479-80.) This study, which was not discussed by respondents' experts, does not substantiate claim 1.

109. CX-7-MCHC-18: Microcrystalline Hydroxyapatite Compound in Prevention of Bone Loss in Corticosteroid-Treated Patients with Chronic Active Hepatitis by A. Stellon, et al., in Postgraduate Medical Journal (1985).

This study did not examine the effects of calcium or MCHC on bone building or bone thickness and cannot substantiate claim 1. (Tr. 920.)

110. CX-7-CAL-3: Osteoporosis: Effects of Calcium by Anthony A. Albanese, et al., in American Family Practitioner (1978).

Dr. Holick agreed with this review article's statement that "bone loss and fracture risk 'may be' minimized or reversed by a daily intake of calcium" provided that the patient is calcium deficient. (Tr. 1892-93.) He also agreed that the statement that bone loss in elderly women may be decelerated or reversed by taking calcium supplements is "a reasonable

comment." (Tr. 1894.) This article therefore provides some substantiation for claim 1.

111. CX-7-CAL-4: Problems of Bone Health in Elderly by Anthony A. Albanese, et al., in New York State Medical Journal (1975).

I agree with Dr. Holick that this review article does not substantiate claim 1. (Tr. 921-22, 1820-23, 2203.) None of respondents' experts testified about the merits of this review.

112. CX-7-CAL-8: Spinal Bone Density and Calcium Intake in Healthy Postmenopausal Women by Mark Andon, Linda Strause, et al., in American Journal of Clinical Nutrition (1991).

Although Dr. Strause, one of the authors of this study, testified that its results substantiate some claims for calcium (Tr. 2746-47), I accept Dr. Holick's criticism that this study did not examine the effects of calcium or MCHC on bone building, or bone thickness, and does not, therefore, substantiate claim 1. (Tr. 738.)

113. CX-7-CAL-9: Symposium: Required versus Optimal Nutrient Intakes: A look at Calcium -- Supplemental Trials With Calcium Citrate Malate: Evidence in Favor of Increasing the Calcium RDA During Childhood and Adolescence by Mark B. Andon, Tom Lloyd and Velimir Matkovic, in American Institute of Nutrition (1994).

This review article does not provide substantiation for claim 1 since it deals with the calcium RDA for children. (Tr. 738-40.) Although it claims that other studies "suggest" an affirmative answer, it cautions that "an important question which cannot be addressed is whether increased calcium intake during youth provides for a sustained increase in bone mass in adulthood." (P. 1416S.) This article does not clearly support claim 1 and I reject it as substantiation.

114. CX-7-CAL-11: Calcium Intake and Bone Health by Louis V. Avioli and Robert P. Heaney, in Calcified Tissue International (1991).

This is an editorial which recommends that despite the lack of unanimity, the RDA for calcium should be increased. This editorial does not substantiate a finding that calcium builds bone or increases bone thickness. (Tr. 743-44.)

115. CX-7-CAL-14: Dietary Modification with Dairy Products for Preventing Vertebral Bone Loss in Premenopausal Women: A Three-Year Prospective Study, by Daniel Baran, et al., in Journal of Clinical Endocrinology and Metabolism (1990).

This article reports the results of a randomized double-blind prospective study which concluded that "After 30 months of dairy product supplementation, the bone density of the experimental group was significantly greater than that of the controls" ($P < 0.02$). (P. 266.)

Despite the criticism that this study involves a confounding factor, vitamin D, Dr. Heaney testified, and I find, that this article substantiates claim 1 (Tr. 2461).

116. CX-7-CAL-16: Coffee-Associated Osteoporosis Offset by Daily Milk Consumption by Elizabeth Barrett-Connor, in Journal of the American Medical Association (1994).

This retrospective study is irrelevant and does not substantiate a finding that calcium builds bone or increases bone thickness. (Tr. 748.)

117. CX-7-CAL-23: Calcium, Estrogen, and Progestin in the Treatment of Osteoporosis by Neil Breslau, in Rheumatic Disease Clinics of North America (1994).

This is a review article which does not substantiate the claim that calcium or MCHC builds bone or increases bone thickness. (Tr. 386-88.) Respondents' experts did not discuss this article.

118. CX-7-CAL-31: Dietary Calcium and Bone Mineral Status of Children and Adolescents by Gary Chan, in American Journal Dis. Child.

This study concludes that there is an association between bone mineral content and dietary calcium intake, but this does not establish that calcium or MCHC builds bone or increases bone thickness. (Tr. 528-29, 879-80.)

119. CX-7-CAL-33: Calcium and Vitamin D Supplements: Effects on Calcium Metabolism in Elderly People by Marie-Claire Chapuy, Pierre Meunier, et ano., in American Journal of Clinical Nutrition (1987).

This report of a randomized, controlled study does not substantiate claim 1 because none of respondents' experts testified about its merits.

120. CX-7-CAL-35: Vitamin D_3 and Calcium to Prevent Hip Fractures in Elderly Women by Marie C. Chapuy, Pierre Delmas, Pierre Meunier, et al., in The New England Journal of Medicine (1992).

Dr. Raisz testified that this randomized, placebo-controlled study showed that calcium plus vitamin D, in a deficient population, decreased the incidence of fractures by 20%. (Tr. 84.) Thus, even though vitamin D was involved (Tr. 883), it provides some substantiation for the claim that calcium or MCHC increases bone thickness. (Strause, Tr. 2760-61.)

121. CX-7-CAL-36: Bone Gain and Loss in Premenopausal Women by Cyrus Cooper, in British Medical Journal (1993).

This review article, whose merits were not discussed by respondents' experts, does not substantiate claim 1. (Tr. 937.)

122. CX-7-CAL-37: Osteoporosis: Recent Advances in Pathogenesis and Treatment by C. Cooper, et al., in Quarterly Journal of Medicine (1994).

This is a review article which concludes that physical activity, calcium, and vitamin D are important for bone health. It does not examine calcium in relation to claim 1 and does not substantiate a finding that calcium or MCHC builds bone or increases bone thickness. (Tr. 760-61, 833-34.) Also, the merits of this study were not discussed by respondents' experts.

123. CX-7-CAL-39: Management of Fractures in Patients with Osteoporosis by Charles N. Cornell, in Orthopedic Clinics of North America (1990).

This review by an orthopedic surgeon is irrelevant to claim 1 because it merely states that calcium supplements should be given to patients with fractures. (P. 139.) (Tr. 884-86.)

124. CX-7-CAL-41: Calcium Intake and Bone Mass: A Quantitative Review of the Evidence by Robert Graham Cumming, in Calcified Tissue International (1990).

Dr. Holick rejected this meta-analysis (a review of six intervention studies) because it is a review. However, a meta-analysis, which statistically analyzes a significant body of work in prior studies (Lachance, Tr. 1661-63) is entitled to greater weight than a single study. (Raisz, Tr. 216.) Dr. Strause, Dr. Lachance and Dr. Heaney testified that this analysis substantiates claim 1. (Tr. 1663, 2764-65, 2403-05, 2408.) I accept their conclusion.

125. CX-7-CAL-42: A Controlled Trial of the Effect of Calcium Supplementation on Bone Density in Postmenopausal Women by Bess Dawson-Hughes, et al., in The New England Journal of Medicine (1990).

Dr. Heaney testified that this study by Dr. Dawson-Hughes, a leading expert in calcium, demonstrated a clear calcium effect in late menopausal women, and that it mainly substantiated claim 3 but it could possibly or plausibly substantiate claim 1. (Tr. 2411-15.) I find that this study provides some substantiation for that claim.

126. CX-7-CAL-47: Exercise and Its Interaction With Genetic Influences in the Determination of Bone Mineral Density by John A. Eisman, et al., in American Journal of Medicine (1991).

Dr. Holick claims that this article looks only at the influence of genetics and exercise on bone health (Tr. 942), but it concludes that "Their data [in a meta-analysis, which was reviewed] suggest that dietary calcium

intake plays a role in the determination and maintenance of peak bone mass." (P. 5B-6S.) Dr. Lachance testified that this article substantiates claim 1. (Tr. 1647-49.) I agree.

127. CX-7-CAL-48: Calcium Supplementation Reduces Vertebral Bone Loss in Perimenopausal Women: A Controlled Trial in 248 Women Between 46 and 55 Years of Age by Petra J.M. Elders, Paul Lips, et al., in Journal of Clinical Endocrinology and Metabolism (1991).

This study does not substantiate claim 1 because none of respondents' experts testified about its merits. (See also, Tr. 942, 948.)

128. CX-7-CAL-54: Symposium: Required Versus Optimal Intakes: A Look at Calcium -- Consumption of Calcium in the U.S.: Food Sources and Intake Levels by Kathryn Fleming, et ano., in American Institute of Nutrition (1994).

This is a review article which did not look at calcium or MCHC as they relate to claim 1. (Tr. 947.) This article was not discussed by respondents' experts.

129. CX-7-CAL-55: Relationships Between Usual Nutrient Intake and Bone-Mineral Content of Women 35-65 Years of Age: Longitudinal and Cross-Sectional Analysis by Jo L. Freudenheim, et al., American Journal of Clinical Nutrition (1986).

This is a study which looked at a variety of interventions. It would, therefore, be difficult to conclude that only calcium had the observed effect. (Tr. 948.) This article was not discussed by any of respondents' experts.

130. CX-7-CAL-59: Management of Osteoporosis and Paget's Disease -- An Appraisal of the Risks and Benefits of Drug Treatment by Carlo Gennari, et al., in Drug Safety (1994).

This is a review article which looked at a variety of treatments for osteoporosis and is not directly relevant to claim 1. (Tr. 890.) None of respondents' experts discussed this article.

131. CX-7-CAL-64: Lifetime Calcium Intake and Physical Activity Habits: Independent and Combined Effects on the Radial Bone of Healthy Premenopausal Caucasian Women by Lydia Halioua and John J.B. Anderson, in American Journal of Clinical Nutrition (1989).

Dr. Holick testified that this retrospective study does not provide substantiation for claim 1 because the subjects' calcium came from milk, which contains vitamin D. (Tr. 952.) None of respondents' experts testified as to the merits of this study.

132. CX-7-CAL-65: Attempts to Prevent Disuse Osteoporosis by Treatment With Calcitonin, Longitudinal Compression and Supplementary Calcium and Phosphate by David A. Hantman, et al., in Journal of Clinical Endocrinology and Metabolism (1973).

Dr. Holick testified that this study, which involved men at strict bed rest, and was not discussed by respondents' experts, is irrelevant to claim 1 because bone loss from bed rest does not mimic osteoporosis. (Tr. 952-53.) Dr. Lachance disagreed (Tr. 1681) but the study concluded that further studies are needed to confirm the effectiveness of mineral supplements on osteoporosis. (P. 856-57.) This study does not substantiate claim 1.

133. CX-7-CAL-68: Bone Mass, Nutrition, and Other Lifestyle Factors by Robert P. Heaney, in American Journal of Medicine (1993).

This study by Dr. Heaney substantiates claim 1. It concludes:

> of 43 studies published since 1987-88 relating calcium intake to bone health, 27 (63%) showed a beneficial effect of calcium. (P. 5A-31S.) (Tr. 1673-76.)

134. CX-7-CAL-69: Calcium Nutrition and Bone Health in The Elderly by Robert P. Heaney, J.C. Gallagher, C.C. Johnston, Robert Neer, Michael Parfitt, G. Donald Wheadon, et ano, in American Journal of Clinical Nutrition (1982).

Dr. Lachance testified that he saw nothing wrong with citing this review by the most eminent authority on calcium (Tr. 1677) as substantiation for claim 1 but this is not an unqualified endorsement and I reject it as substantiation.

135. CX-7-CAL-70: Effect of Calcium on Skeletal Development, Bone Loss and Risk of Fractures by Robert P. Heaney in American Journal of Medicine (1991).

This review article by Dr. Heaney which states that "calcium is not the cause of bone health but simply a necessary condition for it" (P. 5B-27S) does not directly substantiate claim 1. (Tr. 954-55.)

136. CX-7-CAL-71: Nutritional Factors in Bone Health in Elderly Subjects: Methodological and Contextual Problems by Robert P. Heaney, in American Journal of Clinical Nutrition (1989).

This article does not directly address calcium or MCHC relative to claim 1 and does not substantiate that claim. (P. 1183.)

137. CX-7-CAL-72: Nutritional Factors In Osteoporosis by Robert P. Heaney, in Annual Review of Nutrition (1993).

This review article discusses the effect of calcium on osteoporosis (claim 5). Its relevance to claim 1 is not evident. (Tr. 957.)

138. CX-7-CAL-76: Dietary Calcium and Risk of Hip Fracture: 14-Year Prospective Population Study by Troy L. Holbrook, Elizabeth Barrett-Connor, et ano., in The Lancet (1988).

This study does not substantiate claim 1 because, while it discusses hip fractures and the effect of calcium, it does not establish that calcium builds bone. (Tr. 956-60.)

139. CX-7-CAL-78: Effect of Calcium Supplementation on Urinary Hydroxyproline in Osteoporotic Postmenopausal Women by Michael Horowitz, B. E. C. Nordin, et al., in American Journal of Clinical Nutrition (1984).

This document, a study of postmenopausal women, does not substantiate claim 1 because the authors did not measure the subjects' bone density. (Tr. 584-85, 962-63.) None of respondents' experts discussed the merits of this article.

140. CX-7-CAL-83: The Relationship of Dietary Calcium Intake to Radiographic Bone Density in Normal and Osteoporotic Persons by Lewis M. Hurxthal, et ano., in Calcified Tissue Research (1969).

This is a study correlating estimates of lifetime calcium intake to bone mineralization. Dr. Holick testified that this study is of no value because the authors did not consider a number of variables that impact upon bone density, such as vitamin D, trace minerals, vitamin K and exercise. (Tr. 588-90.) None of respondents' experts discussed the merits of this study.

141. CX-7-CAL-85: Calcium Supplementation and Increases in Bone Mineral Density in Children by C. Conrad Johnston, et al., in New England Journal of Medicine (1992).

This is a double-blind, placebo-controlled study in which one group of twins was given calcium and another a placebo. The authors conclude that during the formative years bone density can be increased by the ingestion of calcium supplements. (P. 83-84.) Dr. Holick rejected this study because it dealt with the formative years. (Tr. 594, 966-67). Nevertheless, it substantiates claim 1 (Strause, Tr. 2779) which is not limited to calcium intake in adults.

142. CX-7-CAL-86: Premenopausal Bone Loss -- A Risk Factor for Osteoporosis by C. Conrad Johnston, et ano., in New England Journal of Medicine (1990).

This editorial does not substantiate a finding that calcium or MCHC builds bone or increases bone thickness. (Tr. 968-69.) None of respondents' experts testified about this editorial.

143. CX-7-CAL-95: New Strategies to Prevent Hip Fracture by Douglas P. Kiel, in Hospital Practice (1994).

This review article, which was not discussed by respondents' experts, suggests various ways to avoid hip fractures including calcium supplementation, but it does not directly substantiate claim 1. (Tr. 899-900, 2068.)

144. CX-7-CAL-99: Physical Activity and Calcium Intake in Fracture of the Proximal Femur in Hong Kong by E. Lau, et al., in British Medical Journal (1988).

This study concludes that exercise and calcium are important to bone health but offers no substantiation for claim 1 according to Dr. Holick and Dr. Heaney. (Tr. 972, 2468.)

145. CX-7-CAL-104: A Review of Calcium Preparations by David I. Levenson, et ano., in Nutrition Reviews (1994).

This is a review article which encourages adequate calcium intake but which is not directly relevant to claim 1. (Tr. 900-01.) None of respondents' experts discussed this review.

146. CX-7-CAL-105: Prevention and Osteoporosis Management by Angelo A. Licata, in Cleveland Clinic Journal of Medicine (1994).

This is a review article which concludes that women should have an adequate intake of calcium. It does not substantiate claim 1. (Tr. 796-97.) This review was not discussed by respondents' experts.

147. CX-7-CAL-107: Calcium Supplementation and Bone Mineral Density in Adolescent Girls by Tom Lloyd, et al., in Journal of the American Medical Association (1993).

