DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

# WARNING LETTER

OCT 16 2001

Mr. Klee Irwin
President and Chief Executive Officer
Omni Nutraceuticals, Inc.
5310 Beethoven Street
Los Angeles, California 90066

Ref: 02-HFD-312-02

Dear Mr. Irwin:

This letter concerns *INHOLTRA® JOINT PAIN™ CAPLETS* and *INHOLTRA® JOINT PAIN PLUS™ CAPLETS* (Inholtra products), which are marketed by your firm as combination drug-dietary supplement products. According to the respective package labeling, each tablet of *INHOLTRA® JOINT PAIN™ CAPLETS* contains, among other ingredients, 325 mg of acetaminophen and 375 mg of glucosamine sulfate, and *INHOLTRA® JOINT PAIN PLUS™ CAPLETS* contains, among other ingredients, 325 mg of acetaminophen, 187.5 mg of glucosamine sulfate, and 150 mg of chondroitin sulfate. Both products are labeled for use as "A NEW TWO-IN-ONE SOLUTION" to "[t]emporarily relieve[] minor aches and pains due to: headache, backache, muscular aches, and the minor pain of arthritis..." and "for Long Term Joint Health." The labeling for *INHOLTRA® JOINT PAIN™ CAPLETS* specifies that it is "the only product to combine the fast pain relief of Acetaminophen with the healthy long-term joint support of the Inholtra Glucosamine," while the labeling for *INHOLTRA® JOINT PAIN PLUS™ CAPLETS* specifies that it is "the only product to combine the fast pain relief of Acetaminophen with the healthy long-term joint support of the Inholtra Glucosamine and Chondroitin complex." (Emphasis added.)

In addition, the respective package labeling contains a "DRUG FACTS" panel for the acetaminophen and a "Supplement Facts" panel for glucosamine sulfate for *INHOLTRA® JOINT PAIN™ CAPLETS* and for glucosamine sulfate and chondroitin sulfate for *INHOLTRA® JOINT PAIN PLUS™ CAPLETS*. The labeling for both products also contains a disclaimer that states that the glucosamine sulfate in the former and the glucosamine sulfate and chondroitin sulfate in the latter is/are "...not intended to diagnose, treat, cure, or prevent any disease...," and that the

claims made for these ingredients "...have not been evaluated by the Food and Drug Administration."

As formulated and labeled, the Inholtra products described above are "drugs" under section 201(g)(1)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) because they are intended to cure or mitigate a disease (e.g., "relieves minor aches and pain due to...arthritis" and "combine the fast pain relief of acetaminophen with the healthy long-term joint support of [Inholtra Glucosamine (or) the Inholtra Glucosamine and Chondroitin complex."].[1] These products are also "drugs" under section 201(g)(1)(C) of the Act because they are intended to affect the structure or function of the body (e.g., "relieves minor aches and pains due to...muscular aches"). Notwithstanding your attempt to market these Inholtra products as combination drug-dietary supplements, the presence of the acetaminophen, with its intended use to relieve arthritis pain, renders the entire product a drug. This is true even though the acetaminophen in these Inholtra products is combined with other ingredients like glucosamine and chondroitin that separately could be marketed as dietary supplements. When, as here, a drug and dietary ingredients are combined into a single product, there is no provision in the Act, as amended by the Dietary Supplement Health and Education Act of 1994 (DSHEA), that exempts any part of that product from the scope of section 201(g).[2]

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[1] In its final rule on structure/function claims for dietary supplements, FDA stated that, since joint pain is a characteristic symptom of arthritis, claims related to the maintenance or support of joints are implied disease claims when made in conjunction with claims about pain relief. See 65 Fed. Reg. 1000 at 1030 (Jan. 6, 2000). Therefore, in the context of the other claims in the products' labeling, the claims that glucosamine or glucosamine and chondroitin provide "healthy long-term joint support" is an implied claim to treat or prevent arthritis and thus implicates section 201(g)(1)(B) of the Act.

[2] In addition, the presence of acetaminophen excludes these Inholtra products from the definition of a dietary supplement under section 201(ff)(3)(B) of the Act because acetaminophen is a new drug that has been approved under section 505(a). See Pharmanex v. Shalala, 221 F.3d 1151, 1154 (10th Cir. 2000). FDA first approved a New Drug Application for acetaminophen in April 1950, and acetaminophen was not marketed as a food or a dietary supplement before that date. Moreover, these Inholtra products are not dietary supplements within the meaning of Section 201(ff)(1) of the Act because they include acetaminophen, which is an active drug ingredient that is not a dietary ingredient under 201(ff)(1)(A)-(F).

Under section 201(g)(1)(D) of the Act, the glucosamine sulfate or glucosamine sulfate and chondroitin sulfate used in combination with the acetaminophen are also drugs since they are components of the finished drug product. See Title 21 of the Code of Federal Regulations, Part 210.3(b)(3) [21 CFR 210.3(b)(3)]. Based on the labeling claims made for them (e.g., "Long Term Joint Health"), the glucosamine sulfate and chondroitin sulfate are also "active" drug ingredients under 21 CFR 201.66(b)(2).

