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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Seattle District
Pacific Region
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Bothell, WA 98021-4421

Telephone: 425-486-8788
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March 17, 2005

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

IN REPLY REFER TO: SEA 05-16

Truman J. Berst, Founder
Alternative Health & Herbs Remedies
37386 Soap Creek Road
Corvallis, Oregon 97330

WARNING LETTER

Dear Mr. Berst:

During an inspection of your manufacturing facility located at 425 Jackson Street SE, Albany, Oregon, on September 13-17, 2004, FDA Investigators Terri L. Dodds and Dawn E. Barkans found significant deviations from the Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals (Title 21, Code of Federal Regulations (CFR), Parts 210 and 211, and Part 200, Subpart C). These deviations cause your drug products, such as your single ingredient herbal tinctures and multi-ingredient tincture formulas intended for ophthalmic use, including but not limited to Squaw Vine, Parsley Herb, Mistletoe (European), and Licorice Root tinctures, to be adulterated within the meaning of Section 501(a)(2)(B) [21 U.S.C. § 351(a)(2)(B)], of the Federal Food, Drug, and Cosmetic Act (the Act). In addition, several of your products bear direction for use or statements, either on their labels or on your Internet website, www.healthherbs.com, indicating that they may be used as ophthalmic (eye) rinses or otherwise applied directly to the eye for the treatment of various conditions. Based on their intended use to either affect the structure of the body, or to cure, mitigate, treat, or prevent disease, these products are drugs as defined in section 201(g) of the Federal Food, Drug, and Cosmetic Act (Act).

The CGMP violations include, but are not limited to, the following:

1. Failure to establish and follow written procedures designed to prevent microbiological contamination of drug products purporting to be sterile. Such procedures shall include validation for any sterilization process [21 CFR 211.113(b)]. Specifically, the ophthalmic drug products currently manufactured at your firm are neither processed using aseptic

technique nor terminally sterilized to prevent microbial contamination. Our investigators noted that you have not validated your manufacturing process through media fills to assure the sterility of any ophthalmic drug product manufactured at your facility. They also noted that your firm filters ophthalmic products such as the Eye Rinse Concentrate Formula and Elderberry Herbal Tincture through non-sterile [redacted] cm filter paper to remove large particulates. A sterilizing filter is not used in the manufacture of these products.

Our investigators collected samples of your Eye Rinse Concentrate Herbal Formula, White Willow Bark Herbal Tincture, Fennel Seed Herbal Tincture, and Elderberry Flower Herbal Tincture drug products during the September 2004 inspection. Our analysis showed that these samples tested positive for microbial growth.

We acknowledge that since the inspection, you have issued a Voluntary Recall (December 02, 2004) for all lots of Eye Rinse Concentrate Formula, Elderberry Flower Herbal Tincture, White Willow Bark Herbal Tincture and Fennel Seed Herbal Tincture. However, on January 03, 2005, our investigators revealed that your Elderberry Flower, White Willow Bark and Fennel Seed Herbal Tinctures were still available for purchase at your retail outlets. As of our last teleconference on February 1, 2005, you firm has yet to provide us with the status of the recall efforts.

We also acknowledge that you have destroyed the current stock of Eye Rinse Concentrate Formula and have removed references to ophthalmic uses from the other three products. However, you still manufacture other ophthalmic products such as Licorice Root, Mistletoe (European), Squaw Vine, and Parsley Herb tinctures. The Code of Federal Regulations (CFR) states within 21 CFR 200.50 that "... all preparations offered or intended for ophthalmic use, including preparations for cleansing the eyes should be sterile."

2. Failure to clean and sterilize drug product containers and closures to assure they are suitable for their intended use [21 CFR 211.94(c)]. Specifically, ophthalmic drug product containers and closures are not cleaned and sterilized prior to the filling and finishing of ophthalmic herbal tinctures. Our investigators noted that containers are never cleaned and sterilized prior to filling ophthalmic drug product. Caps and droppers are only rinsed with water when broken glass is found on or in the dropper tubes. In all other instances, the caps and droppers are not cleaned and sterilized prior to utilizing them in the capping of ophthalmic drug product containers. These observations, along with your practice of storing containers and closures in a manner that exposes them to your facility's uncontrolled environment, severely increases the risk of microbial contamination of the ophthalmic drug products that your firm manufactures.