This is a double-blind, controlled study which concludes that increasing the calcium intake of calcium-deficient girls will increase bone density in puberty. It substantiates claim 1. (Raisz, Tr. 153.) (See Heaney, Tr. 2422-25.)

148. CX-7-CAL-110: Histological Osteomalacia Due to Dietary Calcium Deficiency in Children by Pierre J. Marie, et al., in New England Journal of Medicine (1982).

This is a report of a study which concludes that low calcium intake may be associated with osteomalacia. This conclusion offers no direct substantiation for claim 1. (Tr. 802-03.) None of respondents' experts testified about this report.

149. CX-7-CAL-113: Calcium Metabolism and Calcium Requirements During Skeletal Modeling and Consolidation of Bone Mass by V. Matkovic, American Journal of Clinical Nutrition (1991).

This is a review article that concludes that one's calcium requirement is highest during infancy and adolescence. It does not, however, directly substantiate claim 1 (Tr. 978-79) and respondents' experts did not testify regarding the merits of this article.

150. CX-7-CAL-114: Factors that Influence Peak Bone Mass Formation: A Study of Calcium Balance and the Inheritance of Bone Mass in Adolescent Females by Velimir Matkovic, et al., in American Journal of Clinical Nutrition (1990).

This study of adolescent females found that the main determinant of calcium balance was calcium intake. Dr. Holick rejected this study because the difference in bone mass between two groups of subjects, one receiving more calcium supplementation than the other, was not statistically significant. (Tr. 979-80.)

Dr. Heaney, on the other hand, concluded that despite this fault (Tr. 2666), the study substantiates claim 1. (Tr. 2466-69.) I accept Dr. Heaney's judgment.

151. CX-7-CAL-117: Required Versus Optimal Intakes: A Look at Calcium by Gregory D. Miller and Connie M. Weaver in Journal of Nutrition (1994).

This review article, which was not discussed by respondents' experts, does not substantiate a finding that calcium or MCHC builds bone or increases bone thickness. (Tr. 632-33, 982.)

152. CX-7-CAL-120: Recommended Dietary Allowances, National Research Counsel of the National Academy of Sciences (1989).

Dr. Holick testified that this document is irrelevant to claim 1. (Tr. 427-28, 634, 984.) None of respondents' experts discussed this document which offers no clear substantiation for claim 1. However, it does support claim 5. (F. 308.)

153. CX-7-CAL-125: Epidemiology of Osteoporosis by Michael C. Nevitt. This is a chapter in the book entitled Rheumatic Disease Clinics of North America (1994).

This chapter is an epidemiological review which states that "population studies show a consistent, but small, increase in bone mass associated with higher dietary calcium intake" (p. 547). Dr. Holick rejected this statement because it does not derive from a study. (Tr. 984-86.) None of respondents' experts disagreed with this conclusion.

154. CX-7-CAL-129: Calcium Requirement and Calcium Therapy by B. E. C. Nordin, et al., in Clinical Orthopaedics and Related Research (1979).

This is a review article which does not directly substantiate claim 1 since it is a general discussion of calcium and bone health. (Tr. 908.) None of respondents' experts discussed the merits of this review.

155. CX-7-CAL-138: Dietary Risk Factors for Age-Related Bone Loss and Fractures by A. M. Parfitt, in The Lancet (1983).

This article discusses risk factors for age-related bone loss but was not discussed by respondents' experts and does not substantiate claim 1. (Tr. 815-16.)

156. CX-7-CAL-141: Effect of Calcium Supplementation on Forearm Bone Mineral Content in Postmenopausal Women: A Prospective, Sequential Controlled Trial by Karen J. Polley, B. E. C. Nordin, et al., in Journal of Nutrition (1987).

This controlled intervention study, whose merits were not discussed by respondents' experts, concluded that calcium supplementation decreases but does not stop bone loss. Dr. Holick rejected this study as substantiation for claim 1, as I do. (Tr. 819, 991-92.)

157. CX-7-CAL-143: The Effects of Calcium Supplementation (Milk Powder or Tablets) and Exercise on Bone Density in Postmenopausal Women by Richard Prince, et al., in Journal of Bone and Mineral Research (1995).

In this randomized, placebo-controlled study, all subjects lost bone, including the calcium group. This study does not substantiate claim 1 (Tr. 650, 913), although it substantiates claim 3. (Heaney, Tr. 2432-33.) (F. 236.)

158. CX-7-CAL- 145: Anti-Fracture Efficacy of Calcium in Elderly Women by Robert Recker, D.B. Kimmel, et al., in Journal of Bone and Mineral Research (1994).

Dr. Heaney testified that this abstract, which showed a significant gain in bone mass with increased calcium intake, taken alone, would not substantiate claim 1, but it gains credibility when considered with other work. (Tr. 2300-01.) It thus substantiates claim 1.

159. CX-7-CAL-146: Bone Gain in Young Adult Women by Robert R. Recker, Robert P. Heaney, Donald B. Kimmel, et al., in Journal of the American Medical Association (1992).

This is a five-year, prospective, longitudinal study which substantiates claim 1. (Tr. 2473.) The study concluded that:

gain in bone was enhanced by increased self-selected calcium intake (adjusted for protein intake) and increased self-selected activity. (P2607.)

160. CX-7-CAL-151: Effect of Calcium Supplementation on Bone Loss in Postmenopausal Women by Ian Reid, et al., in New England Journal of Medicine (1993).

This double-blind, randomized, controlled study of calcium supplementation found that bone mineral density declined in both groups of women, but the loss was significantly greater in the placebo group. (P. 461.) I accept Dr. Strause's opinion that this study substantiates claim 1. (Tr. 2786-87.)

161. CX-7-CAL-152: Long-Term Effects of Calcium Supplementation on Bone Loss and Fractures in Postmenopausal Women: A Randomized Controlled Trial by Ian Reid, et al., in American Journal of Medicine (1995).

This follow-up study to CAL-151 substantiates claim 1.

162. CX-7-CAL-172: Chapter 5, Calcium and Phosphorus by Louis V. Avioli, Modern Nutrition in Health and Disease (988).

This book chapter discusses calcium but does not examine the longitudinal effects of calcium or MCHC on the building of bone or bone thickness and does not substantiate claim 1. (Tr. 1002-03.) None of respondents' experts discussed this chapter.

163. CX-7-CAL-174: Physical Activity and Calcium Modalities for Bone Mineral Increase in Aged Women by Everett L. Smith, et al., in Medicine And Science In Sports And Exercise (1981).

This is a study which evaluated the effects of physical activity on bone health. This study, which respondents' experts did not discuss, does not substantiate claim 1. (Tr. 1003-04.)

164. CX-7-CAL-177: Bone Health and Prevention of Osteoporosis in Active and Athletic Women by Christine M. Snow-Harter, in Clinics in Sports Medicine (1994).

This review article, according to Dr. Lachance, substantiates the conclusion that calcium builds bone (Tr. 1651), but I agree with Dr. Holick that this study does not directly substantiate claim 1. (Tr. 338, 842, 1007.)

165. CX-7-CAL-184: Calcium Supplementation Increases Bone Density in Adolescent Girls by Dorothy Teegarden and Connie M. Weaver in Nutrition Reviews.

This is a review article which concludes that calcium is a necessary component of bone development but does not directly substantiate claim 1. (Tr. 1009-10.) This review was not discussed by any of respondents' experts.

166. CX-7-CAL-185: Calcium Balance in Osteoporotic Patients on Long-Term Oral Calcium Therapy With and Without Sex Hormones by N. C. Thalassinos, et al., in Clinical Science (1982).

This study examined the effects of increased calcium and hormones on calcium balance. It did not employ bone mineral density measurements to determine whether calcium intake had any effect on bone, and does not substantiate claim 1. (Tr. 693-94, 1011.) None of respondents' experts testified with respect to this claim.

167. CX-7-CAL-189: Evaluation of Publicly Available Scientific Evidence Regarding Certain Nutrient-Disease Relationships: Calcium and Osteoporosis by Robert P. Heaney (1991).

This report by Dr. Heaney, one of respondents' experts, was written for the Center for Food Safety & Applied Nutrition and was reviewed by two experts, including Dr. Raisz. It states, inter alia, that "peak bone mass appears to be related to intake of calcium during the years of bone mineralization. . . ." (p. 3), and that "achieving peak bone mass is a good, and possibly the best known, preventative against late life osteoporosis."

(P. 1.) Although this is a report (Tr. 702-04, 845-46, 917, 1109), it is by the most eminent expert in the field, and I accept Dr. Heaney's and Dr. Lachance's conclusion that it substantiates claim 1. (Tr. 1667-68, 2322-23.)

168. CX-7-CAL-190 and 191: Food Labeling: Health Claims; Calcium and Osteoporosis.

These are regulations issued by the Food and Drug Administration in 1992 and contain guidelines as to claims which may be made by manufacturers about the relationship between calcium and osteoporosis. The regulations provide substantiation for claim 1 insofar as they announce that calcium is important for achieving genetically programmed bone mass. (P. 2665.) (See Tr. 1784: "The [regulations] talk about building bone mass during adolescence and early adulthood.")

169. CX-7-CAL-192: Public Health Reports, National Conference on Women's Health Series, Special Topic On Osteoporosis, United States Department of Health and Human Services ("HHS") (1987).

This document is a compilation of papers presented at a conference on women's health. This document was not discussed by respondents' experts and I accept Dr. Holick's opinion that it does not substantiate claim 1. (Tr. 490, 1015.)

170. CX-7-CAL-193: Consensus Conference Statement on Optimal Calcium Intake, National Institute of Health Consensus Conference, and HHS (1994).

Dr. Heaney testified that this report stresses the importance of calcium throughout life (Tr. 2624), but it does not directly substantiate claim 1. (Tr. 918.)

171. CX-7-CAL-194 and 195: Consensus Development Conference Statement - Osteoporosis, National Institute of Health Consensus Conference, HHS (1984).

This article stresses adequate nutrition, including calcium, along with weight-bearing exercise and estrogen replacement. This article substantiates claim 1. (Heaney, Tr. 2402-03.)

172. CX-7-CAL-198: Healthy People 2000, National Health Promotion and Disease Prevention Objectives, HHS (1991).

None of respondents' experts are cited as substantiating the conclusions in this document. However, it states, as does CAL-189, that peak bone mass appears to be related to intake of calcium during the years of bone mineralization (P. 120), and it substantiates claim 1.

173. CX-7-CAL-203: Effects of Nutritional Supplementation of Bone Mineral Status of Children with Rheumatic Diseases Receiving Corticosteroid Therapy by Barbara D. Warady, Barbara P. Lukert, et al., in The Journal of Rheumatology (1994).

This article whose merits were not discussed by respondents' experts does not substantiate claim 1. (Tr. 1025.)

174. CX-7-CAL-204: A Meta-Analysis of the Effect of Calcium Intake on Bone Mass in Young and Middle Aged Females and Males by Desiree Welten, et al., in Journal of Nutrition (1995).

This analysis' main finding was that the studies published to date show a small but significant positive correlation between calcium intake and bone mass in females. (P2809.) This meta-analysis substantiates claim 1 because "It shows a direct relationship between dietary calcium and bone mass" (Strause, Tr. 2795), and a clear effect from calcium supplementation. (Tr. 2406.)

175. CX-7-CAL-205: Effects of High Calcium Intakes on Bones, Blood and Soft Tissue: Relationship of Calcium Intake to Balance Osteoporosis by G. Donald Whedon, in Federation Proceedings (1959).

Dr. Holick testified that no reliance could be placed on this article because it is a 1959 review. (Tr. 1027.) Despite Dr. Lachance's disagreement (Tr. 1645), I agree with Dr. Holick.

2. Claim 2: Bone Builder or MCHC Restores Lost Bone

176. CX-7-MCHC-7: Non-Hormonal Treatment of Osteoporosis by Allan St.J. Dixon, in British Medical Journal (1983).

This article, which was not discussed by respondents' experts, does not substantiate the claim that Bone Builder or MCHC restores lost bone. (Tr. 872.)

177. CX-7-MCHC-8: Extracts of Bone Contain a Potent Regulator of Bone Formation by R. H. Drivdahl, G. A. Howard and D. J. Baylink, in Biochimica et Biophysica Acta. (1982).

This study is irrelevant because it deals with the activity in the bone cells of two-day old chicks and did not examine the effect of calcium in restoring lost bone. (Tr. 872.)

178. CX-7-MCHC-10: Vitamin D, Hydroxyapatite and Calcium Gluconate in Treatment of Cortical Bone Thinning in Postmenopausal Women With Primary Biliary Cirrhosis by Owen Epstein, Sheila Sherlock, et al., in The American Journal of Clinical Nutrition (1982).

This study concluded that calcium supplements "prevented or retarded" cortical bone thinning. (P. 426.) It did not conclude that calcium or MCHC restored lost bone. (Tr. 347-50, 513, 873-74.)

179. CX-7-MCHC-13: The Use of a Whole Bone Extract in the Treatment of Fractures by T. J. Mills, et al., in Manitoba Medical Review (1965).

This study compared ossopan to a placebo and Dr. Heaney testified that it could be construed as substantiation for claim 2 if fracture healing was considered to be restoring bone. (Tr. 2469-70.) I reject this equivocal conclusion and find that this study does not substantiate claim 2 because bone mineral density was not measured. (Tr. 874.)

180. CX-7-MCHC-17: Examination of New Bone Growth on Aluminum Oxide Implant Contact Surfaces After Oral Administration of Ossein-Hydroxyapatite Compound to Rats by K. H. Schmidt, et ano., in Current Medical Research and Opinion (1988).

Even though rat studies may sometimes be valuable (Tr. 2212), this unusual animal study provides no insight into impact of calcium or MCHC on the restoration of lost bone. (Tr. 875.) This study was not discussed by any of respondents' experts.

181. CX-7-CAL-3: Osteoporosis: Effects of Calcium by Anthony A. Albanese, et al., in American Family Practitioner (1978).

Dr. Holick testified that the following statement from this review article is a "reasonable comment":

> These results suggest that under conditions of low calcium intake due to inadequate consumption of dairy products, bone loss in elderly women may be decelerated or reversed by taking calcium supplements. (Tr. 1894.)

This review substantiates claim 2.

182. CX-7-CAL-33: Calcium and Vitamin D Supplements: Effects on Calcium Metabolism in Elderly People by Marie-Claire Chapuy, Pierre Meunier, et ano., in American Journal of Clinical Nutrition (1987).

This report of a study does not discuss the restoration of lost bone and therefore does not substantiate claim 2. (Tr. 757-59, 883.) None of respondents' experts discussed the merits of this report.

183. CX-7-CAL-39: Management of Fractures in Patients with Osteoporosis by Charles N. Cornell, in Orthopedic Clinics of North America (1990).

This review article discusses fracture healing through mechanical means and the aggressive use of vitamin D and calcium in elderly

osteoporotic patients. Its direct relevance to claim 2, however, is not clear. (Lachance, Tr. 1655.)

184. CX-7-CAL-56: Increase of Bone Mineral Density by Calcium Supplement with Oyster Shell Electrolysate by T. Fujita, et al., in Bone and Mineral (1990).

This study suggests that calcium supplementation can reduce age-related bone loss (p. 89) but is not directly relevant to claim 2. (Tr. 888-89.) This study was not discussed by respondents' experts.

185. CX-7-CAL-69: Calcium Nutrition and Bone Health in The Elderly by Robert P. Heaney, J.C. Gallagher, C.C. Johnston, Robert Neer, Michael Parfitt, G. Donald Wheadon, et ano., in American Journal of Clinical Nutrition (1982).

This review article by Dr. Heaney is rejected as substantiation for claim 2 because it is not clear, as respondents claim, that Drs. Lachance and Strause endorse it as substantiation. (See Tr. 1675, 2774-75.)

186. CX-7-CAL-95: New Strategies to Prevent Hip Fracture by Douglas P. Kiel, in Hospital Practice (1994).

This review article, not discussed by any of respondents' experts, does not substantiate claim 2. (Tr. 899-900, 2068.)

