DEPARTMENT OF HEALTH AND HUMAN SERVICE

Public Health Service 35065d

Food and Drug Administration
Kansas City District
Southwest Region
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Lenexa, Kansas 66214-3340

Telephone: (913) 752-2100

April 29, 2004

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER
Ref. KAN 2004-08

Mary Barnes, President
Vita-Erb, Ltd.
1358 North Stewart Ave.
Springfield, MO 65802

Dear Ms. Barnes:

This letter follows the February 19 through March 4 and the October 27 through November 12, 2003, inspections of your firm by representatives of the federal Food and Drug Administration (FDA). This letter does not address the deviations from the current good manufacturing practice regulations (Title 21 of the Code of Federal Regulations, Parts 210 and 211 (21 CFR 210 and 211)) observed during those inspections. The significance of those observations, many of which have been noted and brought to your attention previously, remains under active consideration.

We have reviewed a substantial number of product labels gathered during the inspections noted above and, based on that review, we have concluded that many of the over-the-counter (OTC) drug products manufactured and marketed by your firm violate the new drug and misbranding provisions of the federal Food, Drug, and Cosmetic Act (the Act). This letter concerns the following products:

- Vita-Erb THE ORIGINAL CELL REVITALIZER
- CELL PROTECTOR™
- bite out®
- Obediencé® Medicated Shampoo-C-S-S
- HANDCLEANER, WATERLESS CREAM FORM - ANTIMICROBIAL
- Vita-Erb ARTHRITIS PAIN FORMULA
- Valley-of-Youth R-Thritis Relief Roll-On
- Obediencé® Medicated Shampoo-S-S
- flows™ Herbal Foot & Body Soak
- PES 828® PAIN RELIEVING GEL WITH ILEX
- P.E.S. CLEAN - INSTANT ANTISEPTIC HAND CLEANER
- MEDI-DERM ANALGESIC LOTION

- DOCTOR'S BEST™ DRY SKIN CREME

During the inspections, our investigators obtained immediate container labels, promotional labeling, and formulation information for these products. Based on their respective labels and labeling, these products are intended for various uses, described below, that cause them to be "drugs" under section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act). The marketing of these products violates one or more sections of the Act as follows:

Vita-Erb THE ORIGINAL CELL REVITALIZER and CELL PROTECTOR™

According to their labels, these products contain, among other ingredients, Folic Acid, Vitamin B-6, Vitamin B-12, Iron, Salicylic Acid, and Tannins, and they are intended for oral administration. During the referenced inspections, Mr. Moses Barnes of your firm acknowledged that shipments of these products are accompanied by copies of letters signed by [redacted] who is a co-owner of your firm and serves as your technical consultant. These letters bear the following statements:

> "The predominant compound in the Tannins is Epigallocatechin-3-Gallate (EGCG) . . . . In the test tube, cancerous mouse and human cells (skin, lymph system and prostate) and normal human skin cells were contacted with EGCG. This treatment led to apoptosis (programmed death) of the cancer cells, but left the healthy cells unharmed . . . . Also research at the Medical College of Ohio indicates that EGCG inhibits production of urokinase, an enzyme that cancer cells need in order to grow. . . . In addition Masami Suganuma and his research group of Saitama Prefectural Cancer Research Center (Japan) have found in "in vitro" testing that when EGCG is combined with a cancer-preventive drug the preventive effect dramatically increases. . . . Many people have taken Cell Revitalizer with and without chemotherapy and some in each case have seen their cancers go into remission with disappearance of tumors. Others who have not had remission have achieved a significant improvement in quality of life during their period of survival. In all cases tolerance to chemotherapy side effects improved dramatically. . . ."

We are not aware of products like Vita-Erb [redacted], as formulated and labeled, having been marketed on or before the inception of the OTC Drug Review (May 11, 1972); nor these products the subject of a final determination by FDA under 21 CFR § 330.14. Accordingly, they are not deferred to that review.

Because we are not aware of any data establishing that these drugs, as formulated and labeled, are generally recognized as safe and effective, they are "new drugs" as defined

by section 201(p) of the Act. Under section 505(a) of the Act, a new drug must be the subject of an approved application to be legally marketed in the United States. Since these drugs are not so approved, their marketing in the United States violates section 505(a) of the Act.

