U.S. Department of Health & Human Services

U.S. Food and Drug Administration



## Inspections, Compliance, Enforcement, and Criminal Investigations

### Allure Labs, Inc. 5/24/11

Department of Health and Human Services

Public Health Service
Food and Drug Administration
San Francisco District
Pacific Region
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Alameda, CA 94502-7070
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**WARNING LETTER**

**Via UPS**
**Delivery Signature Requested**

May 24, 2011

Swarnjit S. Dhatt, President and CEO
Allure Laboratories, Inc.
30901 Wiegman
Hayward, CA 94544

Dear Mr. Dhatt:

During our October 18, 2010 through November 22, 2010 inspection of your pharmaceutical manufacturing facility, Allure Laboratories, Inc., located at 30901 Wiegman, Hayward, California, investigator(s) from the Food and Drug Administration (FDA) identified significant violations of Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations, Parts 210 and 211. These violations cause your drug product(s) to be adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 351(a)(2)(B)] in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing, or holding do not conform to, or are not operated or administered in conformity with, CGMP.

As described below, some of the drugs you manufacture are unapproved new drugs without an approved application, and by delivering them for introduction into interstate commerce, you are in violation of sections 301(d) and 505(a) of the Act [21 U.S.C. §§ 331(d) and 355(a)]. These unapproved new drugs are misbranded pursuant to sections 502(f)(1), 502(c), 502(e)(1)(A), and 503(b)(4) of the Act [21 U.S.C. §§ 352(f)(1), 352(c)(1), 352(e)(1)(A), and 353(b)(4)], and by delivering them for introduction into interstate commerce you are in violation of section 301(a) of the Act [21 U.S.C. § 331(a)].

We have reviewed your firm's response dated December 12, 2010, and note that it lacks sufficient corrective actions.

We acknowledge your second written response, dated February 3, 2011, to the Form FDA 483. However, because this response was received more than 15 business days after the Form FDA 483 was issued, this second response has not been considered. We plan to evaluate this response to the Form FDA 483, along with any other written material provided, as a direct response to this Warning Letter.

Specific violations observed during the inspection include, but are not limited, to the following:

**CGMP Violations**

1. Your firm has failed to establish an adequate quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging material, labeling, and drug products [21 C.F.R. § 211.22(a)]. For example,

A. Your Quality Control Unit (QCU) failed to reject a lot of Honeysuckle component (lot **(b)(4))** after it failed specifications for yeast, mold, and Aerobic Plate Count. The lot was released and used to manufacture three lots of **(b)(4)** Moisturizing Face Screen (lots **(b)(4)**).

B. Your QCU failed to detect an employee miscalculating the microbial results for three lots of **(b)(4)** Moisturizing Face Screen (lots **(b)(4)**) finished products by not applying a dilution factor of $10^{-2}$. The correct calculation of the results would have shown that these products were Out-of-Specification (OOS). The three lots of **(b)(4)** Moisturizing Face Screen were released and distributed by the QCU based on the erroneous results.

C. Your QCU failed to detect multiple discrepancies in sample weights and dilution factors between the analyst's notebook and the *Calculation Sheet*. As a result, incorrect data was recorded for multiple products and finished products not meeting specifications were released. Specifically, a lot of **(b)(4)** SPF 30 (lot **(b)(4)**) was released and distributed even though it did not meet the established specification of **(b)(4)**% label claim. The correct calculation would have reported a **(b)(4)**% label claim.

Your QCU did not require a second, independent person to review the raw data, calculations and records before releasing these lots for distribution.

In your response, your firm states that you have removed the employees responsible for the laboratory data errors from employment. However, you have not explained in any detail how you intend to handle all affected lots or whether you would report these issues to the own-label distributors. Additionally, your response did not propose a timeframe for completing the proposed corrective actions. We acknowledge the results of the retesting for Zinc and Titanium performed by the third party laboratory. However, the response does not include any documentation of the procedure by which your firm qualified the laboratory or demonstrated its use of a validated methodology. Finally, your response failed to provide a plan to ensure that the QCU will carry out its responsibilities in the future.

2. Your firm has failed to establish appropriate written procedures designed to prevent objectionable microorganisms in products not required to be sterile [21 C.F.R. § 211.113(a)].

For example, your firm's microbial limit specifications for finished product permits a microbial load in your drug product that could allow the presence of objectionable and potentially pathogenic organisms in your topical OTC drug products. In addition, your firm does not specifically test for *Staphylococcus aureus* or *Pseudomonas aeruginosa* that should be absent from topical drug preparations.

In your response, your firm states that you will review all raw material specifications to determine if the current specifications should be changed or whether to add further quality control tests. Your response, however, is inadequate because you do not mention a similar review for the appropriateness of your current specifications as it is applied to finished products and fails to propose a timeframe for completion.