187. CX-7-CAL-129: Calcium Requirement and Calcium Therapy by B. E. C. Nordin, et al., in Clinical Orthopaedics and Related Research (1979).

This review, whose merits were not discussed by respondents' experts, concludes that bone loss in the elderly can be reduced by consumption of calcium or vitamin D. It does not substantiate claim 2. (Tr. 641-42.)

188. CX-7-CAL-143: The Effects of Calcium Supplementation (Milk Powder or Tablets) and Exercise on Bone Density in Postmenopausal

Women by Richard Prince, et al., in Journal of Bone and Mineral Research (1995).

This study concludes that calcium supplementation plus increased exercise will reduce bone loss in the hip bone. It does not substantiate a claim that calcium or MCHC restores lost bone. (Tr. 650, 913.) Respondents' experts did not discuss the merits of this study.

189. CX-7-CAL- 145: Anti-Fracture Efficacy of Calcium in Elderly Women by Robert Recker, D.B. Kimmel, et al., in Journal of Bone and Mineral Research (1994).

This is an abstract of a study which concluded that increasing calcium intake causes a significant reduction in the risk of further vertebral fractures in women. (Tr. 914.) This abstract is not scientifically valid considered alone (Tr. 914) but it gains credibility when viewed in the context of other work on calcium effects. (Heaney, Tr. 2300-01.) It therefore offers some substantiation for claim 2.

190. CX-7-CAL-152: Long-Term Effects of Calcium Supplementation on Bone Loss and Fractures in Postmenopausal Women: A Randomized Controlled Trial by Ian Reid, et al., in American Journal of Medicine (1995).

This study, a follow-up to CAL-151, substantiates claim 2. (F. 160.)

191. CX-7-CAL-182: The Role of Trace Elements in Bone Metabolism by Linda Strause, P. Saltman, et al., in Nutritional Aspects of Osteoporosis (1991).

Dr. Strause testified that this article should be read in conjunction with CX-7-CAL-161, 162 and 181 as demonstrating the efficacy of calcium and trace minerals in improving the spinal bone mineral density of women involved in a 2 year clinical trial. (Tr. 2792.) This article substantiates claim 2.

192. CX-7-CAL-193: Consensus Conference Statement on Optimal Calcium Intake, HHS (1994).

This document recommends the optimal RDA for calcium. While Dr. Heaney testified that this document shows the importance of calcium (Tr. 2634-35), it does not substantiate a finding that calcium or MCHC will restore lost bone. (Tr. 918.)

3. Claim 3: Bone Builder or MCHC Halts or Prevents Bone Loss or Bone Thinning

193. CX-7-MCHC-4: Effects of Calcium Supplements on Femoral Bone Mineral Density and Vertebral Fracture Rate in Vitamin-D Replete Elderly Patients by T. Chevalley, J. P. Bonjour, et al. , in Osteoporosis International (1994).

Dr. Holick rejected this report of a double-blind, placebo-controlled study, with two groups, calcium-supplemented or non-supplemented, which found, over a period of 18 months, no significant change in bone density. (Tr. 720-21.)

Dr. Heaney testified that this criticism is unsound since individuals in this age group are typically losing bone at the rate of three percent. No change is a decided improvement over a three percent loss per year. (Tr. 2393.) (See also Tr. 2761-63.) This study which found that calcium supplements could be of benefit in preventing bone loss in the elderly (P. 251) substantiates claim 3.

194. CX-7-MCHC-5: Therapy of Osteoporosis With an Ossein-Hydroxyapatite-Compound Evaluated With Quantitative Computed Tomography by M. A. Dambacher, et ano., in Journal of Bone Mineral Research (1987).

This abstract substantiates claim 3 because the ossein-hydroxyapatite treated patients remained unchanged in their bone density while the untreated subjects lost bone. (Heaney, Tr. 2448-49, 2465.)

195. CX-7-MCHC-10: Vitamin D, Hydroxyapatite and Calcium Gluconate in Treatment of Cortical Bone Thinning in Postmenopausal Women With

Primary Biliary Cirrhosis by Owen Epstein, Sheila Sherlock, et. al., in The American Journal of Clinical Nutrition (1982).

This study found that "in postmenopausal patients with PBC (primary biliary cirrhosis), calcium supplements given in addition to parenteral vitamin D prevents or retards pathological bone thinning." (PP. 429-30.) Dr. Holick criticized this study because the patients had PBC and were given vitamin D (Tr. 725), but Dr. Heaney testified that the vitamin D given to all patients did not invalidate this study. (Tr. 2394.) The same is true as to PBC. (Tr. 2773-74.) Nevertheless, there is no clear conclusion with respect to this study. It does not substantiate claim 3.

196. CX-7-MCHC-14: Microcrystalline Calcium Hydroxyapatite Compound in Corticosteroid-Treated Rheumatoid Patients: A Controlled Study, by Kjell Nilsen, et al., British Medical Journal (1978).

This is an abstract of a controlled study of patients with steroid-induced osteoporosis. Dr. Holick testified that this study does not support claim 3 because all of the subjects had rheumatoid arthritis and all lost bone. (Tr. 727.) The authors stated that the results of the trial suggest that MCHC has a significant prophylactic effect in preventing the development of osteoporosis in corticosteroid-treated rheumatoid patients. (P. 1124.) Dr. Heaney testified that this paper substantiated claim 3 (Tr. 2470), and I accept his conclusion.

197. CX-7-MCHC-15: Clinical Trial of Microcrystalline Hydroxyapatite Compound (`Ossopan') in the Prevention of Osteoporosis Due to Corticosteroid Therapy by A. Pines, et al., in Current Medical Research and Opinion (1984).

This is a study involving steroid-treated subjects in which the MCHC group continued to lose bone; while Dr. Heaney believes that it substantiates claim 3 (Tr. 2472), I disagree, for there was no statistically significant difference between the groups which were studied. (Holick, Tr. 919-20.)

198. CX-7-MCHC-16: Comparison of the Treatment of Ossein-Hydroxyapatite Compound and Calcium Carbonate in Osteoporotic

Females by P. Ruegsegger, et al., in Osteoporosis International (1995).

This randomized double-blind study showed that ossein-hydroxyapatite is more effective than calcium carbonate in preventing further bone loss in postmenopausal osteoporosis. (P. 33.) Dr. Strause testified that this study substantiates claim 3 (Tr. 2785-86) as did Dr. Heaney. (Tr. 2439-40, 2774-75.)

199. CX-7-CAL-2: Effect of a Calcium Supplement on Serum Cholesterol, Calcium, Phosphorus and Bone Density of "Normal, Healthy" Elderly Females by Anthony A. Albanese, et al., in Nutrition Reports International (1973).

This is a study which Dr. Holick criticized as being confounded by vitamin D. (Tr. 731-31.) None of respondents' experts testified about the merits of this study.

200. CX-7-CAL-3: Osteoporosis: Effects of Calcium by Anthony A. Albanese, et al., in American Family Practitioner (1978).

Dr. Holick testified that the following statement in this review article was reasonable: "bone loss and fracture risk may be minimized or reversed by a daily intake of approximately 1 Gm of calcium derived from the diet or through supplements." (Tr. 1892-93.) He came to the same conclusion with respect to this statement:

> These results suggest that under conditions of low calcium intake due to inadequate consumption of dairy products, bone loss in elderly women may be decelerated or reversed by taking calcium supplements. (Tr. 1894.)

This review article substantiates claim 3.

201. CX-7-CAL-5: Calcium Supplementation with and without Hormone Replacement Therapy to Prevent Postmenopausal Bone Loss by John F. Aloia, et al., in Annals of Internal Medicine (1994).

This is a report of a three-arm, placebo-controlled randomized trial which found that "in this healthy population of early postmenopausal white women, calcium augmentation of the diet retarded bone loss from the entire skeleton." (P. 102.) This study substantiates claim 3. (Heaney, Tr. 2460-61.)

202. CX-7-CAL-8: Spinal Bone Density and Calcium Intake in Healthy Postmenopausal Women by Mark Andon, Linda Strause, et al., in American Journal of Clinical Nutrition (1991).

This cross-sectional study by Dr. Strause and others found that:

> subjects consuming less than the population mean of dietary calcium had significantly lower BMD [Bone Mineral Density] than did subjects with intakes above the mean. (P. 001.)

Dr. Strause testified that this study substantiates claim 3 despite the fact that it is not an intervention study. (Tr. 2745-47.) Dr. Holick disagreed. (Tr. 738.) I accept his judgment.

203. CX-7-CAL-11: Calcium Intake and Bone Health by Louis V. Avioli and Robert P. Heaney, in Calcified Tissue International (1991).

I reject this editorial, whose merits were not discussed by respondents' experts, as support for claim 3. (Tr. 733-34.)

204. CX-7-CAL-14: Dietary Modification with Dairy Products for Preventing Vertebral Bone Loss in Premenopausal Women: A Three-Year Prospective Study, by Daniel Baran, et al., in Journal of Clinical Endocrinology and Metabolism (1990).

Dr. Holick rejected this article as being confounded by vitamin D (Tr. 523-25) and Dr. Heaney testified that it supports claim 3 only by inference. (Tr. 2461.) I reject this article as substantiation for claim 3.

205. CX-7-CAL-15: Symposium: Required Versus Optimal Intakes: A Look at Calcium -- The Role of Calcium Intake in Preventing Bone

Fragility, Hypertension, and Certain Cancers by M. Janet Barger-Lux and Robert Heaney.

In this review article from a symposium, Dr. Heaney states:

> Although one commonly reads that the nutritional effect of calcium on bone status is "controversial", that term is no longer appropriate. Of 43 studies published since 1988 and recently examined by Heaney (1993a), 27 found a statistically significant association between calcium intake and bone mass, bone loss, or bone fragility; 16 did not find a significant effect. Those 16 failed studies are all fully explainable on two grounds: investigator control of calcium intake and timing of the study relative to menopause. (P. 1408S.)

Considering the reputation of Dr. Heaney, this article substantiates claim 3.

206. CX-7-CAL-16: Coffee-Associated Osteoporosis Offset by Daily Milk Consumption by Elizabeth Barrett-Connor, in Journal of the American Medical Association (1994).

This study, contrary to Dr. Holick's claim (Tr. 748), refers to calcium (in milk). (P. 282.) Nevertheless, it is not directly relevant to claim 3.

207. CX-7-CAL-23: Calcium, Estrogen, and Progestin in the Treatment of Osteoporosis by Neil Breslau, in Rheumatic Disease Clinics of North America (1994).

This review was not discussed by respondents' expert witnesses, and I reject it as substantiation for claim 3.

208. CX-7-CAL-32: Effects of Increased Dietary Calcium Intake Upon the Calcium and Bone Mineral Status of Lactating Adolescent and Adult Women by Gary M. Chan, et al., in American Journal of Clinical Nutrition (1987).

Dr. Holick rejected this study because its results cannot be extrapolated to the general population. (Tr. 756-57). Respondents' experts did not discuss this exhibit. It does not substantiate claim 3.

209. CX-7-CAL-33: Calcium and Vitamin D Supplements: Effects on Calcium Metabolism in Elderly People by Marie-Claire Chapuy, Pierre Meunier, et ano., in American Journal of Clinical Nutrition (1987).

I reject this article as support for claim 3 because respondents' transcript citation (Tr. 2582-83) makes no reference to a CX number.

210. CX-7-CAL-37: Osteoporosis: Recent Advances in Pathogenesis and Treatment by C. Cooper, et ano., in Quarterly Journal of Medicine (1994).

This article merely concludes that physical activity, vitamin D and calcium are needed for bone health. (Tr. 760-61.) It does not directly substantiate claim 3, and its merits were not discussed by respondents' experts.

211. CX-7-CAL-41: Calcium Intake and Bone Mass: A Quantitative Review of the Evidence by Robert Graham Cumming, in Calcified Tissue International (1990).

This meta-analysis, concluded that calcium supplements might prevent nearly half the rate of bone loss that occurs in elderly women, but was rejected by Dr. Holick. (Tr. 762.) However, Dr. Raisz agreed with this article's recommendation of high calcium intake for postmenopausal women (Tr. 218-21) and Drs. Lachance and Heaney testified that it substantiates claim 3. (Tr. 1660-63, 2405-08, 2414.)

212. CX-7-CAL-42: A Controlled Trial of the Effect of Calcium Supplementation on Bone Density in Postmenopausal Women by Bess Dawson-Hughes, et al., in The New England Journal of Medicine (1990).

This double-blind, placebo controlled study was rejected by Dr. Holick because subjects on a higher calcium diet still lost bone. (Tr. 763.)

Dr. Heaney, on the other hand, testified that the study showed a clear calcium effect in late menopausal women. (Tr. 2411, 2415; see also Strause, Tr. 2766-67.) This article substantiates claim 3.

213. CX-7-CAL-43: Dietary Calcium Intake and Bone Loss From the Spine in Healthy Postmenopausal Women by Bess Dawson-Hughes, et al., in American Journal of Clinical Nutrition (1987).

None of respondents' experts stated that this study substantiates claim 3. It is therefore rejected.

214. CX-7-CAL-48: Calcium Supplementation Reduces Vertebral Bone Loss in Perimenopausal Women: A Controlled Trial in 248 Women Between 46 and 55 Years of Age by Petra J. M. Elders, Paul Lips, et al., in Journal of Clinical Endocrinology and Metabolism (1991).

This randomized controlled study found:

> In conclusion, calcium supplementation retards lumbar bone mineral loss in perimenopausal women by decreasing bone turnover during the first year of supplementation. (P. 539.)

The results of this study substantiate claim 3. (Heaney, Tr. 2466.)

215. CX-7-CAL-49: Long-term Effect of Calcium Supplementation on Bone Loss in Perimenopausal Women by Petra M. Elders, Paul Lips, et al., in Journal of Bone and Mineral Research (1994).

Dr. Holick rejected this article as substantiation (Tr. 770) and none of respondents' experts testified that it substantiated claim 3.

216. CX-7-CAL-55: Relationships Between Usual Nutrient Intake and Bone-Mineral Content of Women 35-65 Years of Age: Longitudinal and Cross-Sectional Analysis by Jo L. Freudenheim, et al., in American Journal of Clinical Nutrition (1986).

Dr. Holick testified that this study does not substantiate claim 3 because all of its subjects experienced bone loss. (Tr. 549-51, 772-73.)

Since none of respondents' experts specifically disagreed, I reject the study as substantiation.

217. CX-7-CAL-57: The Crush Factor Syndrome in Postmenopausal Women by J. C. Gallagher, A. Horsman, B.E.C. Nordin, et al., in Clinics in Endocrinology and Metabolism (1973).

This article, whose merits were not discussed by respondents' experts, does not substantiate claim 3. (Tr. 773.)

218. CX-7-CAL-59: Management of Osteoporosis and Paget's Disease -- An Appraisal of the Risks and Benefits of Drug Treatment by Carlo Gennari, et al., in Drug Safety (1994).

This article, which was not discussed by respondents' experts, does not substantiate claim 3. (Tr. 775.)

219. CX-7-CAL-68: Bone Mass, Nutrition, and Other Lifestyle Factors by Robert P. Heaney, in American Journal of Medicine (1993).

This article by Dr. Heaney found that although failed calcium studies left some questions:

> In all [of six new randomized controlled studies] supplemented calcium and/or vitamin D slowed bone loss or reduced fractures. (P. 5A-30A.)

This article substantiates claim 3. (Lachance, Tr. 1673-77.)

220. CX-7-CAL-70: Effect of Calcium on Skeletal Development, Bone Loss and Risk of Fractures by Robert P. Heaney, in American Journal of Medicine (1991).

This review article found:

> [T]he conclusion from all these studies seems inescapable: low-calcium intakes contribute to age-related bone loss, and high intakes reduce such loss. (P. 5B-25-6S.)

This article substantiates claim 3. (Tr. 2774-75.)

221. CX-7-CAL-71: Nutritional Factors in Bone Health in Elderly Subjects: Methodological and Contextual Problems by Robert P. Heaney, in American Journal of Clinical Nutrition (1989).

This review article by Dr. Heaney which concludes that most studies show a beneficial effect of calcium on bone mass and bone loss (P. 1185) substantiates claim 3. (Strause, Tr. 2774-75.)