3. Failure to have control systems for your firm's operations necessary to prevent contamination of drug product during aseptic processing [21 CFR 211.42(c)(10)]. Specifically, your firm manufactures ophthalmic drug products in a non-aseptic area that has not been designed to facilitate proper cleaning, maintenance and aseptic operations. For example, the concrete flooring in the manufacturing area is not sealed and is significantly cracked, the walls consist of painted concrete blocks which are stained in several areas, and a canvas covering, which is torn in many places, has been fastened to the ceiling studs. All of

the counter tops in the manufacturing area consist of particle board lined with wood laminate. The laminate has been chipped from the edge of the counters, exposing the particle board. Your manufacturing area has several wooden storage shelves, and the ceiling lighting fixtures are not appropriately designed to facilitate cleaning. The cleaning and disinfecting within the aseptic area is inadequate, as the manufacturing area was visibly dusty.

Additionally, our inspection revealed that the HVAC system is not designed to maintain a "Class 100" or ISO "Class 5" environment within the manufacturing area used for ophthalmic drug products. Also, the air supplied to the manufacturing area has not been filtered through high-efficiency particulate air (HEPA) filters, and there is no control of room pressurization to ensure that the manufacturing area will maintain significant positive pressure relative to the adjacent rooms within your facility.

Furthermore, our investigators noted that you do not perform environmental monitoring of your manufacturing area. You have also not established any written procedures for environmental monitoring that specifically address issues such as sample location, sample frequency, sampling technique, sample size, analytical techniques, interpretation of results, acceptance criteria, and corrective actions in the event of failures.

Finally, your personnel do not practice aseptic gowning technique designed to provide a barrier between the body and the ophthalmic drug product, and prevent microbial contamination of the ophthalmic drug product.

4. Failure to establish written standards or specifications, methods of testing, and methods of cleaning and sterilizing drug product containers and closures [21 CFR 211.94(d)]. Specifically, your firm does not have any written procedures, standards or specifications for cleaning and sterilizing containers and closures used in the manufacture of your ophthalmic herbal tinctures.

5. Failure to conduct appropriate laboratory testing on any batches of ophthalmic drug products required to be free of objectionable microorganisms [21 CFR 211.165(b)]. Specifically, your firm does not test any batches of ophthalmic drug products to ensure that they are free of objectionable microorganisms.

6. Failure to establish a written testing program designed to assess the stability characteristics, appropriate storage conditions and expiration dates of drug products [21 CFR 211.166]. Specifically, your firm does not perform any testing to establish appropriate expiration dates and storage conditions for your ophthalmic drug products. During the inspection, our investigators inquired as to how your firm determined whether a drug product had lost its effectiveness. Your firm replied that your drug products do not usually "go bad." Yet, your firm acknowledged that some products cause the rubber bulb of the cap and dropper to disintegrate over time. Additionally, your firm has stated that the single herb tinctures and tincture formulas have an expiration date of approximately 3 to 10 years. There is no data to assure the stability of drug product over the stated expiration period.

7. Failure to prepare batch records and control records for each batch of ophthalmic drug product produced [21 CFR 211.188]. Specifically, your firm does not have written batch records for any batch of ophthalmic herbal tincture manufactured at your facility, which describe steps such as the extraction and filtration of the tinctures or filling of these tinctures into bulk storage containers and final containers and closures. You also do not retain copies of all ophthalmic drug product labeling used.

8. Failure to establish and follow written procedures for the cleaning of equipment used in the manufacture, processing, packing and holding of drug products [21 CFR 211.67(b)]. Specifically, your firm does not have any written procedures for cleaning and maintenance of equipment and utensils used in the manufacture of ophthalmic drug products. There are no other procedures which sufficiently address various aspects of cleaning such as: the assignment of responsibility for the cleaning and maintenance of equipment; the methods, equipment and materials used in the cleaning operations; the protection of cleaned equipment and the inspection for cleanliness in equipment prior to use. Additionally, you have not determined whether your cleaning agents, such as dish soap and household bleach effectively remove contamination from equipment product contact surfaces. Furthermore, the equipment and utensils are scrubbed by a bottle washing brush that is left in the sink between uses.

