DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Kerry W. Mettert
Director, Quality and Regulatory
ParaPRO, LLC
11550 North Meridian Street, Suite 400
Carmel, IN 46032-4565

RE: NDA # 022408
Natroba (spinosad) topical suspension, 0.9%
MA #18

Dear Mr. Mettert,

The Office of Prescription Drug Promotion (OPDP), Division of Consumer Drug Promotion (DCDP) of the U.S. Food and Drug Administration (FDA) has reviewed a video news release (VNR) (NAT-PRL-000 natrobapkg_HDMP4.mp4) for Natroba (spinosad) topical suspension, 0.9% (Natroba) submitted by ParaPRO, LLC (ParaPRO) under cover of Form FDA 2253. The VNR is misleading in that it presents efficacy claims for Natroba, but fails to communicate any risks associated with its use, presents an unsubstantiated superiority claim, and inadequately communicates the full indication for the drug. Thus, the VNR misbrands the drug in violation of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), 21 U.S.C. 352(a), (n); 321(n). *See* 21 CFR 202.1(e)(3)(ii); (e)(5) & (e)(6)(ii).

Background

Below is the indication and summary of the most serious and most common risks associated with the use of Natroba.[1]

The FDA-approved product labeling (PI) for Natroba states that it is a pediculicide indicated for the:

- Topical treatment of head lice infestation in patients four (4) years of age and older.

The Adjunctive Measures subsection of the Indications and Usage section of the PI also states the following:

> NATROBA Topical Suspension should be used in the context of an overall lice management program:

[1] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.

- Wash (in hot water) or dry-clean all recently worn clothing, hats, used bedding and towels.
- Wash personal care items such as combs, brushes and hair clips in hot water.
- A fine-tooth comb or special nit comb may be used to remove dead lice or and nits.

The PI for Natroba includes a Warning and Precaution regarding benzyl alcohol toxicity. Natroba contains benzyl alcohol and is not recommended for use in neonates and infants below the age of 6 months. Systemic exposure to benzyl alcohol has been associated with serious adverse reactions and death in neonates and low birth-weight infants. The most common adverse events associated with Natroba were application site erythema and ocular erythema.

Omission of Risk Information

Promotional materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials. The VNR is misleading in that it presents various efficacy claims for Natroba, but fails to communicate any risk information. For example, the VNR includes claims made by a narrator (identified in the VNR as Clark Powell reporting from Indianapolis) such as:

> The FDA has approved what could be a game changing medication in the war against head lice; one that doesn't require nit combing to be effective. It's called Natroba. It is a topical medicine whose active ingredient is derived from a naturally occurring soil microbe. It is approved for kids 4 years and up and studies show it's about twice as effective as permethrin – the most commonly used over the counter product.

The VNR, however, entirely omits **all** risk information, including the warning and precaution regarding benzyl alcohol toxicity and the most frequently reported adverse events from the PI. By omitting the most serious and frequently occurring risks associated with the drug, the VNR misleadingly suggests that Natroba is safer than has been demonstrated.

Unsubstantiated Superiority Claim

Promotional materials are misleading if they represent or suggest that a drug is more effective than another drug, when this has not been demonstrated by substantial evidence or substantial clinical experience. As noted above, the VNR claims that Natroba "could be a game changing medication in the war against head lice; one that doesn't require nit combing to be effective." This claim misleadingly implies that Natroba represents a new or different approach in the treatment of head lice, one that is a significant advance over other currently available products, when this has not been demonstrated by substantial evidence or substantial clinical experience. While we acknowledge that Natroba does not require nit combing to be effective, there are several other prescription products currently available for the treatment of head lice infestation that also do not require nit combing to be effective. Furthermore, we are not aware of any adequate, well-controlled studies demonstrating that Natroba offers a significant advantage over other prescription drugs already available for this

condition. Therefore, the claim that Natroba is a "game changing" medication for the treatment of head lice is not supported by substantial evidence or substantial clinical experience.

Inadequate Communication of Indication

The VNR fails to adequately communicate Natroba's full approved indication. While we acknowledge that the VNR communicates that Natroba is indicated for topical treatment of head lice infestation in patients four years of age and older, it fails to convey that Natroba should be used in the context of an overall lice management program. Specifically, the Adjunctive Measures subsection of the Indications and Usage section of the PI states the following:

> NATROBA Topical Suspension should be used in the context of an overall lice management program:
> - Wash (in hot water) or dry-clean all recently worn clothing, hats, used bedding and towels.
> - Wash personal care items such as combs, brushes and hair clips in hot water.
> - A fine-tooth comb or special nit comb may be used to remove dead lice or and nits.

Thus, the VNR fails to adequately communicate the full approved indication for Natroba.

Conclusion and Requested Action

For the reasons discussed above, the VNR misbrands Natroba in violation of the FD&C Act, 21 U.S.C. 352(a), (n); 321(n). *See* 21 CFR 202.1(e)(3)(ii); (e)(5) & (e)(6)(ii).

OPDP requests that ParaPRO immediately cease the dissemination of violative promotional materials for Natroba such as those described above. Please submit a written response to this letter on or before March 7, 2013, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Natroba that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, Division of Consumer Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266** or by facsimile at (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. Please refer to MA #18 in addition to the NDA number in all future correspondence relating to this particular matter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Natroba comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Carrie Newcomer, PharmD
Regulatory Review Officer
Division of Consumer Drug Promotion
Office of Prescription Drug Promotion

{See appended electronic signature page}

Michael Sauers
Acting Deputy Director
Division of Consumer Drug Promotion
Office of Prescription Drug Promotion

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

CARRIE A NEWCOMER
02/21/2013

MICHAEL A SAUERS
02/21/2013