222. CX-7-CAL-72: Nutritional Factors In Osteoporosis by Robert P. Heaney, in Annual Review of Nutrition (1993).

This review article by Dr. Heaney substantiates claim 3. (Heaney, Tr. 2380-81.) It states:

> What the study clearly shows is that women with low intakes [of calcium] lose bone [and] that calcium supplements reduce or prevent that loss. . . . (P. 301.)

223. CX-7-CAL-73: Editorial: A Unified Concept of Osteoporosis by Robert P. Heaney, in American Journal of Medicine (1965).

This editorial (Tr. 783) by Dr. Heaney does not directly substantiate claim 3.

224. CX-7-CAL-77: Biochemical Effects of Calcium Supplementation in Postmenopausal Osteoporosis by M. Horowitz, B.E.C. Nordin, et al., in European Journal of Clinical Nutrition (1988).

This study, which was not discussed by respondents' experts, reported that the data "do not prove that calcium supplementation is a useful preventative or therapeutic measure in postmenopausal osteoporosis." (P. 777.) It does not substantiate claim 3.

225. CX-7-CAL-78: Effect of Calcium Supplementation on Urinary Hydroxyproline in Osteoporotic Postmenopausal Women by Michael

Horowitz, B. E. C. Nordin, et al., in American Journal of Clinical Nutrition (1984).

This short-term study, whose merits were not discussed by respondents' experts, does not substantiate claim 3. (Tr. 584-86, 962-63.)

226. CX-7-CAL-104: A Review of Calcium Preparations by David I. Levenson, et ano., in Nutrition Reviews (1994).

This article, which was not discussed by respondents' experts, does not substantiate claim 3.

227. CX-7-CAL-105: Prevention and Osteoporosis Management by Angelo A. Licata, in Cleveland Clinic Journal of Medicine (1994).

This review, which was not discussed by respondents' experts, does not substantiate claim 3. (Tr. 796-97.)

228. CX-7-CAL-109: Osteoporosis - A Mineral Deficiency Disease? by Leo Lutwack, in Journal of the American Dietetic Association (1964).

This review, which was not discussed by respondents' experts, does not substantiate claim 3. (TR. 801.)

229. CX-7-CAL-110: Histological Osteomalacia Due to Dietary Calcium Deficiency in Children by Pierre J. Marie, et al., in New England Journal of Medicine (1982).

This report of a study concludes that calcium deficiency is the cause of osteomalacia. It offers no direct substantiation for claim 3 and was not discussed by respondents' experts. (Tr. 802-03.)

230. CX-7-CAL-122: Biochemical Effects of a Calcium Supplement in Osteoporotic Postmenopausal Women with Normal Absorption and Malabsorption of Calcium by Allan G. Need, B. E. Christopher Nordin, et al., in Mineral Electrolyte Metabolism (1987).

Because this study reported that calcium alone did not prevent bone loss (Tr. 809), it does not substantiate claim 3.

231. CX-7-CAL-123: Comparison of Calcium, Calcitriol, Ovarian Hormones and Nandrolone in the Treatment of Osteoporosis by A. G. Need, B.E.C. Nordin, et al., in Maturitas (1986).

This study substantiates claim 3. (Heaney, Tr. 2471.)

232. CX-7-CAL-125: Epidemiology of Osteoporosis by Michael C. Nevitt, in Rheumatic Disease Clinics of North America (1994).

This book chapter does not substantiate claim 3 because it is an epidemiologic study which concludes that a variety of factors may be related to bone health. (Tr. 810.)

233. CX-7-CAL-129: Calcium Requirement and Calcium Therapy by B. E. C. Nordin, et al., in Clinical Orthopaedics and Related Research (1979).

This is a review article which found that individuals treated with calcium experienced a significant decline in the density of wrist bone. (Tr. 641-42.) None of respondents' experts testified as to the merits of this review. It does not substantiate claim 3.

234. CX-7-CAL-138: Dietary Risk Factors for Age-Related Bone Loss and Fractures by A. M. Parfitt, in The Lancet (1983).

Respondents' experts did not discuss this review, and it does not substantiate claim 3.

235. CX-7-CAL-141: Effect of Calcium Supplementation on Forearm Bone Mineral Content in Postmenopausal Women: A Prospective, Sequential Controlled Trial by Karen J. Polley, B. E. C. Nordin, et al., in Journal of Nutrition (1987).

This study of postmenopausal women showed that they were losing bone at a significant rate when consuming a mean calcium intake of just

over 700 mg daily. They ceased to lose bone when their mean calcium intake was raised to about 1400 mg. (P. 1934.) This study substantiates claim 3. (Heaney, Tr. 2472.)

236. CX-7-CAL-143: The Effects of Calcium Supplementation (Milk Powder or Tablets) and Exercise on Bone Density in Postmenopausal Women by Richard Prince, et al., in Journal of Bone and Mineral Research (1995).

Dr. Heaney testified that this randomized, controlled study demonstrated that calcium slowed or stopped bone loss at the hip and substantiates claim 3. (Tr. 2432-33.)

237. CX-7-CAL- 145: Anti-Fracture Efficacy of Calcium in Elderly Women by Robert Recker, D.B. Kimmel, et al., in Journal of Bone and Mineral Research (1994).

This abstract concludes that increasing calcium intake results in a significant gain in bone mass, and Dr. Heaney testified that its conclusion has not changed. (Tr. 2300.) This abstract substantiates claims 1 and 2, but not 3 since it does not discuss bone loss.

238. CX-7-CAL-149: The Effect of Milk Supplements on Calcium Metabolism, Bone Metabolism and Calcium Balance by Robert R. Recker and Robert P. Heaney, in The American Journal of Clinical Nutrition (1985).

This relatively short term study by Dr. Recker offers no direct substantiation for claim 3 since its main conclusion is merely that milk is a good source of calcium. (P. 261.) (Tr. 824.)

239. CX-7-CAL-150: Calcium Supplements in the Prevention of Steroid-Induced Osteoporosis by I. R. Reid, et ano., in The American Journal of Clinical Nutrition (1986).

This article when read in conjunction with other evidence substantiates the claim that calcium is important for bone health and substantiates claim 3. (Heaney, Tr. 2356-59, 2473.)

240. CX-7-CAL-151: Effect of Calcium Supplementation on Bone Loss in Postmenopausal Women by Ian Reid, et al., in New England Journal of Medicine (1993).

Although all subjects in this study continued to lose bone (Tr. 828), it found that a calcium supplement of 1000 mg per day had a beneficial effect on bone loss in normal postmenopausal women. (P. 462.) This study substantiates claim 3. (Strause, Tr. 2787; Heaney, Tr. 2473.)

241. CX-7-CAL-152: Long-Term Effects of Calcium Supplementation on Bone Loss and Fractures in Postmenopausal Women: A Randomized Controlled Trial by Ian Reid, et al., in American Journal of Medicine (1995).

This follow-up study to CAL-151 substantiates claim 3. (F. 160.)

242. CX-7-CAL 171: Short-term Changes in Calcium but Not Protein Intake Alter the Rate of Bone Resorption in Healthy Subjects as Assessed by Urinary Pyridium Cross-Link Excretion by Sue A. Shapses, et al., in Journal of Nutrition (1995).

This study did not measure bone mineral density. None of respondents' experts challenged this conclusion. I therefore agree with Dr. Holick that this study does not substantiate claim 3. (Tr. 836-37.)

243. CX-7-CAL-172: Chapter 5, Calcium and Phosphorus by Louis V. Avioli, in Modern Nutrition in Health and Disease (1988).

This book chapter offers no direct substantiation for claim 3. It was not discussed by respondents' experts.

244. CX-7-CAL-173: Calcium Supplementation and Bone Loss in Middle-Aged Women by Everett L. Smith, et al., in American Journal of Clinical Nutrition (1989).

Dr. Holick rejected this article as substantiation for claim 3 and none of respondents' experts challenged his testimony. (Tr. 838.)

245. CX-7-CAL-181: Spinal Bone Loss in Postmenopausal Women Supplemented with Calcium and Trace Minerals by Linda Strause, Paul Saltman, et al., in Journal of Nutrition (1994).

This randomized, controlled study by Dr. Strause found that:

> spinal bone loss in a small group of older postmenopausal women was slowed by supplementation with calcium as CCM [calcium citrate malate] and was halted by supplementation with a mineral cocktail. . . . (P. 1063.)

Although the group of women in this study given calcium still lost bone (Tr. 843), Drs. Heaney and Strause testified that it substantiates claim 3 and I accept their judgment. (Tr. 2789-92, 2475-76.)

246. CX-7-CAL-182: The Role of Trace Elements in Bone Metabolism by Linda Strause, P. Saltman, et al., in Nutritional Aspects of Osteoporosis (1991).

This review article, according to Dr. Strause, should be read in conjunction with CAL-181, 161 and 162 as substantiation for claim 3. (Tr. 2789-92.)

247. CX-7-CAL-189: Evaluation of Publicly Available Scientific Evidence Regarding Certain Nutrient-Disease Relationships: Calcium and Osteoporosis by Robert P. Heaney.

This report for the FDA by Dr. Heaney substantiates claim 3. (Tr. 2323.) Although he warned that "an adequate calcium intake cannot be expected to prevent or reverse the bone loss and fragility due to other factors" (P. 39), he concluded:

> The bulk of the evidence, particularly for the better designed studies, supports the hypothesis that a higher calcium intake is more protective of bone than is a lower one. (P. 25.)

248. CX-7-CAL-191: Food Labeling: Health Claims; Calcium and Osteoporosis.

These are regulations promulgated by the FDA which announces the claims which may be made in connection with the association between calcium intake and the prevention of osteoporosis.

This document states that an adequate calcium intake is linked to a reduced risk of osteoporosis through the mechanism of slowing the rate of bone loss (Tr. 1784) and substantiates claim 3.

249. CX-7-CAL-192: Public Health Reports, National Conference on Women's Health Series, Special Topic On Osteoporosis, HHS (1987).

This document does not substantiate claim 3. None of respondents' experts discussed it.

250. CX-7-CAL-193: Consensus Conference Statement on Optimal Calcium Intake, HHS (1994).

This is a general description of the benefits of calcium and does not substantiate claim 3.

251. CX-7-CAL-194: Consensus Development Conference Statement - Osteoporosis, HHS (1984).

This document states that: "It seems likely that an increase in calcium intake to 1,000 to 1,500 mg a day . . . well before menopause will reduce the risk of osteoporosis in postmenopausal women. Increased calcium intake may prevent age-related bone loss in men as well." (P. 7.) It substantiates claim 3. (Tr. 2403.)

252. CX-7-CAL-204: A Meta-Analysis of the Effect of Calcium Intake on Bone Mass in Young and Middle Aged Females and Males by Desiree Welten, et al., in Journal of Nutrition (1995).

This meta-analysis states:

> The . . . results of the intervention trials are based on only four studies. This limits the interpretation, but it is worthwhile pointing out that the amount of bone loss prevented by calcium supplementation was quite large. (P. 2811.)

This analysis substantiates claim 3. (Heaney, Tr. 2406-07.)

253. CX-7-CAL-205: Effects of High Calcium Intakes on Bones, Blood and Soft Tissue: Relationship of Calcium Intake to Balance in Osteoporosis by G. Donald Whedon, in Federation Proceedings (1959).

Despite Dr. Lachance's belief that this review article substantiates claim 3 (Tr. 1645-46), I agree with Dr. Holick that it does not do so. (Tr. 864.)

4. Claim 4: Bone Builder or MCHC Restores Bone Strength

254. CX-7-MCHC-4: Effects of Calcium Supplements on Femoral Bone Mineral Density and Vertebral Fracture Rate in Vitamin-D Replete Elderly Patients by T. Chevalley, J. P. Bonjour, et al., in Osteoporosis International (1994).

This study does not specifically examine bone strength, according to Dr. Holick (Tr. 1034-35), and does not substantiate claim 4.

255. CX-7-MCHC-10: Vitamin D, Hydroxyapatite and Calcium Gluconate in Treatment of Cortical Bone Thinning in Postmenopausal Women With Primary Biliary Cirrhosis by Owen Epstein, Sheila Sherlock, et. al., in The American Journal of Clinical Nutrition (1982).

This report of a study found an increase in cortical bone thickness in subjects receiving ossopan (P. 428) but it did not directly measure bone strength. (Tr. 1036-37.) It does not substantiate claim 4.

256. CX-7-MCHC-13: The Use of a Whole Bone Extract in the Treatment of Fractures by T. J. Mills, et al., in Manitoba Medical Review (1965).

Dr. Holick testified that this study does not substantiate claim 4 because it looks only at fracture healing. (Tr. 1037.) Dr. Heaney testified that this study could be viewed as substantiating claim 4 if fracture healing was considered to be restoring strength to the broken bone. (Tr. 2470.) Since Dr. Heaney did not so construe this study, I find that it does not substantiate claim 4.

257. CX-7-CAL-33: Calcium and Vitamin D Supplements: Effects on Calcium Metabolism in Elderly People by Marie-Claire Chapuy, Pierre Meunier, et ano., in American Journal of Clinical Nutrition (1987).

The merits of this study were not discussed by respondents' experts and it does not, therefore, substantiate claim 4.

258. CX-7-CAL 35: Vitamin D_3 and Calcium to Prevent Hip Fractures in Elderly Women: by Marie C. Chapuy, Pierre Delmas, Pierre Meunier, et al., in The New England Journal of Medicine (1992).

This is a further study by the authors of CAL-33. It does not substantiate claim 4. (Tr. 936.)

259. CX-7-CAL-37: Osteoporosis: Recent Advances in Pathogenesis and Treatment by C. Cooper, et ano., in Quarterly Journal of Medicine (1994).

This review article does not substantiate claim 4. (Tr. 1040-41.) None of respondents' experts commented on this article.

260. CX-7-CAL-59: Management of Osteoporosis and Paget's Disease -- An Appraisal of the Risks and Benefits of Drug Treatment by Carlo Gennari, et al., in Drug Safety (1994).

This chapter from a book, which respondents' experts did not discuss, does not substantiate claim 4. (Tr. 1044.)

261. CX-7-CAL-65: Attempts to Prevent Disuse Osteoporosis by Treatment with Calcitonin, Longitudinal Compression and Supplementary Calcium and Phosphate by David A. Hantman, et al., in Journal of Clinical Endocrinology and Metabolism (1973).

Dr. Heaney testified that there is presumptive proof that calcium restores bone strength. This is not direct evidence of such a relationship. In fact, Dr. Heaney tried to get NIH funds to establish this claim. (Tr. 2657.)

262. CX-7-CAL-69: Calcium Nutrition and Bone Health in The Elderly by Robert P. Heaney, J.C. Gallagher, C.C. Johnston, Robert Neer, Michael Parfitt, G. Donald Whedon, et ano., in American Journal of Clinical Nutrition (1982).

Dr. Strause and Dr. Lachance testified that this review article substantiates claim 4 (Tr. 2774, 1677) but Dr. Heaney, one of its authors, made no such claim. I find that this article does not directly substantiate claim 4.

263. CX-7-CAL-72: Nutritional Factors In Osteoporosis by Robert P. Heaney, in Annual Review of Nutrition (1993).

This article does not substantiate claim 4. (Tr. 1047.) Dr. Heaney's review recognizes a general consensus that decreased mass produces a decrease in bone strength but cautions that there is disagreement about how much of a strength reserve bone possesses. (P. 289.)

264. CX-7-CAL-76: Dietary Calcium and Risk of Hip Fracture: 14-Year Prospective Population Study by Troy L. Holbrook, Elizabeth Barrett-Connor, et ano., in The Lancet (1988).

This study does not discuss bone strength and therefore does not substantiate claim 4. (Tr. 1047, 959-60.)

265. CX-7-CAL-87: Risk Prediction in Osteoporosis: A Theoretic Overview by C. Conrad Johnston, et ano., in American Journal of Medicine (1991).

This review article does not directly address the issues of restoration of bone strength. (Tr. 1049.) Dr. Heaney testified that it is likely that an increase in bone mass will be accompanied by an increase in bone strength (Tr. 2657), but did not state that this article substantiated claim 4.