9. Failure to withhold each lot of component, drug product containers, and closures, from use in the manufacture of ophthalmic herbal tinctures until the lot has been sampled, tested or examined as appropriate [21 CFR 211.84(a)]. For example, your general procedure for the manufacture of herbal tinctures requires Distilled Water. You utilize water purchased from the [redacted] without performing any testing to determine whether it is "distilled." In addition, you have no documented testing or assurance from your vendor that the water meets the "distilled" quality as required by your procedures. Furthermore, you have not provided assurance through testing that this water is free of objectionable microbial organisms. In fact, our investigators observed that your firm consistently leaves the cap to the [redacted] water jug open, thus exposing the water to your facility's uncontrolled environment.

   We acknowledge that, during the inspection, you stated that you have purchased a [redacted] Water Purifier. However, our investigators noted that your employees did not use water from this equipment in the manufacture of ophthalmic drug products.

10. Failure to adequately investigate any written and oral complaints regarding drug products manufactured by your firm [21 CFR 211.198(b)]. Specifically, our investigators noted that although your firm began recording complaints from customers in April 2004 and offered refunds to them for the returned drug product, you have failed to follow-up on the complaints to determine the exact problem with the returned drug product. You have also failed to establish whether other lots of the same drug might have similar defects. Furthermore, you did not record the complainant, lot number of the drug product unit in question, or a reply to the complainant. On two occasions, customers complained of "pain" and "not feeling good"

after taking Truman's CAC (colon and liver cleanser) Liquid. You replied "Well yah – it cleans you out." Based on your assessment of these customers' complaints, it is evident that your firm does not adequately investigate and resolve complaints regarding the drug products that you manufacture.

11. Failure to have adequate written procedures for production and process controls designed to assure that drug products have the identity, strength, quality, and purity they purport to possess [21 CFR 211.100(a)]. Your firm's procedures for the manufacturing of ophthalmic drug products do not describe the entire manufacturing process. For example, your procedures do not explain the filtering step that occurs in the manufacturing of final drug product. Your procedures also do not include other essential information such as the identification of equipment to be used in the manufacturing process, the in-process controls or sampling of product for analysis, the assignment of lot numbers for each batch of drug product, a description of the containers and closures used in the filling and finishing of drug product, and instructions on the use of the correct labels and labeling for each drug product.

12. Failure to establish written procedures that describe in sufficient detail the receipt, identification, storage, handling, sampling, testing, and approval or rejection of components and drug product containers and closures [21 CFR 211.80(a)]. Specifically, your firm does not have any written procedures describing the receipt, identification, storage, handling, sampling, testing and approval or rejection of components and drug product containers and closures.

13. Failure to establish and follow written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, examination, and/or testing of labeling and packaging materials [21 CFR 211.122(a)]. Specifically, your SOP on creating labels does not address the processes of controlling label receipt, storage, handling, sampling, issuance, and reconciliation.

14. Failure to exercise strict controls over labeling issued for use in drug product labeling operations [21 CFR 211.125(a)]. Specifically, your firm currently does not issue labels, review them for accuracy, or reconcile them; any extra labels from a labeling campaign are stored under the labeling area in cardboard boxes for use with future lots of drug product. Furthermore, the original labeling stored on your computer database has not been reviewed or approved for accuracy. In addition, your firm fails to have adequate SOP's for review and approval of labels for finished drug products.

15. Failure to have a quality control unit that has the responsibility and authority to approve or reject all components, in-process materials, drug products, and all procedures or specifications impacting on the identity, strength, quality, and purity of the drug products [21 CFR 211.22]. All of the above deficiencies are indicative of your Quality Control Unit's inability to meet the requirements impacting the identity, strength, quality and purity of your drug products.

Additionally, the products cited below fail to comply with the Act and final regulations as follows:

Eye Rinse Concentrate Formula 1036 contains various herbal ingredients and bears directions for use on the label to place in an eye rinse cup and flush the eye. Neither the ingredients in the product nor the labeled directions for use and warnings comply with the final regulations for OTC ophthalmic drug products at 21 C.F.R. Part 349. We are not aware of any evidence that the ingredients in this product are generally recognized as safe and effective for ophthalmic use.

