9-12-91 BBO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

CERTIFIED MAIL - RETURN RECEIPT REQUESTED

WARNING LETTER

Los Angeles District
1521 West Pico Boulevard
Los Angeles, California 90015-248
Telephone (213) 252-7583

September 9, 1991

WL-27-1

Mr. Elliott Balbert
President
Natrol, Inc.
20371 Prairie Street, #2
Chatsworth, California 91311

RE: Natrol Ester C 4,400 mg
with Mineral Complex
Natrol Ester C 2,000 mg
Natrol Ester C 1,000 mg
Natrol Ester C 2,000 mg
with Bioflavonoid Complex
Natrol SAF Stress & Anxiety Formula
Natrol High
Natrol ACE

Dear Mr. Balbert:

An inspection of your firm indicates that you market the above referenced products. These products are in violation of both food and drug sections of the Federal Food, Drug, and Cosmetic Act (Act).

FOOD CHARGES:

Our review of the label for "Natrol A-Beta Carotene C-Vitamin C E-Vitamin E Plus Herbal extracts" capsules marketed by your firm reveals that it is adulterated in violation of Section 402(a)(2)(c) of the Federal Food, Drug, and Cosmetic Act (Act). The label lists the ingredient chaparral herb that contains nordihydroguaiaretic acid (NDGA) which has been prohibited from use in food because it represents a potential risk to the public health.

The analysis of "Natrol Ester C 4,400 mg. Vitamin C Activity with Mineral Complex" tablets and "Natrol Ester C 1,000 mg. Vitamin C Activity" 275 mg. tablets marketed by your firm reveals that these products are misbranded within the meaning of Section 403(a)(1) of the Federal Food, Drug, and Cosmetic Act as follows:

> The declarations "4,400 mg. Vitamin C Activity" (Natrol Ester C 4,400 mg. Vitamin C Activity...label) and "1,000 mg. Vitamin C Activity" (Natrol Ester C 1,000 mg Vitamin C Activity...label) as declared in the identity statements for these foods are false and misleading since they represent and suggest that these products contain 4,400 and 1,000 milligrams of Vitamin C per serving, respectively, which is contrary to fact. Whereas, a serving of these products (as indicated on the information panel) contains 1100 and 275 milligrams of Vitamin C per serving, and 1096 and 232 milligrams per serving by analysis, respectively.

Further, our review of the labeling for:

-"Natrol Ester C 4,400 mg. Vitamin C Activity with Mineral Complex" Calcium - Magnesium-Zinc-Potassium-Sodium tablets;

-"Natrol Ester C 1,000 mg. Vitamin C Activity" 275 mg. tablets;

-"Natrol SAF Stress and Anxiety Formula" capsules;

-"Natrol High A Vitamin Formula now with Ester C" capsules;

-"Natrol Ester C 2,000 mg. Vitamin C Activity with Bioflavonoid Complex" 550 mg. tablets; and capsules;

-"Natrol A-Beta Carotene C-Vitamin C E-Vitamin E Plus Herbal extracts and other Select Ingredients" capsules; and

-"Natrol Ester C 2,000 mg. Vitamin C Activity" 550 mg. capsules;

marketed by your firm reveals that these products are misbranded in violation of Section 403(a)(1) of the Federal Food, Drug, and Cosmetic Act. The statements: super nutrient; enters the blood stream faster and shows levels 4 times higher in the white blood cells than conventional ascorbic acid; 4 tablets of Ester-C with Mineral Complex is equivalent to 4, 440 mg. of ordinary Vitamin C (ascorbic acid) activity; this form of Vitamin C is superior to regular ascorbic acid and delivers four times the normal amount to the system; for example, 275 mg. of Ester C is equivalent to 1000 mg. of regular Vitamin C activity; Ester C is four times more bioavailable than regular Vitamin C; 550 mg. of Ester C with metabolites is equivalent to 2,000 mg. of activity; and the term "poly" in calcium polyascorbate; are false and misleading in that they are unsubstantiated and imply superiority claims.

Additionally, the substances:

-GABA, L-Tyrosine, Siberian Ginseng and inositol in "Natrol" SAF Stress and Activity Formula capsules:

-Citrus bioflavonoid complex with hesperidin and rutin in "Natrol" Ester C 2,000 mg. Vitamin C Activity with Bioflavonoid Complex 550 mg. tablets and capsules;

-bilberry, echinacea, china chlorella, chlorophyll, RNA/DNA complex, citrus bioflavonoids, and glutathione in "Natrol" A-Beta Carotene C-Vitamin C E-Vitamin E capsules;

which are not vitamins or minerals may not be listed except as a part of a list of all the ingredients of such products and the labeling may not give prominence to or emphasize such substances under Sections 403(a)(2) and 411(b)(2).