Moreover, based on their formulations and labeling, these Inholtra products are "new drugs" under section 201(p) of the Act and 21 CFR 310.3(h) because these products are not generally recognized as safe and effective for their respective labeled uses. Neither of these products is subject to the Food and Drug Administration's (FDA's) Over-The-Counter (OTC) Drug Review because no other product formulated with these active ingredients and labeled for these intended uses has ever been commercially marketed, and the agency has never proposed that such a product be included in this Review. Thus, these Inholtra products violate section 505(a) of the Act because they are new drugs and neither is the subject of an approved New Drug Application (NDA).

The Inholtra products described in this letter are also misbranded under section 502(f)(1) of the Act because they lack adequate directions for use as defined in 21 CFR 201.5, 21 CFR 310.201(a)(1)(vii), and 21 CFR 369.21. Under these regulations, the labeling for an OTC drug product that contains acetaminophen is required to specify the duration of administration and contain specific acetaminophen warnings. The respective labeling for these Inholtra products includes the statement, "[s]top use and ask a doctor if...pain gets worse or lasts more than 10 days...," but does not warn consumers about the need to consult a physician before giving acetaminophen drug products to children under three years of age. In addition, this "stop use" statement is much less prominent than other, conflicting statements on the respective bottle labels, cartons, and carton inserts that promote the "long term" use of these products for maintaining joint health. For example, the respective principal display panels of the package labeling and front panels of the bottle labels contain the phrase "[l]ong [t]erm." The respective carton end-flaps also state that the Inholtra product inside is "the only product to combine the fast pain relief of

Acetaminophen with the healthy long-term joint support of [Inholtra Glucosamine (or) the Inholtra Glucosamine and Chondroitin complex.]" In addition, the respective carton inserts include the statement, "[w]e've combined these powerful pain fighters with clinically proven ingredients like Glucosamine and Chondroitin for long term joint health...."

These Inholtra products are likewise misbranded under section 502(f)(2) of the Act because their respective labeling lacks adequate warnings. These Inholtra products are marketed for long-term joint health, but their respective warnings state only that they should not be taken "if...pain gets worse or lasts more than 10 days." (Emphasis added). The labeling for these products does not bear a warning limiting use for long-term joint health. In fact, use of the phrase "[l]ong [t]erm" implies the products should be taken consistently over a long period of time. This contradiction raises serious safety concerns because these products contain acetaminophen, which, if used incorrectly, have the potential to cause hepatotoxicity. In addition, protracted pain may be a symptom of a more serious condition. Under 21 CFR 310.201(a)(1)(vii) and 21 CFR 369.21, over-the-counter use of acetaminophen for the temporary relief of pain is limited to 10 days unless otherwise directed by a doctor. This is true regardless of the other intended uses for which the acetaminophen product is sold.

Finally, the Inholtra products described above are misbranded under section 502(e)(1)(A)(ii) of the Act because their respective labeling fails to identify glucosamine sulfate for *INHOLTRA® JOINT PAIN™ CAPLETS* and glucosamine sulfate and chondroitin sulfate for *INHOLTRA® JOINT PAIN PLUS™ CAPLETS* as active drug ingredients. See 21 CFR 201.10.

The violations described in this letter are not meant to be all-inclusive. It is your responsibility to ensure that all drug products manufactured and distributed by your firm comply with the Act. Federal agencies are advised of the issuance of all Warning Letters pertaining to drugs and devices so that they may take this information into account when considering the award of contracts. We request that you take action immediately to correct these violations. Failure to do so may result in regulatory action without further notice and may include seizure and/or injunction.

Please respond to this office in writing within fifteen (15) working days of receipt of this letter. Your response should describe the specific actions you will take, or have taken, to correct the violations described above. It should also include an explanation of each step being taken to prevent recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which corrections will be completed. Your reply should be directed to Mr. Kevin M. Budich, Compliance Officer, as follows:

Food and Drug Administration
OTC Compliance Team, HFD-312
7520 Standish Place, Room 168
Rockville, Maryland 20855

If you have any questions about the content of this letter, you may contact Mr. Budich at 301-827-7354.

Sincerely,

David J. Horowitz, Esq.
Acting Director
Office of Compliance
Center for Drug Evaluation and Research

cc:
HF-11 (Dotzel)
HF-11 (Mayl)
HFC-200 (Taylor)
HFC-210
HFC-120
GCF-1 (McConagha)
GCF-1 (Kempic)
GCF-1 (Wion)
GCF-1 (Nickerson)
HFD-205
HFD-560 (Ganley)
HFD-560 (Katz)
HFD-560 (Rachanow)
HFS-811 (Moore)
HFD-330 (Ogram)
HFD-300 (Horowitz)
HFD-300 (RATS# _____ )
HFD-314 (Aronson)
HFD-310 Reg File
HFD-312 DLNDC
HFD-312 (Budich)
HFD-312 (Heller)
HFA-224
HFR-PA200 (Cruse)
HFR-PA240 (Sawyer)
File # DRU - 5.1101 and 6.1503 (w/cc of labeling)
DRAFT:KMBudich(HFD-312):kmb:8/2/01
REVISIONS:WAMcConagha(GCF-1)/LNickerson(GCF-1)/SLMayl(HF-11)/
RJMoore(HFS-811)/LMKatz(HFD-560)/GMRachanow(HFD-
560)/DJHorowitz(HFD-300):kmb:8/2/01 - 10/15/01
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