266. CX-7-CAL-95: New Strategies to Prevent Hip Fracture by Douglas P. Kiel, in Hospital Practice (1994).

Dr. Holick testified that this review article does not substantiate claim 4 (Tr. 1053) and none of respondents' experts discussed it.

267. CX-7-CAL-104: A Review of Calcium Preparations by David I. Levenson, et ano., in Nutrition Reviews (1994).

This review article does not discuss bone strength and it does not substantiate claim 4. (Tr. 900-01.) This review was not discussed by respondents' experts.

268. CX-7-CAL-129: Calcium Requirement and Calcium Therapy by B. E. C. Nordin, et al., in Clinical Orthopaedics and Related Research (1979).

This review article, whose merits were not discussed by respondents' experts, does not evaluate bone strength and does not substantiate claim 4. (Tr. 1056.)

269. CX-7-CAL- 145: Anti-Fracture Efficacy of Calcium in Elderly Women by Robert Recker, D.B. Kimmel, et al., in Journal of Bone and Mineral Research (1994).

This study does not directly measure bone strength and does not substantiate claim 4 (Tr. 1106), although there is a presumption that if fracture risk decreases, bone strength is increased. (Tr. 1351-52.)

270. CX-7-CAL-152: Long-Term Effects of Calcium Supplementation on Bone Loss and Fractures in Postmenopausal Women: A Randomized

Controlled Trial by Ian Reid, et al., in American Journal of Medicine (1995).

This study, according to Dr. Holick, does not substantiate claim 4 because the authors did not specifically measure bone strength. (Tr. 1107.)

Dr. Raisz, in apparent reference to this study, testified that: "The only measure of bone strength in human is the incidence of fractures (Tr. 84-85), and he [Reid] had a small study in which the incidence of spine fractures was reduced with calcium alone." (Tr. 85.) Nevertheless, this article does not directly substantiate claim 4.

271. CX-7-CAL-189: Evaluation of Publicly Available Scientific Evidence Regarding Certain Nutrient-Disease Relationships: Calcium and Osteoporosis by Robert P. Heaney, for FDA (1991).

Although this report by Dr. Heaney substantiates other claims, it does not critically examine bone strength (Tr. 1109) and Dr. Heaney did not testify that it substantiates claim 4.

272. CX-7-CAL-193: Consensus Conference Statement on Optimal Calcium Intake, HHS (1994).

This Consensus Conference report whose message is that calcium is important throughout life (Heaney, Tr. 2624) does not substantiate claim 4. (Tr. 1101.)

5. Claim 5: Bone Builder or MCHC Halts, Prevents Or Treats Osteoporosis

273. CX-7-MCHC 10: Vitamin D, Hydroxyapatite and Calcium Gluconate in Treatment of Cortical Bone Thinning in Postmenopausal Women With Primary Biliary Cirrhosis by Owen Epstein, Sheila Sherlock, et. al., in The American Journal of Clinical Nutrition (1982).

Dr. Holick testified that this study could not be relied upon because it dealt with patients who had primary biliary cirrhosis and received vitamin D

(Tr. 513), but Dr. Heaney testified that the bone loss in these patients is the same as bone loss in osteoporotic patients. (Tr. 2659.)

Dr. Strause, who discounted Dr. Holick's vitamin D objection, testified that this article substantiates claim 5. (Tr. 2773-74.) Dr. Heaney made no such claim. This study does not substantiate claim 5.

274. CX-7-MCHC-14: Microcrystalline Calcium Hydroxyapatite Compound in Corticosteroid-Treated Rheumatoid Patients: A Controlled Study, by Kjell Nilsen, et al., in British Medical Journal (1978).

This abstract of a 1978 controlled study stated that:

> [T]he results of this trial suggest that MCHC has a significant prophylactic effect in preventing the development of osteoporosis in corticosteroid-treated rheumatoid patients. (P. 1124.)

This study substantiates claim 5. (Heaney, Tr. 2470-72.)

275. CX-7-MCHC-15: Clinical Trial of Microcrystalline Hydroxyapatite Compound (`Ossopan') in the Prevention of Osteoporosis Due to Corticosteroid Therapy by A. Pines, et al., in Current Medical Research and Opinion (1984).

Dr. Holick testified that there was no statistically significant difference between the MCHC-treated and untreated groups in this study (Tr. 517-18, 727-28, 919) and I reject it as substantiation.

276. CX-MCHC 16: Comparison of the Treatment Effects of Ossein-Hydroxyapatite Compound and Calcium Carbonate in Osteoporotic Females by P. Ruegsegger, et al., in Osteoporosis International (1995).

Dr. Holick did not testify regarding this study and Dr. Heaney claimed that it "supports claims three and five. Three at least." (Tr. 2474-75.) While it does support claim 3, this equivocal endorsement does not establish that this study substantiates claim 5.

277. CX-7-MCHC-17: Examination of New Bone Growth on Aluminum Oxide Implant Contact Surfaces After Oral Administration of Ossein-Hydroxyapatite Compound to Rats by K. H. Schmidt, in Current Medical Research and Opinion (1988).

This study, which was not discussed by respondents' experts, does not substantiate claim 5. (Tr. 519.)

278. CX-7-MCHC-19: Prospective Trial of Ossein-Hydroxyapatite Compound in Surgically Induced Postmenopausal Women by J. J. Stepan, et al., in Bone (1989).

Dr. Heaney testified that this controlled study substantiates claim 5 only by implication. (Tr. 2476.) I reject it as substantiation.

279. CX-7-CAL-14: Dietary Modification with Dairy Products for Preventing Vertebral Bone Loss in Premenopausal Women: A Three-Year Prospective Study, by Daniel Baran, et al., in Journal of Clinical Endocrinology and Metabolism (1990).

I reject this study since it substantiates claim 5 only by inference. (Heaney, Tr. 2461-62.)

280. CX-7-CAL-31: Dietary Calcium and Bone Mineral Status of Children and Adolescents, by Gary M. Chan, in American Journal Dis. Child (1991).

This study, whose merits were not discussed by respondents' experts, does not substantiate claim 5 because it does not address osteoporosis. (Tr. 528-29.)

281. CX-7-CAL-36: Bone Gain and Loss in Premenopausal Women by Cyrus Cooper, in British Medical Journal (1993).

This review concludes that studies:

suggest that oestrogen status, exercise and calcium nutrition are the most important, modifiable contributors to peak bone mass.

This review, whose merits were not discussed by respondents' experts, does not substantiate the claim that calcium, or MCHC, halts, prevents or treats osteoporosis. (Tr. 531.)

282. CX-7-CAL-39: Management of Fractures in Patients with Osteoporosis, by Charles N. Cornell, in Orthopedic Clinics of North America (1990).

This review article's discussion of bone fractures provides no direct substantiation of claim 5. (Tr. 884-85.)

283. CX-7-CAL-41: Calcium Intake and Bone Mass: A Quantitative Review of the Evidence by Robert Graham Cumming, in Calcified Tissue International (1990).

This meta-analysis concludes:

In summary, in the published literature up to October 1989, there is a consistent positive effect of calcium supplements in tablet form in postmenopausal women at all bone sites except the vertebrae. This supports the recommendation of a high calcium intake for these women, particularly in the early post menopausal years. (P. 199.)

I accept Dr. Heaney's conclusion that this meta-analysis substantiates claim 5. (Tr. 2406-08.)

284. CX-7-CAL-42: A Controlled Trial of the Effect of Calcium Supplementation on Bone Density in Postmenopausal Women by Bess Dawson-Hughes, et al., in The New England Journal of Medicine (1990).

This double-blind, placebo controlled study concluded:

> On the basis of this study, we recommend that healthy postmenopausal women whose dietary calcium intake is low be urged to increase their calcium intake to 800 mg per day in order to eliminate bone loss. (P. 883.)

This study substantiates claim 5 because it demonstrated a clear calcium effect in late menopausal women. (Heaney, Tr. 2411-15.)

285. CX-7-CAL-43: Dietary Calcium Intake and Bone Loss From the Spine in Healthy Postmenopausal Women by Bess Dawson-Hughes, et al., in American Journal of Clinical Nutrition (1987).

This double-blind, placebo controlled study which was rejected by Dr. Holick (Tr. 537-38) was not cited by respondents' experts as substantiation for claim 5.

286. CX-7-CAL-48: Calcium Supplementation Reduces Vertebral Bone Loss in Perimenopausal Women: A Controlled Trial in 248 Women Between 46 and 55 Years of Age by Petra J. M. Elders, Paul Lips, et al., in Journal of Clinical Endocrinology and Metabolism (1991).

The report of this randomized, controlled study stated:

> We conclude that calcium supplementation retards lumbar bone loss in the first year of calcium supplementation by reducing bone turnover. (P. 533.)

Dr. Holick testified that this study showed only a marginal effect on osteoporosis the first year. (Tr. 540.) Dr. Heaney concluded that this study substantiates claim 5 only by implication (Tr. 2466) and I therefore reject it as substantiation.

287. CX-7-CAL-49: Long-Term Effect of Calcium Supplementation on Bone Loss in Premenopausal Women, by Petra J. M. Elders, Paul Lips, et al., in Journal of Bone and Mineral Research (1994).

The authors of this randomized, controlled study reported that:

> [C]alcium supplements were observed to be most effective in those women in whom the baseline calcium intake was low, the mean age was high, and there was clinical evidence of osteoporosis. (P. 967.)

This study only substantiates claim 5 by implication (Heaney, Tr. 2466) and I reject it as substantiation.

288. CX-7-CAL-55: Relationships Between Usual Nutrient Intake and Bone-Mineral Content of Women 35-65 Years of Age: Longitudinal and Cross-Sectional Analysis by Jo L. Freudenheim, et al., in American Journal of Clinical Nutrition (1986).

None of respondents' experts discussed the merits of this study. It does not substantiate claim 5.

289. CX-7-CAL-57: The Crush Factor Syndrome in Postmenopausal Women by J. C. Gallagher, A. Horsman, B.E.C. Nordin, et al., in Clinics in Endocrinology and Metabolism (1973).

This review article does not substantiate claim 5. (Tr. 552, 773.) None of respondents' experts discussed the merits of this article.

290. CX-7-CAL-64: Lifetime Calcium Intake and Physical Activity Habits: Independent and Combined Effects on the Radial Bone of Healthy Premenopausal Caucasian Women by Lydia Halioua and John J. B. Anderson, in American Journal of Clinical Nutrition (1989).

This study, which was not discussed by any of respondents' experts, does not substantiate claim 5. (Tr. 558-59.)

291. CX-7-CAL-65: Attempts to Prevent Disuse Osteoporosis by Treatment with Calcitonin, Longitudinal Compression and Supplementary Calcium and Phosphate by David A. Hantman, et al., in Journal of Clinical Endocrinology and Metabolism (1973).

This study, whose merits were not discussed by any of respondents' experts, does not substantiate claim 5. (Tr. 562.)

292. CX-7-CAL-68: Bone Mass, Nutrition, and Other Lifestyle Factors by Robert P. Heaney, in American Journal of Medicine (1993).

This review article by Dr. Heaney substantiates claim 5. (See F. 133, 219.)

293. CX-7-CAL-69: Calcium Nutrition and Bone Health in the Elderly by Robert P. Heaney, J.C. Gallagher, C.C. Johnston, Robert Neer, Michael Parfitt, G. Donald Whedon, et ano., in American Journal of Clinical Nutrition (1982).

This very early article does not substantiate claim 5. (Tr. 571.)

294. CX-7-CAL-70: Effect of Calcium on Skeletal Development, Bone Loss and Risk of Fractures by Robert P. Heaney, in American Journal of Medicine (1991).

This review by Dr. Heaney states that:

> The conclusion from all these studies seems inescapable: low calcium intake contributes to age-related bone loss, and high intakes reduce such loss. (PP. 5B-25S-26S.)

This review substantiates claim 5. (Tr. 2775.)

295. CX-7-CAL-72: Nutritional Factors In Osteoporosis by Robert P. Heaney, Annual Review of Nutrition (1993).

Dr. Heaney testified that this article by him, and particularly the statements on p. 303, has been reflected in FDA regulations requiring calcium as a component of every therapeutic regimen for osteoporosis. (Heaney, Tr. 2386.) His article states:

> The goals of treatment of osteoporosis, in addition to symptom control and rehabilitation, include arrest of further bone loss and, where possible, restoration of lost bone mass.

However, for any of these modalities to produce these effects, calcium intakes must be sufficient to prevent further bone loss and/or support the laying down of new bone, without taking calcium from other regions of the skeleton.

Hence, calcium supplementation, usually beyond what can feasibly be provided by diet alone, constitutes an essential component of virtually every therapeutic regimen for this disorder. (P. 303.)

296. CX-7-CAL-73: Editorial: A Unified Concept of Osteoporosis by Robert P. Heaney, in American Journal of Medicine (1965).

This early editorial by Dr. Heaney, whose merits were not discussed by respondents' experts, does not substantiate claim 5. (Tr. 576-78.)

297. CX-7-CAL-77: Biochemical Effects of Calcium Supplementation in Postmenopausal Osteoporosis by M. Horowitz, B.E.C. Nordin, et al., in European Journal of Clinical Nutrition (1988).

This study, whose merits were not discussed by respondents' experts, involved 20 women, and concluded that the data collected "[does] not prove that calcium supplementation is a useful preventative or therapeutic measure in postmenopausal osteoporosis." (P. 777.) It does not substantiate claim 5.

298. CX-7-CAL-78: Effect of Calcium Supplementation on Urinary Hydroxyproline in Osteoporotic Postmenopausal Women by Michael Horowitz, B. E. C. Nordin, et al., in American Journal of Clinical Nutrition (1984).

This study, whose merits were not discussed by respondents' experts, does not substantiate claim 5. (Tr. 584-86, 962-63.)

299. CX-7-CAL-83: The Relationship of Dietary Calcium Intake to Radiographic Bone Density in Normal and Osteoporotic Persons by Lewis M. Hurxthal, et ano., in Calcified Tissue Research (1969).

This study does not substantiate claim 5. (Tr. 589-90.)

300. CX-7-CAL-84: Osteoporosis Associated With Rheumatoid Arthritis: Pathogenesis and Management by Ian Joffe and Solomon Epstein, in Seminars in Arthritis and Rheumatism (1991).

This review, which was not discussed by respondents' experts, does not substantiate claim 5. (Tr. 593, 894-95.)

301. CX-7-CAL-85: Calcium Supplementation and Increases in Bone Mineral Density in Children by C. Conrad Johnston, et al., in New England Journal of Medicine (1992).

This double-blind controlled study of identical twins demonstrates the importance of calcium supplements to peak bone mass which is a critical indication of future risk of osteoporosis. (Strause, Tr. 2779-80.) It substantiates claim 5.

302. CX-7-CAL-104: A Review of Calcium Preparations by David I. Levenson, et ano., in Nutrition Reviews (1994).

This review article was not discussed by respondents' experts. It does not substantiate claim 5. (Tr. 900-01.)

303. CX-7-CAL-107: Calcium Supplementation and Bone Mineral Density in Adolescent Girls by Tom Lloyd, et al., in Journal of the American Medical Association (1993).

This study does not directly substantiate claim 5. It does so only by inference. (Heaney, Tr. 2423-24.) I reject it as substantiation.

304. CX-7-CAL-109: Osteoporosis - A Mineral Deficiency Disease? by Leo Lutwack, in Journal of the American Dietetic Association (1964).

This review article, which was not discussed by respondents' experts, does not substantiate claim 5. (Tr. 624-25.)

305. CX-7-CAL-112: Bone Status and Fracture Rates in Two Regions of Yugoslavia by Velimir Matkovic, B.E.C. Nordin, et al., in The American Journal of Clinical Nutrition (1979).

This epidemiological study, according to Dr. Holick and Dr. Raisz, is significantly flawed. (Tr. 627-30, 163-64.) Nevertheless, when asked what clinical trial he was relying on when he observed that if one does not replace lost calcium it may lead to osteoporosis, Dr. Holick cited this study. (Tr. 1156.) This study, which concluded that calcium intake was the main factor influencing cortical bone mass, substantiates claim 5. (Strause, Tr. 2781-82; Heaney, Tr. 2468-69.)