DRUG CHARGES:

Promotional materials, namely the booklet entitled "The Key to the Power of Vitamin C and Its Metabolites" and the pamphlet entitled "Ester-C in the News" state or suggest that the above referenced products, each of which contain "Ester-C" as an ingredient, help to strengthen the immune system, enhance interferon production, normalize blood cholesterol and prevent such disease conditions as hypercholesterolemia, hepatitis infection, periodontal disease, cancer, polio, heart disease, Epstein Barr/Chronic Fatigue Syndrome, colds and influenza.

Because such labeling includes statements which represent and suggest that these products are intended to be used in the cure, mitigation, treatment, or prevention of disease, or are intended to affect the structure or any function of the body of man, these products are drugs within the meaning of Section 201(g) of the Federal Food, Drug, and Cosmetic Act (Act). Further we are unaware of any substantial scientific evidence which demonstrates that these drugs are generally recognized as safe and effective for the aforementioned disease conditions. Accordingly, marketing of these drugs is a violation of the Act as follows:

SECTION	BRIEF DESCRIPTION
502(a)	The referenced articles of drug are misbranded in that their labeling is false and misleading by representations and suggestions that there is substantial scientific evidence to establish that the articles are safe and effective for the aforementioned disease conditions.
502(f)(1)	They are further misbranded in that their labeling fails to bear adequate directions for use for the conditions for which they are being offered and they are not exempt from this requirement under regulation 21 CFR 201.115, since the articles are new drugs within the meaning of Section 201(p) and no approval of any applications filed pursuant to Section 505(b) is effective for these drugs. Additionally, the drugs are misbranded in that their labeling does not contain adequate directions for use as this term is defined in 21 CFR 201.5, since the conditions for which they are offered are not amenable to self diagnosis and treatment by the laity; therefore adequate directions for use cannot be written under which the layman can use these drugs safely and for the purposes for which they are intended.

505(a) The articles are drugs within the meaning of Section 201(g) of the Act which may not be introduced or delivered for introduction into interstate commerce under Section 505(a) of the Federal Food, Drug, and Cosmetic Act, since they are new drugs within the meaning of Section 201(p) of the Act and no approval of any applications filed pursuant to Section 505(b) are effective for such drugs.

Our review of the formulation, product labels, and promotional material (labeling) distributed with your products indicates the following:

SAF Stress & Anxiety Formula

Each capsule contains gamma amino butyric acid (GABA), vitamins, minerals, amino acids, and Siberian Ginseng.

The labeling for SAF STRESS & ANXIETY FORMULA states in part: "FOR PAIN, STRESS AND ANXIETY... Magnesium and Siberian Ginseng have also been associated with prompt overall calmative effects...can actually mimic the tranquilizing effects of Valium and Librium...Tyrosine plays an important role in fighting all kinds of stress...Take two capsules twice a day or as desired..."

The listed ingredients in SAF STRESS & ANXIETY FORMULA have a long history of use as daytime sedatives (to relieve stress, anxiety, and nervous tension). Therefore, based on the product's formulation, name (SAF STRESS & ANXIETY FORMULA) and labeling (to calm you, fight stress), we regard this product to be a drug subject to the final order for OTC Daytime Sedatives (21 CFR 310.519). This regulation states that there are no ingredients that can be generally recognized as safe and effective for use as an OTC daytime sedative, and that any such product introduced into interstate commerce after December 24, 1979 is subject to regulatory action.

Natrol High

Each capsule contains vitamins, MaHuang, Siberian Ginseng, Damiana, Solomon Seal, Gotu Kola, Capsicum, Ginger, Juniper Berry.

The labeling for Natrol High states in part: "PACKED WITH POWER...TOO POOPED TO POP?...it's time for NATROL HIGH...The country's best picker upper!...STAY ALERT, FEEL ALIVE WITH NATROL HIGH..."

Based on the product name, and its intended use, we would regard Natrol High to be a drug subject to the final monograph concerning OTC Stimulant Drug Products published in the February 29, 1988 Federal Register and codified in 21 CFR 340.

Only one ingredient, caffeine, in a form suitable for oral adminstration, when used as a stimulant within the limits established in 21 CFR 340, has been determined to meet monograph conditions. All other ingredients, including the following specifically reviewed as stimulants, ammonium chloride, ginseng, and vitamins, are considered nonmonograph ingredients and are prohibited from use as active ingredients in OTC stimulant drug products in the absence of an approved NDA.

On or after March 1, 1989, no OTC drug product that is subject to the monograph (21 CFR 340 - Stimulant Drug Products for OTC use) that contains a monograph condition, i.e., a condition that would cause the drug to be not generally recognized as safe and effective may be introduced into interstate commerce. Natrol High is not in compliance with the terms of the final monograph in that it contains ingredients not allowed in 21 CFR 340.10. Further, the indications found on the product labeling are not included in 21 CFR 340.50(b) and are not acceptable.