These drugs are intended and labeled for use by the general public for the prevention of serious diseases (e.g., cancer) that require the supervision of a physician. However, "adequate directions for use," as described at 21 CFR § 201.5, cannot be written for this use. Therefore, these drugs are misbranded under section 502(f)(1) of the Act. The drugs are further misbranded under section 502(f)(2) of the Act, because their respective labels fail to bear the warning required by 21 CFR § 201.314(a) for all oral OTC salicylate-containing drugs.

In addition, [redacted]™ is misbranded under section 502(a) of the Act, as described in 21 CFR § 201.1(h)(2), in that the firm name ("R&P Research") is not qualified on the label and, as such, is represented as the product's manufacturer. This is not true, since the product is actually manufactured by Vita-Erb. [redacted]™ is further misbranded under section 502(b)(1) of the Act, as described in 21 CFR § 201.1(i), in that the label does not disclose the address for the labeled distributor [redacted] and there is no listing for this firm in a current telephone directory.

bite out®

Based on the label, this product contains, among other ingredients, hydrocortisone, 1.0 percent, and it is intended and labeled for topical application for the temporary relief of itching associated with insect bites. This product is subject to FDA's Enforcement Policy for marketed external analgesic drug products containing from 0.5 to 1 percent hydrocortisone. This policy was published in the Federal Register of August 30, 1991 (56 FR 43025). However, bite out® doe s not comply fully with this policy in that (1) the labeled statement of use does not include "Other uses of this product should be only under the advice and supervision of a physician (or "doctor")" and (2) the existing warnings statements do not include, "Do not use for the treatment of diaper rash."

Since bite out® does not comply with the referenced enforcement policy, it is not permitted to market pending establishment under the OTC drug review of a final monograph covering external analgesic drug products.. Therefore, it is a "new drug" as defined by section 201(p) of the Act. This drug is not the subject of an approved application and, therefore, its marketing in the United States violates section 505(a) of the Act.

Because bite out® does not bear the statement of use or comply fully with the warnings statements required by the agency's enforcement policy for hydrocortisone-containing drugs (noted above), the existing directions and warnings on the label are not adequate. Therefore, this product is misbranded under sections 502(f)(1) and 502(f)(2) of the Act.

Obediencé® Medicated Shampoo-C-S-S

According to the label, this product contains, among other ingredients, coal tar extract (equivalent to 0.5% coal tar USP), sulfur (2%), and salicylic acid (2%) and it is intended for topical application to control dandruff. Based on this intended use, Obediencé® Medicated Shampoo-C-S-S is subject to the final OTC drug monograph for dandruff control drug products (21 CFR 358, Subpart H). It does not, however, comply with this monograph as follows:

(1) the triple combination of active ingredients identified on the label is not permitted by the final monograph (21 CFR § 358.720),

(2) the label fails to bear the warnings "Use caution in exposing skin to sunlight after applying this product. It may increase your tendency to sunburn for up to 24 hours after application" and "Do not use for prolonged periods without consulting a doctor," which are required for coal tar-containing antidandruff preparations (21 CFR § 358.750(c)(2)(i) and (ii)),

(3) the label fails to bear the required warning "If condition worsens or does not improve after regular use of this product as directed, consult a doctor" (21 CFR § 358.750(c)(1)(iii)),

(4) the label bears the warning statements "For external use only" and "Avoid contact with the eyes. If contact occurs, rinse eyes thoroughly with water," which are required by 21 CFR § 358.750(c)(1)(i) and (c)(1)(ii). However, these statements are not placed under a "Warnings" heading, also required by this regulation,

(5) the label fails to include the statement "For best results use at least twice a week or as directed by a doctor" as part of the required directions for use (21 CFR § 358.750(d)(1)), and

(6) the label does not bear a required statement of identity, in that the principal display panel does not identify the product as a "Dandruff Shampoo" or "Antidandruff Shampoo." (21 CFR § 358.750(a)(1))

Since Obediencé™ Medicated Shampoo-C-S-S does not comply with the referenced final OTC drug monograph, it is not generally recognized as safe and effective for its labeled uses. Therefore, it is a "new drug" as defined by section 201(p) of the Act. Because Obediencé™ Medicated Shampoo-C-S-S is not the subject of an approved application, its marketing in the United States violates section 505(a) of the Act.

Moreover, because this product's labeled directions and warnings do not comply with the final OTC drug monograph, it is misbranded under sections 502(f)(1) and 502(f)(2) of the Act.