306. CX-7-CAL-113: Calcium Metabolism and Calcium Requirements During Skeletal Modeling and Consolidation of Bone Mass by V. Matkovic, in American Journal of Clinical Nutrition (1991).

This review of calcium balance studies does not substantiate claim 5. (Tr. 631.)

307. CX-7-CAL-117: Required Versus Optimal Intakes: A Look at Calcium by Gregory D. Miller and Connie M. Weaver, in Journal of Nutrition (1994).

This article, whose merits were not discussed by respondents' experts, does not substantiate claim 5. (Tr. 633.)

308. CX-7-CAL-120: Recommended Dietary Allowances, 10th edition, published by the National Research Counsel of the National Academy of Sciences in 1989.

Although none of respondents' experts discussed this publication, it is obviously relevant to and supports claim 5.

> In the subcommittee's judgment, the most promising nutritional approach to reduce the risk of osteoporosis in later life is to ensure a calcium intake that allows the development of each individual's genetically programmed peak bone mass during the formative years. . . . (P. 178.)

309. CX-7-CAL-123: Comparison of Calcium, Calcitriol, Ovarian Hormones and Nandrolone in the Treatment of Osteoporosis by A. G. Need, B.E.C. Nordin, et al., in Maturitas (1986).

This study substantiates claim 5. (Tr. 2471.)

310. CX-7-CAL-128: The Calcium Deficiency Model for Osteoporosis by B. E. C. Nordin, et ano., in Nutrition Reviews (1989).

This review article, whose merits were not discussed by respondents' experts, does not substantiate claim 5. (Tr. 639-40.)

311. CX-7-CAL-129: Calcium Requirement and Calcium Therapy by B. E. C. Nordin, et al., in Clinical Orthopaedics and Related Research (1979).

This review article, whose merits were not discussed by respondents' experts, does not substantiate claim 5. (Tr. 641-42.)

312. CX-7-CAL-130: Calcium Supplementation of the Diet: Justified by Present Evidence by B. E. Christopher Nordin and Robert P. Heaney, in British Medical Journal (1990).

Although Dr. Heaney did not testify that this article supports claim 5, it is an important article which summarizes as of 1990 the evidence justifying calcium supplementation:

> In a recent review Kanis and Passmore concluded that there was no case for supplementation of the diet with calcium for the prevention or treatment of osteoporosis. We consider that present evidence, taken as a whole, points to a different conclusion. (P. 1.)

Dr. Heaney testified that the view expressed in the article is not only his, but that of the FDA, NIH and others. (Tr. 2364-65.)

313. CX-7-CAL-134: Treatment of Spinal Osteoporosis on Postmenopausal Women by B. E. C. Nordin, et al., in British Medical Journal (1980).

This study, whose merits were not discussed by respondents' experts, does not substantiate claim 5. (Tr. 646.)

314. CX-7-CAL-143: The Effects of Calcium Supplementation (Milk Powder or Tablets) and Exercise on Bone Density in Postmenopausal Women by Richard Prince, et al., in Journal of Bone and Mineral Research (1995).

Dr. Holick testified that this randomized, controlled study does not substantiate claim 5 for, although those subjects taking some form of calcium had less bone loss, all subjects lost bone. (Tr. 650.)

Dr. Heaney, however, testified that this study demonstrates that calcium slowed or stopped bone loss at the hip, but he was not certain that this evidence related to claim 5. (Tr. 2432.) This study does not substantiate claim 5.

315. CX-7-CAL- 145: Anti-Fracture Efficacy of Calcium in Elderly Women by Robert Recker, D.B. Kimmel, et al., in Journal of Bone and Mineral Research (1994).

Dr. Holick testified that this abstract's conclusion that increasing calcium intake causes a significant reduction in the risk of further vertebral fractures in elderly women was reasonable (Tr. 1844), and Dr. Heaney testified:

> if you reduce the risk of vertebral fractures, you are treating or preventing osteoporosis. (Tr. 2301.)

This abstract substantiates claim 5.

316. CX-7-CAL-146: Bone Gain in Young Adult Women by Robert R. Recker, Robert P. Heaney, Donald B. Kimmel, et al., in Journal of the American Medical Association (1992).

None of respondents' experts discussed the merits of this study. It does not substantiate claim 5. (Tr. 658.)

317. CX-7-CAL-148: Effect of Estrogens and Calcium Carbonate on Bone Loss in Postmenopausal Women by Robert R. Recker, Robert P. Heaney, et ano., in Annals of Internal Medicine (1977).

Dr. Heaney testified that this study, contrary to Dr. Holick's conclusion (Tr. 660), substantiates claim 5 because the calcium group lost less bone and he considered this as slowing the onset of osteoporosis. (Tr. 2398.) This study substantiates claim 5.

318. CX-7-CAL-151: Effect of Calcium Supplementation on Bone Loss in Postmenopausal Women by Ian Reid, et al., in New England Journal of Medicine (1993).

This randomized, double blind controlled study found that a calcium supplement of 1000 mg per day has a beneficial effect on bone loss in normal postmenopausal women. (P. 462.)

However, Dr. Heaney testified that while this study substantiates claim 3 (and 1; Strause, Tr. 2786-87) it substantiates claim 5 only by implication. (Tr. 2473.) I reject this study as substantiation.

319. CX-7-CAL-152: Long-Term Effects of Calcium Supplementation on Bone Loss and Fractures in Postmenopausal Women: A Randomized Controlled Trial by Ian Reid, et al., in American Journal of Medicine (1995).

This study is a follow-up to CX-7-CAL-151 and Dr. Heaney testified that it substantiated claim 5. (Tr. 2474.)

320. CX-7-CAL-161: The Role of Manganese in Bone Metabolism by Paul Saltman and Linda Strause, in The Nutrition Report (1987).

See CX-7-CAL-181.

321. CX-7-CAL-172: Chapter 5, Calcium and Phosphorus by Louis V. Avioli, in the book Modern Nutrition in Health and Disease (1988).

This book chapter, which was not discussed by respondents' experts, does not substantiate claim 5. (Tr. 684, 837-38, 1002-03.)

322. CX-7-CAL-173: Calcium Supplementation and Bone Loss in Middle-Aged Women by Everett L. Smith, et al., in American Journal of Clinical Nutrition (1989).

None of respondents' experts discussed this study. It does not substantiate claim 5. (Tr. 685, 838.)

323. CX-7-CAL-179: Absorption of Calcium in Osteoporosis by Herta Spencer, et al., in American Journal of Medicine (1964).

None of respondents' experts testified that this study substantiated claim 5. It is rejected as substantiation.

324. CX-7-CAL-181: Spinal Bone Loss in Postmenopausal Women Supplemented with Calcium and Trace Minerals by Linda Strause, Paul Saltman, et al., in Journal of Nutrition (1994).

In this randomized, controlled study, Dr. Strause found that:

> In summary, spinal bone loss in a small group of older postmenopausal women was slowed by supplementation with calcium as CCM [calcium citrate malate] and was halted by supplementation with a mineral cocktail composed of CCM along with zinc, manganese and copper. (P. 1063.)

This study, along with those reported in CX-7-CAL-161 and 182, according to Dr. Strause, demonstrate the efficacy of calcium and trace minerals in improving the spinal bone density in her subjects. This study substantiates claim 5. (Tr. 2789-92.)

325. CX-7-CAL-182: The Role of Trace Elements in Bone Metabolism by Linda Strause, P. Saltman, et al., in Nutritional Aspects of Osteoporosis (1991).

See CX-7-CAL-181.

326. CX-7-CAL-185: Calcium Balance in Osteoporotic Patients on Long-Term Oral Calcium Therapy With and Without Sex Hormones by N. C. Thalassinos, et al., in Clinical Science (1982).

This study was not discussed by respondents' experts and does not substantiate claim 5. (Tr. 693-94, 1011.)

327. CX-7-CAL-189: Evaluation of Publicly Available Scientific Evidence Regarding Certain Nutrient-Disease Relationships: Calcium and Osteoporosis by Robert P. Heaney.

This is a report authored by Dr. Heaney for the Center for Food Safety & Applied Nutrition, Life Sciences Research Office of the FDA in 1991 and it states:

> There is general agreement among the documents to the effect that achieving peak bone mass is a good, and possibly the best known, prevention against late-life osteoporosis. (P. 1.)

This report substantiates claim 5. (Heaney, Tr. 2322-23; Lachance, Tr. 1667-68.)

328. CX-7-CAL-191: Food Labeling: Health Claims; Calcium and Osteoporosis, regulations promulgated by the Federal Food and Drug Administration in 1993.

Although this document was not discussed by any of respondents' experts, it offers support for claim 5:

> To summarize, these new findings were consistent with and strengthened the conclusion that adequate calcium intake has a significant impact on bone health and risk of osteoporotic fracture. (P. 755.)

Dr. Holick testified that he agreed with this conclusion. (Tr. 2004.)

329. CX-7-CAL-192: Public Health Reports, National Conference on Women's Health Series, Special Topic On Osteoporosis, HHS (1987).

None of respondents' experts testified about this study and I reject it as substantiation for claim 5.

330. CX-7-CAL-193: Consensus Conference Statement on Optimal Calcium Intake, HHS (1994).

This conference report encourages taking the RDA of calcium to maintain bone health. It does not specifically substantiate claim 5. (Tr. 457-58, 708, 854-55.)

331. CX-7-CAL-194: Consensus Development Conference Statement - Osteoporosis, HHS (1984).

Dr. Raisz testified that he agreed with the Consensus Conference's conclusion that "it seems likely that an increase in calcium intake to 1,000 to 1,500 mg a day, beginning well before the menopause, will reduce the incidence of osteoporosis in post menopausal women. Increased calcium intake may prevent age-related bone loss in men as well." (Tr. 242-43.)

Dr. Heaney testified that the information contained in a Consensus Conference Statement such as this one is accepted as fact although more studies might be needed, and that the purpose of issuing such a statement is to disseminate the information contained therein as widely as possible. (Tr. 2634-35.) This document provides substantiation for claim 5. (Heaney, Tr. 2402-03.)

6. Claim 6: Bone Builder or MCHC Reduces or Eliminates Pain Associated With Bone Ailments

332. CX-7-MCHC-14: Microcrystalline Calcium Hydroxyapatite Compound in Corticosteroid-Treated Rheumatoid Patients: A Controlled Study, by Kjell Nilsen, et al. , in British Medical Journal (1978).

This abstract of a study does not substantiate claim 6 because the authors did not conduct a careful study of pain; also, their comments are merely observational. (Tr. 1117.) None of respondents' experts testified about the merits of this abstract.

333. CX-7-MCHC-15: Clinical Trial of Microcrystalline Hydroxyapatite Compound ('Ossopan') in the Prevention of Osteoporosis Due to Corticosteroid Therapy by A. Pines, et al., in Current Medical Research and Opinion (1984).

Dr. Holick testified that this study does not substantiate claim 6 because the patients were being treated with steroids which causes a specific kind of bone disease. (Tr. 1118.)

Dr. Heaney said that one "could say" this study substantiates claim 6. (Tr. 2472.) This is, at best, lukewarm support for claim 6, and this study does not substantiate it.

334. CX-7-MCHC-18: Microcrystalline Hydroxyapatite Compound in Prevention of Bone Loss in Corticosteroid-Treated Patients with Chronic Active Hepatitis by A. Stellon, et al., in Postgraduate Medical Journal (1985).

This study states that MCHC was associated with resolution of back pain in one of two patients. This anecdotal (Strause, Tr. 2792-93) and insignificant result (Tr. 1120) is further suspect because there is no proof that the pain experienced was bone pain. (Tr. 1128.) This study does not substantiate claim 6.

335. CX-7-CAL-132: The Pathogenesis of Osteoporosis by B. E. C. Nordin, in Lancet (1961).

This review article, whose merits were not discussed by respondents' experts, does not substantiate claim 6 because there is no proof that the pain being treated was bone pain.

336. CX-7-CAL-178: A Reliable In Vivo Measurement of Bone-Mineral Content by James A. Sorenson, et al., in Journal of Bone & Joint Surgery (1967).

This report of a study was not discussed by any of respondents' experts and does not substantiate claim 6. (Tr. 1132-34.)

7. Claim 7: Bone Builder or MCHC is Superior to and/or More Effective than Other Forms of Calcium in the Prevention and Treatment of Bone Ailments

337. CX-7-MCHC-1: The Influence of Ossein-Hydroxyapatite Compound ('Ossopan') on the Healing of a Bone Defect by M. Annefeld, et al., in Current Medical Research and Opinion (1986).

Although this study reported that an ossein-hydroxyapatite compound has a beneficial effect on the process of bone healing, there is no indication that the effect would be the same on humans. (Tr. 324-25.) It does not substantiate claim 7.

338. CX-7-MCHC-6: Calcium Metabolism in Bone Disease: Effects of Treatment with Microcrystalline Calcium Hydroxyapatite Compound and Dihydrotachysterol by C E Dent and I J T Davies, in Journal of the Royal Society of Medicine (1980).

This study involved only three patients with a rare genetic disorder. Its results are not necessarily applicable to the general population and do not substantiate claim 7. (Tr. 334-35.)

339. CX-7-MCHC-7: Non-Hormonal Treatment of Osteoporosis by Allan St.J. Dixon, in British Medical Journal (1983).

This editorial was not discussed by respondents' experts and does not substantiate claim 7.

340. CX-7-MCHC-8: Extracts of Bone Contain a Potent Regulator of Bone Formation by R. H. Drivdahl, G. A. Howard and D. J. Baylink, in Biochimica et Biophysica Acta. (1982).

There is no reason to believe that this study of two-day old chicks is relevant to bone health to humans. (Tr. 339-40, 472, 2114.) Dr. Strause testified that this article suggests that MCHC may be superior to other forms of calcium (Tr. 2770), but this equivocal conclusion does not establish that this study substantiates claim 7.

341. CX-7-MCHC-10: Vitamin D, Hydroxyapatite and Calcium Gluconate in Treatment of Cortical Bone Thinning in Postmenopausal Women With Primary Biliary Cirrhosis by Owen Epstein, Sheila Sherlock, et al., in The American Journal of Clinical Nutrition (1982).

This report of a study states:

> we conclude that in postmenopausal women with PBC [primary biliary cirrhosis], calcium supplements given in addition to parenteral vitamin D prevents or retards pathological bone thinning. The provision of calcium and phosphate in the form of HA [hydroxyapatite] offers additional benefits as both minerals are absorbed in PBC. (PP. 429-30.)

Despite Dr. Holick's complaint that this study involved women with severe bone disease and the administration of vitamin D (Tr. 347-50), Dr. Heaney and Dr. Strause saw no problem with these variables. (Tr. 2442-43, 2394, 2659, 2773-74.) However, Dr. Heaney testified that he was not sure how strong the study was. (Tr. 2442.) This study does not substantiates claim 7.

342. CX-7-MCHC-13: The Use of a Whole Bone Extract in the Treatment of Fractures by T. J. Mills, et al., in Manitoba Medical Review (1965).

This study is not relevant to claim 7 because it compared the effects of ossopan against a placebo, not calcium. It does not substantiate claim 7. (Tr. 351.)

343. CX-7-MCHC-14: Microcrystalline Calcium Hydroxyapatite Compound in Corticosteroid-Treated Rheumatoid Patients: A Controlled Study, by Kjell Nilsen, et al., in British Medical Journal (1978).

This abstract of a controlled study does not substantiate claim 7 because it did not compare MCHC to other forms of calcium. (Holick, Tr. 353-54.) None of respondents' experts testified about the merits of this study.

344. CX-7-MCHC-16: Comparison of the Treatment of Ossein-Hydroxyapatite Compound and Calcium Carbonate in Osteoporotic Females by P. Ruegsegger, et al., in Osteoporosis International (1995).

This report of a randomized, double blinded study states:

> The present study shows that OHC (ossein-hydroxyapatite compound] is more effective than CC [calcium carbonate] in preventing further bone loss in postmenopausal women. (P. 33.)