This letter is not meant to represent a comprehensive listing of all violations which may be associated with these products, nor is it meant to represent that other violations may not exist with regard to other products distributed by your firm. In fact, you should review products such as "Calms Kids", (daytime sedative), "Guarana" capsules (stimulant), and "Gingo Biloba" (stimulant) for their compliance with the Over-the-Counter (OTC) drug final monographs.

TAMPER RESISTANT PACKAGING (TRP) REQUIREMENTS

Under 21 CFR 211.132(b) all the drug products referenced in this letter must be packaged in a tamper-resistant package (TRP). The indicator or barrier to entry is required to be distinctive by design (e.g., an aerosol container) or by use of an identifying characteristic (e.g., a pattern, name, registered trademark, logo or picture), which must appear directly on the indicator/barrier.

Under 21 CFR 211.132(c) a TRP labeling statement is required to appear on the retail package and it must disclose the specific tamper-resistant feature of the package, e.g., plastic shrink-wrap over the entire container/closure, and/or a plastic foam seal adhered to the mouth of a bottle. In addition, when the tamper-resistant feature is one that is not distinctive by design, and thereby must bear an identifying characteristic (such as the imprinted statement, "SEALED FOR YOUR PROTECTION"), the TRP labeling statement must refer to that identifying characteristic.

Our review of the labeling for the subject drug products indicates that they lack any TRP statements required by 21 CFR 211.132(c) and, therefore, the products are misbranded under Section 502(a) of the Act in that such statement fails to alert consumers to the specific tamper-resistant feature of the package.

A final rule published in the February 2, 1989, Federal Register amended the tamper-resistant packaging (TRP) regulations to state that the packaging for two-piece hard gelatin capsules subject to the TRP requirements must bear a minimum of two tamper-resistant packaging features unless the capsules are sealed by a tamper-resistant technology. For all other products subject to the TRP requirements, including two-piece hard gelatin capsules sealed with a tamper-resistant technology, a minimum of one tamper-resistant feature is required. Further, all of the TRP tamper-resistant features must be referenced in labeling. In cases where the firm chooses to use two packaging features, each must be referenced in the labeling in accordance with 21 CFR 211.132(c). If a firm chooses to use one tamper-resistant packaging feature plus a sealed capsule, both the packaging feature and the sealed capsule must be referenced in the labeling statement. It is our determination that all the above listed products in capsule dosage form do not conform to the TRP requirements of 21 CFR 211.132.

Consequently, we regard the marketing of the above listed products to be in serious violation of the Federal Food, Drug, and Cosmetic Act, as follows:

SECTION	BRIEF DESCRIPTION
505(a)	The articles cited above are drugs within the meaning of Section 201(g) of the Act which may not be introduced or delivered for introduction into interstate commerce under Section 505(a) of the Act, since they are new drugs within the meaning of Section 201(p) and no approval of an application filed pursuant to Section 505(b) is effective for such drugs.
505(f)(1)	The articles of drug cited above are misbranded in that their labeling fails to bear adequate directions for use, and they are not exempted from this requirement under 21 CFR 201.115, since the articles are new drugs within the meaning of Section 201(p) and no approval of an application filed pursuant to Section 505(b) is effective for such drugs.
502(a)	The articles of drug cited above are misbranded in that their labeling fails to alert consumers to the specific tamper-resistant feature(s) of the package.

The above enumeration of deficiencies should not be construed as an all inclusive list of violations which may be in existence concerning the products. It is your responsibility to ensure that all requirements of the Federal Food, Drug, and Cosmetic Act and regulations promulgated thereunder are being met for this and all your products.

We request that you take prompt action to correct these violations. Until the violations are corrected, we will recommend to other Federal agencies that no contracts be awarded for the subject products. Failure to achieve prompt correction may result in enforcement action being initiated by the FDA without further notice.

Please advise us in writing within fifteen (15) working days after the receipt of this letter to the specific actions you have taken to correct the violations. Your response should include (1) each step that has or will be taken to completely correct the current violation(s) and to prevent the recurrence of similar violations; (2) the time correction will be completed; (3) any reason why the corrective action is not completed with the response time; and (4) any documentation necessary to indicate correction has been achieved.

Your reply should be directed to:

Mr. Thomas L. Sawyer
Director, Compliance Branch
U.S. Food and Drug Administration
1521 West Pico Boulevard
Los Angeles, California 90015-2486

Sincerely,

George J. Gerstenberg
District Director
Los Angeles District Office

cc: [redacted]

State Department of Public Health
Environmental Health Services
Attention: Chief, Food and Drug Branch
714 "P" Street, Room 400
Sacramento, California 95814