Since Obediencé™ Medicated Shampoo-C-S-S is subject to the final monograph for OTC drug products for the control of dandruff, it is also subject to the format and content requirements for OTC drug labeling under 21 CFR § 201.66. The effective date for affected products to comply with these requirements was set forth in the Federal Register of March 17, 1999 (64 FR 13254) as amended in subsequent Federal Register notices of April 15, 1999 (64 FR 18571), June 20, 2000 (65 FR 38191), and April 5, 2002 (67 FR 16304). Because this product does not comply with the format and content requirements for OTC drug labeling, the information included on its labeling is not prominently displayed with such conspicuousness that it may be read and understood at the time of purchase and use. Therefore, Obediencé™ Medicated Shampoo-C-S-S is further misbranded under section 502(c) of the Act.

HANDCLEANER, WATERLESS CREAM FORM - ANTIMICROBIAL

Based on the label, this product is intended for topical application. Though not identified on the label, the referenced inspections disclosed that this product contains triclocarban as its active ingredient. The label represents this product as an effective antimicrobial handcleaner in a cream form that does not require rinsing with water after use.

Triclocarban in a bar soap form for antimicrobial hand cleansing, followed by a water rinse, is deferred to FDA's OTC Drug Review. This ingredient in a leave-on cream form for use without rinsing is not so deferred. Since we are not aware of a product formulated and labeled like HANDCLEANER, WATERLESS CREAM FORM - ANTIMICROBIAL to have been marketed on or before the inception of the OTC Drug Review (May 11, 1972), and this product is not the subject of a final determination by FDA under 21 CFR § 330.14, it is not deferred to that Review.

Because we are not aware of any data establishing that this drug is generally recognized as safe and effective for its labeled uses, it is a "new drug" as defined by section 201(p) of the Act. HANDCLEANER, WATERLESS CREAM FORM - ANTIMICROBIAL

is not the subject of an approved application. Therefore, its marketing in the United States violates section 505(a) of the Act.

In addition, since the label for this product does not identify the active drug ingredient, i.e., triclocarban, it is misbranded under section 502(e)(1)(A)(ii) of the Act.

Vita-Erb ARTHRITIS PAIN FORMULA

According to the label, this product contains, among other ingredients, emu oil, menthol, methyl salicylate, devil's claw, aloe vera, eucalyptus, triethanolamine, camphor, glucosamine sulfate, and chondroitin sulfate, and it is intended for topical application for relieving arthritis pain. Since active and inactive ingredients are not differentiated on the label, all of the identified ingredients are represented as active drug ingredients for the labeled drug uses (21 CFR § 201.66(b)(2)). We are not aware of a product like Vita-Erb ARTHRITIS PAIN FORMULA, as formulated and labeled, having been marketed on or before the inception of the OTC Drug Review (May 11, 1972); nor is this product the subject of a final determination by FDA under 21 CFR § 330.14. Accordingly, it is not deferred to that review.

Because we are not aware of any data establishing that this drug is generally recognized as safe and effective for its labeled uses, it is a "new drug" as defined by section 201(p) of the Act. Since Vita-Erb ARTHRITIS PAIN FORMULA is not the subject of an approved application, its marketing in the United States violates section 505(a) of the Act.

The inspections referenced above disclosed that the formulation for Vita-Erb ARTHRITIS PAIN FORMULA is also marketed by your firm under the name [redacted], and that it is similarly labeled. Thus, the violations described above for Vita-Erb ARTHRITIS PAIN FORMULA apply to this product.

Obediencé™ Medicated Shampoo-S-S

According to its label, this product contains, among other ingredients, sulfur (2%) and salicylic acid (2%), and it is intended for topical application to control dandruff. Based on this intended use, this product is subject to the final OTC drug monograph for dandruff control drug products (21 CFR 358, Subpart H). But it does not comply with this final monograph, as follows:

(1) the label fails to include the statement "For best results use at least twice a week or as directed by a doctor" as part of the directions for use as required by the final monograph (21 CFR § 358.750(d)(1)),

(2) the label fails to bear the warning "If condition worsens or does not improve after regular use of this product as directed, consult a doctor" as required by the final monograph (21 CFR § 358.750(c)(1)(iii)),

(3) the label bears the warning statements "For external use only" and "Avoid contact with the eyes. If contact occurs, rinse eyes thoroughly with water," which are required by 21 CFR § 358.750(c)(1)(i) and (c)(1)(ii). But these statements are not placed under a "Warnings" heading, also required by this regulation, and

(4) the label does not bear a statement of identity as required by the final monograph (21 CFR § 358.750(a)(1)) in that the principal display panel does not identify the product as a "Dandruff Shampoo" or "Antidandruff Shampoo."