Dr. Heaney and Dr. Strause testified that this study substantiates claim 7. (Tr. 2474-75, 2785-86.) Dr. Heaney also testified that this is a well designed, randomized, double-blind, controlled trial which would pass muster, and is one of the better MCHC studies. (Tr. 2439.) This study substantiates claim 7.

345. CX-7-MCHC-17: Examination of New Bone Growth on Aluminum Oxide Implant Contact Surfaces After Oral Administration of Ossein-Hydroxyapatite Compound to Rats by K. H. Schmidt, et ano., in Current Medical Research and Opinion (1988).

This study was not discussed by any of respondents' expert witnesses and does not substantiate claim 7.

346. CX-7-MCHC-20: Quantitation of Growth Factors in Ossein-Mineral Compound by Jan J. Stepan, Subburaman Mohan, David J. Baylink, et al., in Life Sciences (1991).

While this report of a study discusses an ossein-mineral-compound it does not compare it with calcium. (Tr. 368-69.) Dr. Heaney did state that this article provides preliminary evidence of the superiority of MCHC over other forms of calcium (Tr. 2449-50), but he stated, apparently with respect to this article: "Now, whether or not that's true, we don't know." (Tr. 2451.) This report does not substantiate claim 7.

347. CX-7-CAL-20: Instrumental Comparison for the Determination of Cadmium and Lead in Calcium Supplements and Other Calcium-rich Matrices by Bernard P. Bourgoin, et al., in Analyst (1992).

None of respondents' experts testified in opposition to Dr. Holick's testimony that this study does not mention MCHC. (Tr. 381-82.) It therefore does not substantiate claim 7.

348. CX-7-CAL-23: Calcium, Estrogen, and Progestin in the Treatment of Osteoporosis by Neil Breslau, in Rheumatic Disease Clinics of North America (1994).

This review, which was not discussed by respondents' experts, does not substantiate claim 7 because it does not mention MCHC. (Tr. 387-88.)

349. CX-7-CAL-40: Lead-Contaminated Health Food by William H. Crosby, in Journal of the American Medical Association (1977).

This case report, which respondents' experts did not discuss, does not substantiate claim 7. (Tr. 386-88.)

350. CX-7-CAL-161: The Role of Manganese in Bone Metabolism by Paul Saltman and Linda Strause, in The Nutrition Report (1987).

This review article discusses trace minerals and bone health. There is no proof that Bone Builder or MCHC contains these trace minerals. Therefore this study does not substantiate claim 7.

351. CX-7-CAL-162: The Role of Trace Minerals in Osteoporosis by Paul D. Saltman and Linda Strause, in Journal of the American College of Nutrition (1993).

This review article is rejected for the reason given in my analysis of CX-7-CAL-161.

352. CX-7-CAL-181: Spinal Bone Loss in Postmenopausal Women Supplemented with Calcium and Trace Minerals by Linda Strause, Paul Saltman, et al., in Journal of Nutrition (1994).

This study is rejected for the reason given in my analysis of CX-7-CAL-161.

353. CX-7-CAL-182: The Role of Trace Elements in Bone Metabolism by Linda Strause, P. Saltman, et al., in the publication Nutritional Aspects of Osteoporosis (1991).

This study is rejected for the reason given in my analysis of CX-7-CAL-161.

8. Claim 8: Bone Builder/MCHC is More Bioavailable, More Absorbable, or More Effectively Utilized by the Body than Other Forms of Calcium

354. CX-7-MCHC-1: The Influence of Ossein-Hydroxyapatite Compound ('Ossopan') on the Healing of a Bone Defect by M. Annefeld, et al., in Current Medical Research and Opinion (1986).

This rabbit study, which was not discussed by respondents' experts, did not directly compare the bioavailability or absorbability of the calcium products tested. (Tr. 465-66.) It does not substantiate claim 8.

355. CX-7-MCHC-2: Absorption Intestinale de Gluconate de Calcium et de Complexe Ossèino-Minèral: Èvaluation Par Des Dosages Conventionnels by T. Buclin, P. Burckhardt, et ano., in Schweitzer Medical Wschr. (1986).

Dr. Heaney testified that this study showed that MCHC was at least as good as, and possibly superior to, calcium gluconate in terms of bioavailability. (Tr. 2446-47.) He also testified that a study he conducted suggested that MCHC was slightly more bioavailable than calcium carbonate, but the difference was not statistically significant. (Tr. 2641-42.) This study does not substantiate claim 8 because MCHC's superiority is not clearly established. (See also F. 357.)

356. CX-7-MCHC-6: Calcium Metabolism in Bone Disease: Effects of Treatment with Microcrystalline Calcium Hydroxyapatite Compound and Dihydrotachysterol by C E Dent and I J T Davies, in the Journal of the Royal Society of Medicine (1980).

Dr. Strause is cited as testifying that this study substantiates claim 8. I do not agree, for when asked "To that extent, does it also provide some evidence that the MCHC may be superior to some other form of calcium" she stated: "Maybe." (Tr. 2770.) This study does not substantiate claim 8.

357. CX-7-MCHC-10: Vitamin D, Hydroxyapatite and Calcium Gluconate in Treatment of Cortical Bone Thinning in Postmenopausal Women With Primary Biliary Cirrhosis by Owen Epstein, Sheila Sherlock, et al., in The American Journal of Clinical Nutrition (1982).

This report of a study provides some substantiation for claim 8 according to Dr. Strause. (Tr. 2774.) However, this testimony was placed in perspective by Dr. Heaney's observation that:

> So I've just not paid a lot of attention to the MCHC literature over the years, and I probably won't after this trial is over either. Just -- I mean calcium is calcium as far as -- well that's an oversimplification, but there's some truth in it. (Tr. 2447.)

This study does not substantiate claim 8.

358. CX-7-MCHC-13: The Use of a Whole Bone Extract in the Treatment of Fractures by T. J. Mills, et al., in Manitoba Medical Review (1965).

This study, which was not discussed by any of respondents' experts, does not substantiate claim 8. (Tr. 350-51, 476.)

359. CX-7-MCHC-14: Microcrystalline Calcium Hydroxyapatite Compound in Corticosteroid-Treated Rheumatoid Patients: A Controlled Study, by Kjell Nilsen, et al., in British Medical Journal (1978).

This study found that:

> "long-term comparisons of MCHC with, for example, calcium gluconate, are required" to demonstrate its bioavailability or absorbability. (P. 1124.)

This study does not substantiate claim 8. In addition, none of respondents' experts testified about the merits of this study.

360. CX-7-MCHC-15: Clinical Trial of Microcrystalline Hydroxyapatite Compound ('Ossopan') in the Prevention of Osteoporosis Due to Corticosteroid Therapy by A. Pines, et al., in Current Medical Research and Opinion (1984).

This study, whose merits were not discussed by respondents' experts, does not substantiate claim 8. (Tr. 355, 2783 (no direct comparison with another calcium supplement).)

361. CX-7-MCHC-18: Microcrystalline Hydroxyapatite Compound in Prevention of Bone Loss in Corticosteroid-Treated Patients with Chronic Active Hepatitis by A. Stellon, et al., in Postgraduate Medical Journal (1985).

None of respondents' experts discussed the merits of this study, which did not compare MCHC with any other form of calcium. (Tr. 480-81.) It does not substantiate claim 8.

362. CX-7-MCHC-19: Prospective Trial of Ossein-Hydroxyapatite Compound in Surgically Induced Postmenopausal Women by J. J. Stepan, et al., in Bone (1989).

This article did not compare MCHC with another calcium supplement and does not substantiate claim 8. (Tr. 482.)

363. CX-7-MCHC-20: Quantitation of Growth Factors in Ossein-Mineral Compound by Jan J. Stepan, Subburaman Mohan, David J. Baylink, et al., in Life Sciences (1991).

This study does not substantiate claim 8 because it does not directly compare MCHC with other calcium supplements. Dr. Raisz' testimony is not, as respondents claim, contrary to this conclusion:

> Q. There are some reports, not extended trials, that do indicate some superiority of MCHC over other forms?
>
> A. There may be. Whether or not they are fully valid as clinical studies is a different question, and I understood that I was not supposed to be charged with analyzing these studies. (Tr. 239.)

O. Conclusion With Respect To Respondents' Substantiation

364. The parties have taken extreme positions with respect to respondents' substantiation: complaint counsel claim that none of the over 100 studies, trials, articles, editorials, and abstracts offered by respondents substantiate their claims; respondents say that each one of these documents do so.

None of the parties' experts took this position, for many of respondents' scientific papers were not discussed by them at trial (see, e.g., F. 108, 111, 117, 128, 129, 130, 180, 184, 186, 207, 208, 277, 290, 300, 302, 304, 336, 339, 345, 349) which suggests that they were never seriously thought of as substantiation.

365. Similarly, despite Dr. Holick's rejection of all of respondents' papers, he conceded that many of them discuss scientific matters and that their conclusions were reasonable.[6] (See, e.g., Tr. 1993-94, 2208-09, 1907-09, 1856, 2222-23, 2230, 2020-21, 2025-26, 1974, 2078, 2009, 1990-94, 2205-06, 1899, 2208-09, 1907-09, 1856, 2222-24, 1924, 2226, 2230, 2019-20, 2020-21, 2025-26, 2028, 2038, 2039, 2042, 1958-59, 2044, 2068-69, 1974, 2078, 2085.)

366. Furthermore, while Dr. Holick examined, and rejected, all of respondents' substantiation documents, he testified on cross that some did support claims 1, 2, 3 and 5.

CLAIM 1

Q. And, Doctor, do any of the articles support the proposition that calcium builds bone or increases bone thickness, can reduce it or increase it at all?

A. Under certain circumstances, such as during the formative years, as we have discussed previously, the answer is yes. (Tr. 1348.)

CLAIM 2

Q. Doctor, do any of the articles support the proposition that calcium restores lost bone:

---

[6]Defined by Dr. Holick as:

> Reasonable to me, means that its good science and that the conclusions are supported by the facts. (Tr. 1370.)

Dr. Holick qualified this testimony, however, by stating later, that reasonable doesn't necessarily mean that it's of high value scientifically, or that he agrees with a study's conclusions. (Tr. 2034-36.)

A. I would have to answer again, under certain circumstances of calcium nutritional deficiency, the answer probably is yes. (Tr. 1348.)

Q. Page 123, sir. January 16. Starting at line two, were you asked the following questions and did you give the following answers:

Question: "Do any of the articles support the proposition that calcium restores lost bone?"

Answer: "Yes." (Tr. 1349.)

Q. This is the January 16 transcript which you reviewed and signed; is that correct?

A. That's correct.

Q. Did you make any changes on page 123?

A. I did not make any changes. That's correct. (Tr. 1349-50.)

CLAIM 3

Q. Doctor, do any of the articles support the proposition that calcium halts or prevents bone loss or bone thinning?

A. I -- I'd have to go back through each of the individual articles because it depends upon the circumstances. But I believe that -- that the authors may have come to that conclusion. (Tr. 1349.)

Q. Doctor, would you please just go to page 123 of the January 16 transcript of your deposition?

A. What page?

Q. Page 123, sir. January 16. Starting at line two, were you asked the following questions and did you give the following answers:

Question: "Do any of the articles support the proposition that calcium also prevents bone loss or bone thinning?

Answer: "Yes."

Q. Were you asked those questions? Did you give those answers?

A. Yes. (Tr. 1349.)

CLAIM 5

Q. And, Doctor, do some of the articles support the conclusion that calcium halts, prevents and treats osteoporosis?

A. Under certain circumstances, yes. (Tr. 1348.)

And as to respondents' substantiation generally, Dr. Holick testified:

Q. Would you agree that many of the articles you reviewed are good studies regarding very specific issues and that the results support the conclusions of many of the articles?

A. Yes. (Tr. 1348.)

367. Respondents' experts also testified that the scientific papers received in evidence substantiate some of the claims made for Bone Builder.

Claim 1

368. Dr. Heaney testified that while calcium alone does not build the skeleton, it is an essential element in the process and that it builds

bone, or, which is the same thing (Tr. 2496), increases bone thickness (Tr. 2321-22; see also Lachance, Tr. 1645).

Claim 2

369. As to this claim, Dr. Heaney testified:

> So, we need to qualify and put fences around this question of what it means to restore lost bone. Furthermore, the body of evidence with respect to this restoration that I've been talking about is much skimpier than the body of evidence with respect to one, three and five, where the weight of the evidence and the quality of the evidence is so high that there is no serious debate about those issues. But, we could get a good scientific debate about whether I'm right about being able to get back illness related bone loss.
>
> My reading of the evidence is, yes, you can do that, but I'm sure I've got some peers who are going to be skeptics and say, I'm not convinced yet. (Tr. 2342.)

Claim 3

370. Dr. Heaney testified that calcium "prevents bone loss or thinning. That's fact, that's established, that's accepted. I should have thought, by everybody, but if not by everybody, there's clearly a consensus to that effect." (Tr. 2340-41.)

Claim 4

371. As to claim 4, Dr. Heaney testified that it is "probably the weakest of the four claims here" and that he would prefer to say that calcium preserves, but does not restore bone strength. (Tr. 2343.)

Claim 5

372. Dr. Heaney's testimony with respect to claim 5 establishes that calcium halts, prevents or treats osteoporosis. (Tr. 2341-42.) CX-7-

CAL-189 (F. 167) offers solid substantiation for this claim as well as claim 3. (Heaney, Tr. 2322-23.)

373. After considering all of the substantiation offered by respondents, and the expert testimony, I conclude, as does Dr. Heaney, that claims 1, 3, and 5 are substantiated. Two (despite Dr. Holick's testimony (F. 366)) and 4 are not:

> Q Doctor, I wonder if I could impose upon you to again look at the list of eight. At least let's deal with the first five. I wonder if you could tell us which if any of those first five or for which any of those first five might we find evidence?
>
> A One, three, and five, as before. One, three, and five. (Tr.2381.)[7]

Claims 6, 7, 8

374. There is no convincing evidence in the scientific papers offered by respondents which substantiates claims 6, 7, and 8.

375. As to claim 6 (calcium reduces or eliminates pain associated with bone ailments), Dr. Lachance concluded that there was "just not a lot of support" (Tr. 1761) and Dr. Raisz agreed with this assessment. (Tr. 98.)

376. Claims 7 (superiority) and 8 (more bioavailable) also lack convincing documentation. (Raisz, Tr. 98-99; Heaney, Tr. 2592-93, 2447, 2608.)

[7]Dr. Heaney testified that claims 3 and 5 are so "inextricably connected that it's hard to know how to separate them always." (Tr. 2432.)

377. After considering all of the expert testimony with respect to the scientific papers offered by respondents, I find that they substantiate claims 1, 3, and 5.[8] They do not substantiate claims 2, 4, 6, 7, or 8.

III. CONCLUSIONS OF LAW

A. Respondents' Ads And Promotional Materials Made The Representations Alleged In The Complaint

The Commission and its Administrative Law Judges may rely solely on the language in challenged ads and need not resort to extrinsic evidence to determine the meaning which is conveyed to reasonable consumers. Thompson Medical Co., Inc., 104 F.T.C. 648, 788-89 (1984), aff'd, 791 F.2d 189 (D.C. Cir. 1986), cert. denied, 479 U.S. 1086 (1987); Carter Products, Inc. v. FTC, 323 F.2d 523, 528 (5th Cir. 1963).

I do not need to engage in this analysis here, for respondents have conceded that the claims alleged in paragraphs 5 and 8 of the complaint, which summarize the ads listed in paragraph 4 and Exhibits A-D of the complaint, were made. (F. 41.)

B. Respondents' Claims Were Material

The claims made by respondents were material, i.e., they were likely to affect their customers' decision to purchase Bone Builder.

Express claims are presumptively material as are those claims which significantly involve health, safety, or other areas with which the reasonable consumer would be concerned, such as purpose or cost. Cliffdale Associates, 103 F.T.C. 110, 182-83 (1984). Thompson Medical Co., 104 F.T.C. at 816-17.