Antibiotic Formula 1009 contains various herbal ingredients and states on your Internet website that it may be used topically. Your internet website bears claims that the product is useful in more than fifty disease conditions, including abscesses, infection, lupus, and venereal disease. Neither the ingredients in the product nor the labeled directions for use and warnings comply with the final regulations for OTC topical antibiotic drug products at 21 C.F.R. Part 333. We are not aware of any evidence that the ingredients in this product are generally recognized as safe and effective for the product's labeled indications, i.e., the conditions for use listed on your Internet website.

Parsley Herb 3157 contains parsley and is offered on your Internet website for use externally for conjunctivitis, inflammation of the eyelids, and for contusions. Neither the active ingredient in the product not the labeled directions for use and warnings comply with the final regulations for OTC ophthalmic drug products at 21 C.F.R. Part 349. We are not aware of any evidence that this product is generally recognized as safe and effective for its labeled indications.

Eyebright 3124 contains eyebright herb and is offered on your Internet website in a manner that implies that it may be used externally for eye disorders such as failing vision, inflammation, conjunctivitis, ulcers, and itchy eyes with discharge. Neither the active ingredient in the product nor the labeled directions for use and warnings comply with the final regulations for OTC ophthalmic drug products at 21 C.F.R. Part 349. We are not aware of any evidence that this product is generally recognized as safe and effective for its labeled indications.

Squaw Vince 3182 contains squaw vine herb and is offered on your Internet website as an external wash for sore eyes and skin problems. Neither the active ingredient in the product nor the labeled directions for use and warnings comply with the final regulations for OTC ophthalmic drug products at 21 C.F.R. Part 349. We are not aware of any evidence that this product is generally recognized as safe and effective for its labeled indications.

Skin Sores Antibiotic Formula 1046 contains myrrh gum and goldenseal root and is offered on your Internet website for topical use as a general antibiotic for many conditions, including abscesses, appendicitis, bed sores, impetigo, infection, and open sores and ulcers. Neither the ingredients in this product nor the directions for use and warnings comply with the final regulations on OTC topical antibiotic preparations found at 21 C.F.R. Part 333. We are not aware of any evidence that this product is generally recognized as safe and effective for its labeled indications.

Witch Hazel Formula 3199 contains witch hazel (12%) and is offered on your Internet website for use externally as a rinse or gargle for sore throat, as a vaginal douche for vaginitis and leucorrhea, and as a compress for inflamed bed sores, skin irritations, bruises, bites, stings, minor burns, poison ivy, hemorrhoids, bleeding, varicose veins, and nose bleeds. Although witch hazel is acceptable for use in astringent hemorrhoidal preparations under 21 C.F.R. Part 346 and in astringent skin protecant products under 21 C.F.R. Part 347, the labeling for this product does not comply with these final regulations with respect to directions for use and required warnings. Further, we are not aware of any evidence that the active ingredient in this product is generally recognized as safe and effective for the other indications cited.

The above-listed products are not generally recognized as safe and effective for the indications listed on their labeling. Thus, they are new drugs that may not be legally marketed in the United States unless they are the subject of an approved application under section 505 of the Act. Under section 301(d) of the Act, the continued marketing of these products is prohibited. Further, all the products listed above are subject to the final OTC final drug regulations cited above and they are misbranded under section 502(f)(1) of the Act because their directions for use do not comply with those final regulations. They are further misbranded under section 502(f)(2) of the Act because they do not bear the warnings required by the final regulations.

The violations above are not intended to be an all-inclusive list of deficiencies at your firm. It is your responsibility to assure adherence with the requirements of the Federal Food, Drug, and Cosmetic Act and that all of your drug products (ophthalmic and non-ophthalmic) are processed, packed, and held according to Current Good Manufacturing Practice regulations. Failure to promptly correct these deviations may result in regulatory action without further notice. These actions include, but are not limited to, seizure and/or injunction.

Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts.

For your information, we have published several guidance documents, including the "Guidance for Industry, Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice (Sept. 2004)" which may be found at http://www.fda.gov/cder/guidance.

Please advise this office within fifteen days of your receipt of this letter as to the specific actions you have taken or intend to take to correct these violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. Your reply should be directed to the attention of Lisa M. Elrand, Compliance Officer, at the address noted on the letterhead.

Sincerely,

Charles M. Breen
District Director