Since Obediencé™ Medicated Shampoo-S-S does not comply with the referenced final OTC drug monograph, it is not generally recognized as safe and effective for its labeled uses. Therefore, it is a "new drug" as defined by section 201(p) of the Act. And since Obediencé™ Medicated Shampoo-S-S is not the subject of an approved application, its marketing in the United States violates section 505(a) of the Act.

Moreover, because this product's labeled directions and warnings do not comply with the final OTC drug monograph, it is misbranded under sections 502(f)(1) and 502(f)(2) of the Act.

Since Obediencé™ Medicated Shampoo-S-S is subject to the final monograph for OTC dandruff control products, it is also subject to the format and content requirements for OTC drug labeling under 21 CFR § 201.66. The effective date for compliance with the requirements is explained above. Because this product does not comply with the format and content requirements for OTC drug labeling, the information included on its labeling is not prominently displayed with such conspicuousness that it may be read and understood at the time of purchase and use. Therefore, Obediencé™ Medicated Shampoo-S-S is further misbranded under section 502(c) of the Act.

flows™ Herbal Foot & Body Soak

According to the label, this product contains, among other ingredients, calcium peroxide and citric acid, and it is intended for use as a foot and body soak to "revitalize[ ] your cells and increase[ ] blood flow to detoxify and heal." We are not aware of a product like flows™ Herbal Foot & Body Soak, as formulated and labeled, having been marketed on or before the inception of the OTC Drug Review (May 11,

1972); nor is this product the subject of a final determination by FDA under 21 CFR § 330.14. Accordingly, it is not deferred to that review.

Because we are not aware of any scientific data establishing that this drug is generally recognized as safe and effective for its labeled uses, it is a "new drug" as defined by section 201(p) of the Act. Since flows™ Herbal Foot & Body Soak is not the subject of an approved application, its marketing in the United States violates section 505(a) of the Act.

PES 828® PAIN RELIEVING GEL WITH ILEX

Based on the label, this product contains, among other ingredients, menthol (3.32%), ilex herbal extract, aloe vera, triethanolamine, camphor, and Germaben II and it is intended for "***cryotherapy pain relief***" and for "[l]ong lasting relief from neck and back pain, arthritis, sports injuries, and muscle spasms." The label identifies only "Menthol 3.32%" under the heading "**ACTIVE INGREDIENT**."

Although the ingredient "Ilex Herbal Extract" is identified on the label under the heading "**INERT INGREDIENTS**," "**ILEX**" is prominently featured on the label's principal display panel in such a manner as to suggest that it is an "active ingredient," as described in 21 CFR § 201.66(b)(2). We are not aware of a product, formulated with ilex herbal extract and offered for these OTC external analgesic uses, having been marketed on or before the inception of the OTC Drug Review (May 11, 1972); nor is such a product the subject of a final determination by FDA under 21 CFR § 330.14. Accordingly, it is not deferred to that review.

Because we are not aware of any scientific data establishing that a drug, formulated with ilex herbal extract and labeled like PES 828® PAIN RELIEVING GEL WITH ILEX, is generally recognized as safe and effective for its labeled uses, it is a "new drug" as defined by section 201(p) of the Act. Since this product is not the subject of an approved application, its marketing in the United States violates section 505(a) of the Act.

In addition, the label identifies "Germaben II" under the heading "**INERT INGREDIENTS**." The company which holds the trademark for "Germaben® II" describes it as a preservative system comprised of a combination of diazolidinyl urea, methylparaben, propylparaben, and propylene glycol. The presence of these individual ingredients is not identified on the label as required by 21 CFR § 201.10(a). Declaring them solely by the proprietary name "Germaben II" is misleading in that the declaration suggests that a component by that name has some unique composition or role in the formulation when, in fact, it does not. All four of the individual ingredients that

comprise "Germaben® II" are found in many topically applied drug and cosmetic products. Considering the misleading nature of how this component is declared on the label, PES 828® PAIN RELIEVING GEL WITH ILEX is misbranded under section 502(a) of the Act, as described under 21 CFR §§ 201.10(c)(2), (c)(3), and (c)(4).