Respondents do not dispute the materiality of the representations in Bone Builder ads. Thus, the only significant issue outstanding is the level of

[8]And the claim that Bone Builder builds bone or increases bone thickness.

substantiation required for claims 1 through 8 and whether the claims were substantiated.

C. Respondents Have Substantiated Claims 1, 3 and 5

Respondents do not deny the allegations in paragraph 8 of the complaint that statements in their ads and promotional materials described in paragraph 4 and reproduced as exhibits A-D of the complaint represent that "scientific research, including clinical tests, scientific papers and/or scientific studies" provide proof of claims 1-8, but they contest the allegation in paragraph 9 that claims 1-8 have not been substantiated, and they have offered in evidence more than 100 documents to support their assertion.

Complaint counsel reply that respondents' documents do not provide a reasonable basis for their claims because they have not presented the necessary substantiation.

Complaint counsel derive their proposed standard from the Commission's decision in Pfizer, Inc., 81 F.T.C. 1, 23 (1972) and its test for determining the substantiation required where challenged ads do not claim a specific level of substantiation. That test, described later in Thompson Medical Co., 104 F.T.C. 648, 821, considers:

(1) The product involved;

(2) The type of claim;

(3) The benefits of a truthful claim;

(4) The ease of developing substantiation for the claim;

(5) The consequences of a false claim; and,

(6) The amount of substantiation experts in the field agree is reasonable.

Bone Builder is not a drug and its misuse would probably not have severe consequences. (F. 24 n3.) Nevertheless, the benefits of a truthful claim are obvious since it should be used only for treatment of those ailments for which it offers effective treatment, particularly because it is much more expensive than other calcium supplements. (F. 10-11.)

Complaint counsel argue that application of the Thompson standard requires a high level of substantiation -- an expensive, randomized, double-blind, placebo-controlled, prospective study considering the effects of calcium over a one to three year period.

Requiring gold standard clinical trials is appropriate when the product involved has no prior history of scientific analysis. That is not the case here, for there has been recognition of a calcium effect (F. 125) for several years as to some claims. (See F. 370 re prevention of bone loss.) Heaney: "These studies [clinical trials] have been done over and over again. . . ." (re claims 3 and 5). (F. 82.)

After considering the expert testimony in this proceeding and the scientific evidence, including clinical trials, studies, reviews, articles and abstracts, which the experts analyzed, I conclude that at or about the time Metagenics began to advertise Bone Builder (1988 (F. 6)), and certainly when the complaint issued, it possessed convincing scientific evidence which substantiated claims 1, 3, and 5. (F. 205, 373.)

That Mr. Katke was not qualified to judge scientific matters may be relevant (F. 83-86) but the fact remains that some of the scientific studies submitted by him which were published between 1988 and the present do substantiate some of his claims, including the claim that Bone Builder builds bone or increases bone thickness. (F. 59, 377 n.9.)

D. Complaint Counsel's Claim That Respondents' Representations In Paragraphs Five and Eight Were Unqualified

Respondents believe that complaint counsel argue that the claims for Bone Builder are unsubstantiated because they are unqualified. While they are, according to complaint counsel, unqualified, their prima facie case is

not based upon this assertion but upon the proposition that respondents do not possess a reasonable basis for the claims set forth in paragraphs 5 and 8. (Reply to Respondents' Proposed Findings, p. 75.)

E. The Relevance Of Statements Made In Respondents' Ads And Promotional Material

Paragraphs 5 and 8 of the complaint summarize the language used in Metagenics' ads and promotional material. The actual language used in some of these ads is described in paragraph 4, and the ads are attached to the complaint.

Respondents argue that only the summaries in paragraphs 5 and 8 are relevant in this proceeding and that questions about or references to the actual language of the ads should not have been allowed at trial.

I reject this argument, for the complaint was the result of the actual language used in respondents' ads and promotional materials and it is relevant to the product coverage of the following order.

In any event, little testimony about the actual language of the ads and promotional material was elicited during the trial. Expert testimony regarding substantiation was based almost exclusively on the Commission's summaries set forth in paragraphs 5 and 8.

F. The Relevance Of FDA Law

Respondents believe that it is complaint counsel's position that the only claims that may be made for a calcium supplement such as Bone Builder are those specifically enumerated in the FDA's regulations regarding the association between calcium and osteoporosis. Food Labeling: Health Claims: Calcium and Osteoporosis ("Calcium Rule"), 58 Fed. Reg. 2665 (1993). Respondents also argue that their claims are permissible under FDA law.

Complaint counsel have not requested me to limit respondents' advertising for Bone Builder to only those statements contained in the Calcium Rule, although they argue that, with respect to the relationship

between respondents' calcium products and osteoporosis, they are bound by the Rule. (Reply to Respondents' Proposed Findings, p. 5.) Since complaint counsel concede that the Calcium Rule is not dispositive of the issues in this proceeding, this dispute need not be resolved.

G. Respondents' First Amendment Argument

Respondents claim that their First Amendment guarantees would be violated if I accept complaint counsel's supposed argument that even if something is accepted as scientific fact, representation of that fact cannot be made in advertising unless it has been proven through a gold standard trial. Since complaint counsel deny this claim, respondents' First Amendment argument is rejected.

IV. Summary

A. The Commission has jurisdiction over respondents and the acts and practices alleged in the complaint.

B. Respondents made the 8 claims set forth in paragraphs 5 and 8 of the complaint.

C. Respondents did not possess and rely upon a reasonable basis that substantiated claims 2, 4, 6, 7, and 8.

D. Respondents possessed and relied upon a reasonable basis that substantiated representations 1, 3, and 5.

E. The acts and practices of respondents summarized above in parts A, B, and C constitute unfair or deceptive acts or practices and the making of false advertisements in or affecting commerce in violation of Sections 5(a) and 12 of the Federal Trade Commission Act.

V. The Appropriate Order

Although respondents' violations of the FTC Act were limited to Bone Builder, complaint counsel seek a cease and desist order which would prohibit unsubstantiated claims about any food or dietary supplement, food, or drug as "food" and "drug" are defined in Section 15 of the FTC Act.

The issuance of multi-product orders where a violation is limited to a single product is a widely-used method of preventing respondents from engaging in similarly illegal practices in future advertisements for other products. FTC v. Colgate-Palmolive Co., 380 U.S. 374, 395 (1965); ITT Continental Baking Co., Inc. v. FTC, 532 F.2d 207, 223 (2d Cir. 1976).

Deciding whether issuance of a multi-product order is justified requires consideration of (1) The deliberateness and seriousness of respondents' violation; (2) the ease with which the unlawful practices could be transferred to other products and practices; and (3) the respondents' past history of unlawful conduct. FTC v. Colgate-Palmolive Co., 380 U.S. at 395; Sears, Roebuck & Co., 676 F.2d 385, 390 (9th Cir. 1982); Standard Oil Co. of California v. FTC, 577 F.2d 653, 662 (9th Cir. 1978).

All of these factors need not be present to justify a multi-product order where the violation is particularly egregious. Sears, Roebuck & Co., 676 F.2d at 392; Thompson Medical, 104 F.T.C. at 833.

Respondents' violations with respect to claims 2, 4, 6, 7, and 8 were serious and deliberate because they did not rely on the advice of qualified scientists to determine the substantiation for those claims. Respondents should have known that reliance on Mr. Katke's dubious qualifications (F. 83-86) probably would result in unsubstantiated claims about Bone Builder.

Furthermore, the exaggerated language used in the ads for Bone Builder (Cplt., paragraph 4), particularly the comparative statements, suggests that respondents, unless prohibited from doing so, would probably use the same tactics in ads for other products. See Colgate, 380 U.S. at 394-95:

> In this case the respondents produced three different commercials which employed the same deceptive practices. This we believe gave the Commission a sufficient basis for

> believing that the respondents would be inclined to use similar commercials with respect to the other products they advertise. We think it reasonable for the Commission to frame its order broadly enough to prevent respondents from engaging in similarly illegal practices in future advertisements.

Thus, I conclude that a multi-product order requiring respondents to comply with Section 5 of the FTC Act is justified. Kraft, Inc. v. FTC, 970 F.2d 311, 326 (7th Cir. 1992); Sterling Drug Inc. v. FTC, 741 F.2d 1146, 1155-56 (9th Cir. 1984), cert. denied, 470 U.S. 1084 (1985); Sears, Roebuck & Co., 676 F.2d at 395; Litton Industries, 676 F.2d 364, 372 (9th Cir. 1982).

The major cease and desist provisions of the order are contained in parts I through III and cover Bone Builder, MCHC, or any "food or dietary supplement, food or drug." Part I of the order prohibit respondents from making claims 2, 4, 6, 7, and 8 (renumbered as 1, 2, 3, 4 and 5) unless they rely upon competent and reliable scientific evidence as substantiation.

Paragraphs 1, 3, and 5 of part I of complaint counsel's proposed order have been stricken because Bone Builder provides the benefits listed in those paragraphs. Paragraph 9 has been stricken because Bone Builder prevents, treats or cures osteoporosis, and because the other provision of paragraph 9 relating to pain is covered by paragraph 3.

Part II of the proposed order, which refers to Bone Builder, has been stricken because, contrary to the allegations of the complaint, it builds bone or increases bone thickness. I reject the argument that respondents' ads also claim that it restores lost bone. (F. 59.) Thus, respondents can use the name Bone Builder in their ads and on packages of this product.

New Part II prohibits any misrepresentations regarding tests or studies. Part III requires respondents to possess competent and reliable scientific evidence to substantiate claims that Bone Builder or any dietary supplement, food, or drug, will prevent, treat, or cure any disease, disorder, or condition. The words "any representation" have been modified to exclude claims 1, 3, and 5, which have been substantiated.

These provisions allow respondents to rely on any scientific evidence that is competent and reliable. Thus, because the order is limited to substantiation for claims that a supplement can prevent, treat, or cure medical conditions or diseases, it is directly related to the type of violations and products at issue in this case.

Parts IV and V of the order are "safe harbor" provisions that allow respondents to make product representations permitted by the Food and Drug Administration for any food under the Nutrition Labeling and Education Act of 1990, and for any drug under any promulgated tentative or final standard or any new approved drug application.

Parts VI through X of the order are the standard recordkeeping and enforcement provisions requiring respondents to maintain documents substantiating or contradicting their claims, to distribute copies of the order to appropriate individuals and entities, to notify the Commission of any changes in the business of the corporate and individual respondents, and to file a compliance report. The inclusion of Mr. Katke in the order is justified since he was personally responsible for the advertising and marketing of Bone Builder. (F. 2, 84.)

ORDER

I

IT IS ORDERED that respondents Metagenics, Inc., a corporation, doing business as Ethical Nutrients, or under any other name, its successors and assigns, and its officers, and Jeffrey Katke, individually and as an officer of said corporation, and respondents' agents, representatives, and employees, directly or through any corporation, subsidiary, division or other device, in connection with the manufacturing, labeling, advertising, promotion, offering for sale, sale, or distribution of Bone Builder or any food or dietary supplement, food, or drug, as "food" and "drug" are defined in Section 15 of the Federal Trade Commission Act, in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from representing, in any manner, directly or by implication, that such product:

1. restores lost bone;
2. restores bone strength;
3. reduces or eliminates pain associated with bone ailments;
4. is superior to and/or more effective than other forms of calcium in the prevention or treatment of bone ailments; and
5. is more bioavailable, more absorbable, or more effectively utilized by the body than other forms of calcium;

unless, at the time of making such representation, respondents possess and rely upon competent and reliable scientific evidence that substantiates the representation. For purposes of this Order, "competent and reliable scientific evidence" shall mean tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that has been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results.

II

IT IS FURTHER ORDERED that respondents Metagenics, Inc., a corporation, doing business as Ethical Nutrients, or under any other name, its successors and assigns, and its officers, and Jeffrey Katke, individually and as an officer of said corporation, and respondents' agents, representatives, and employees, directly or through any corporation, subsidiary, division or other device, in connection with the manufacturing, labeling, advertising, promotion, offering for sale, sale, or distribution of Bone Builder or any food or dietary supplement, food, or drug, as "food" and "drug" are defined in Section 15 of the Federal Trade Commission Act, in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from misrepresenting, in any manner, directly or by implication, the existence, contents, validity, results, conclusions, or interpretations of any test or study.

III

IT IS FURTHER ORDERED that respondents Metagenics, Inc., a corporation, doing business as Ethical Nutrients, or under any other name, its successors and assigns, and its officers, and Jeffrey Katke, individually and as an officer of said corporation, and respondents' agents, representatives, and employees, directly or through any corporation, subsidiary, division or other device, in connection with the manufacturing, labeling, advertising, promotion, offering for sale, sale, or distribution of Bone Builder or any food or dietary supplement, food, or drug, as "food" and "drug" are defined in Section 15 of the Federal Trade Commission Act, in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from making any representation, in any manner, directly or by implication, that any such product will treat, cure, alleviate the symptoms, prevent, or reduce the risk of developing any disease, disorder, or condition, unless, at the time of making such representation, respondents possess and rely upon competent and reliable scientific evidence that substantiates the representation. Provided, however, that this part does not apply to the claims that Bone Builder builds bone or increases bone thickness, halts or prevents bone loss or bone thinning, or halts, prevents, or treats osteoporosis.

IV

Nothing in this Order shall prohibit respondents from making any representation that is specifically permitted in labeling for any such product by regulations promulgated by the Food and Drug Administration pursuant to the Nutrition Labeling and Education Act of 1990.

V

Nothing in this Order shall prohibit respondents from making any representation for any drug that is permitted in labeling for any such drug under any tentative final or final standard promulgated by the Food and Drug Administration, or under any new drug application approved by the Food and Drug Administration.

VI

IT IS FURTHER ORDERED that for five (5) years after the last date of dissemination of any representation covered by this Order, respondents, or their successors and assigns, shall maintain and upon request make available to the Federal Trade Commission for inspection and copying:

A. Any advertisement making any representation covered by this Order;

B. All materials that were relied upon in disseminating such representation; and

C. All tests, reports, studies, surveys, demonstrations, or other evidence in their possession or control that contradict, qualify, or call into question such representation, or the basis relied upon for such representation, including complaints from consumers, and complaints or inquiries from governmental organizations.

VII

IT IS FURTHER ORDERED that respondent Metagenics, Inc., or its successors and assigns, shall:

A. Within thirty (30) days after the date of issuance of this Order, provide a copy of this Order to each of its operating divisions, subsidiaries, principals, officers, directors, managers and distributors, and to each of its employees, agents, and representatives engaged in the preparation, placement, or dissemination of advertisements, promotional materials, product labels, or other such sales materials covered by this Order, and shall obtain from each such entity or person a signed statement acknowledging receipt of the Order; and

B. For a period of ten (10) years from the date of issuance of this Order, provide a copy of this Order to each of its principals, officers, directors, managers and distributors, and to all employees, agents, and representatives engaged in the preparation, placement, or dissemination of advertisements, promotional materials, product labels, or other such sales materials covered by this Order within three (3) days after the person commences his or her responsibilities, and shall obtain from each such person a signed statement acknowledging receipt of the Order.

VIII

IT IS FURTHER ORDERED that respondents shall notify the Commission at least thirty (30) days prior to any proposed change in the corporate respondent such as a dissolution, assignment or sale resulting in the emergence of a successor corporation, the creation or dissolution of subsidiaries, or any other change in the corporation that may affect compliance obligations under this Order.

IX

IT IS FURTHER ORDERED that for a period of ten (10) years from the date of issuance of this Order, respondent Jeffrey Katke shall provide written notice to the Federal Trade Commission within thirty (30) days of:

A. Any change in his business or employment that may affect compliance obligations arising out of this Order;

B. The discontinuance of his business or employment; and

C. His affiliation with any new business or employment; each such notice to include his business address and telephone number, home address, and a statement describing the nature of the business or employment and his duties and responsibilities.

X

IT IS FURTHER ORDERED that respondents shall, within sixty (60) days after service upon them of this Order, and at such other times as the Commission may require, file with the Commission a report, in writing, setting forth in detail the manner and form in which they have complied with this Order.

Lewis F. Parker
Administrative Law Judge

Dated: October 11, 1996