P.E.S. CLEAN - INSTANT ANTISEPTIC HAND CLEANER

The term "ANTISEPTIC" on the label represents and suggests that this product is effective in killing or inhibiting the growth of microorganisms on the skin to prevent the diseases caused by those microorganisms.

According to the label, this product contains isopropyl alcohol, aloe vera, and emollient gel as "ACTIVE INGREDIENTS." This combination of active ingredients, labeled for this use, is not covered by FDA's OTC Drug Review. We are also not aware of evidence establishing that this combination of ingredients is generally recognized as safe and effective or that this product is deferred to that review for its labeled antiseptic uses. Accordingly, this product is a "new drug" as defined by section 201(p) of the Act. Since it is not the subject of an approved application, its marketing in the United States violates section 505(a) of the Act.

MEDI-DERM ANALGESIC LOTION

According to the label, this product contains "Triethanolamine Salicylate" (or trolamine salicylate, as it is known by its established name), and it is intended for "[f]ast, temporary relief of pains due to Arthritis, Rheumatism, Back, Joints and Muscular Aches," and for "fast temporary relief of the symptoms of Arthritis, Rheumatism." Under FDA's OTC Drug Review, FDA is evaluating external analgesic claims for relieving the pain of arthritis and/or the pain of rheumatism. Claims for relieving other symptoms of arthritis and/or rheumatism, as suggested in this product's label (e.g., "fast temporary relief of the symptoms of Arthritis, Rheumatism"), are not being evaluated under this review.

We are not aware of evidence establishing that trolamine salicylate is generally recognized as safe and effective or that it is deferred to the OTC Drug Review for the symptoms of arthritis or rheumatism (other than for the pain associated with these conditions). Therefore, this product, offered for these broader uses, is a "new drug" as defined by section 201(p) of the Act and requires approval for marketing in the United States. Since MEDI-DERM ANALGESIC LOTION is not the subject of an approved application, its marketing in the United States violates section 505(a) of the Act.

Since trolamine salicylate is not declared on the label by its established name, this product is misbranded under section 502(e)(1)(A)(ii) of the Act.

For your information, topical preparations of trolamine salicylate, 10%, may be marketed OTC for external analgesic use in the treatment of the pain of arthritis, rheumatism, back, joints and muscular aches. As noted above, however, absent an approved application, OTC external analgesics may not be legally marketed for other symptoms of arthritis and/or rheumatism.

DOCTOR'S BEST™ DRY SKIN CREME

This product is intended to mitigate and/or treat eczema. Urea is prominently represented on the label as an active ingredient effective for this use (e.g., "**Dermatologist approved, 20 % urea** cream designed for treatment and relief of eczematous, dry skin") (21 CFR § 201.66(b)(2)). Neither this ingredient nor any of the other ingredients identified on the label is covered by FDA's OTC Drug Review for this use. We are not aware of any evidence establishing that urea, either singly or in combination with the identified ingredients, is generally recognized as safe and effective or that it is deferred to the OTC Drug Review for the labeled use. Therefore, this product is a "new drug" as defined by section 201(p) of the Act.

Since DOCTOR'S BEST™ DRY SKIN CREME is not the subject of an approved application, its marketing in the United States violates section 505(a) of the Act.

Upon revising the labeling to correct the violations noted above, the labeling must also be revised to comply with the final rule covering the format and content requirements for OTC drug labeling (21 CFR § 201.66). Failing to comply with these requirements would cause these products to be misbranded under section 502(c) of the Act. In addition, revised labeling must list all inactive ingredients on the outside container of the retail package, as required by section 502(e)(1)(A)(iii) of the Act.

The violations described above 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, including seizure and/or injunction.

Please send a written response to this office within fifteen working days of receipt of this letter. Your response should describe the specific actions that you will take, or have taken, to

correct the violations described in this letter. Your response should also include an explanation of each step being taken to prevent recurrence of similar violations. If corrective action cannot be completed within fifteen working days, state the reason for the delay and the time within which corrections will be completed. Direct your response to Nadine Nanko Johnson, Compliance Officer, Food and Drug Administration, at the address listed above.

Sincerely,

for/ Charles W. Sedgwick
District Director
Kansas City District