> 3. Your firm has not established scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, in-process materials, and drug products conform to appropriate standards of identity, strength, quality, and purity [21 C.F.R. § 211.160 (b)]. For example,
>
> A. Your firm has failed to provide a scientific justification for how the samples of bulk drugs are representative of the lot when they are collected only from the top of the kettle. Also, the samples are taken using a re-usable spatula sprayed with 70% isopropyl alcohol immediately before use. The presence of the alcohol on the spatulas could affect the validity of the test results.
>
> B. Your firm has failed to validate your Standard Operating Procedure (SOP) **(b)(4)**, "Microbiological Testing of Cosmetics, Raw Materials and Finished Products," to show the absence of growth inhibition by the tested drug products.
>
> C. Your firm has failed to verify the assay methods for zinc oxide, titanium dioxide, and salicylic acid under actual conditions of use to determine the amount of active ingredients in your sunscreen products.

We acknowledge your proposed actions to validate all test methods and establish procedures for sampling, cleaning, preventing cross-contamination, and storing intermediate drug materials. However, your response does not specify any timeframes for completion.

> 4. Your firm does not have adequate written procedures for production and process controls designed to assure that the drug products you manufacture have the identity, strength, quality, and/or purity they purport or are represented to possess [21 C.F.R. § 211.100(a)]. For example,
>
> A. Your firm's mixing operations for bulk drugs have not been validated to ensure homogeneity.
>
> B. Your firm has failed to evaluate the holding time and handling (e.g., transfer from mixing kettles to intermediate storage containers) of bulk drugs during and after intermediate storage to ensure the bulk drugs continue to meet established specifications prior to filling. There has been no testing of finished products to verify that the transfers to intermediate storage containers, and conditions and duration of storage, do not adversely affect the drug products.

We acknowledge your proposed actions to validate the mixing operation and establish holding times for intermediate storage. However, your response does not address the establishment of storage conditions associated with the holding times or specify a timeframe for completion.

> 5. Your firm has failed to ensure that each person engaged in the manufacture, processing, packing, or holding of a drug product has the education, training, and experience, or any combination thereof, to enable that person to perform their assigned functions [21 C.F.R. § 211.25(a)].

For example, the employees of your firm, including a member of your quality control staff, admitted to our investigators that they were unaware of and were not trained to follow your SOP for handling deviations. There were at least two instances in which an OOS investigation was not conducted.

While your response proposes to provide training to all employees, it does not provide documentation that you have initiated the training and does not specify a timeframe for completion. In addition, your response fails to specifically address how the proposed training will ensure that all employees will be trained in SOPs that are relevant to their job functions.

**Unapproved and Misbranded Over-the-Counter (OTC) Drugs**

Your firm manufactures and distributes numerous drug products for over-the-counter (OTC) use. During the inspection noted above, the investigators collected labeling for some of these drug products. As presently formulated, labeled, and promoted, these products are unapproved and/or misbranded drugs in violation of Sections 505(a) and 502 of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. §§ 355 and 352].

These violations are described in more detail below.

**(b)(4) Gel**

Statements found on the label:

• "**(b)(4)**, is a unique, cosmetically elegant roll-on gel formulated for ingrown hairs, razor burn, and bumps resulting from shaving, waxing, tweezing, electrolysis and laser hair removal. **(b)(4)** contains exfoliating and moisturizing ingredients to maximize your results . . . ."

• "vanish" juxtaposed with the following conditions: "Ingrown Hair . . . Waxing/Razor Bumps . . . Razor Burn . . . Roll-On For Men and Women . . . ."

• "Ingredients: SDA-408, Isopropyl Alcohol, Purified Water, Willow Bark Extract, Propylene Glycol, Lactic Acid . . . ."

Based on the above labeling claims, **(b)(4)** Gel is a "drug" as defined by section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 321 (g)(1)), because it is intended to affect the structure or function of the body of man. The above labeling claims for treating ingrown hairs, razor burn, and bumps resulting from waxing, tweezing, electrolysis and laser hair removal are not covered under the OTC Drug Review. In addition, we are not aware of such a product marketed in the United States on or before the inception of that review to be included in it. Moreover, FDA has not considered such a product for inclusion in the OTC Drug Review in accordance with existing regulations (21 C.F.R. §§ 330.10(a)(12) and 330.14).

Thus, **(b)(4)** Gel is a "new drug" under section 201(p) of the Act (21 U.S.C. § 321 (p)), because it is offered for uses not covered by FDA's OTC Drug Review, and we are not aware of any data establishing this product as generally recognized safe and effective for its labeled uses. "New drugs" may not be legally marketed in the United States without an approved application under section 505(a) of the Act (21 U.S.C. § 355(a)). Since **(b)(4)** Gel is not so approved, its marketing in the United States violates sections 301(d) and 505(a) of the Act [21 U.S.C. §§ 331(d) and 355(a)].

Further, during the FDA inspection in October and November of 2010, a batch record for **(b)(4)** Gel was obtained. This batch record disclosed that **(b)(4)** Gel is manufactured with Aspirin, however, its label does not declare Aspirin as an ingredient. This omission of an ingredient on its label causes **(b)(4)** Gel to be misbranded under section 502(e)(1)(A) of the Act, 21 U.S.C. § 352(e)(1)(A).

Last, **(b)(4)** Gel is misbranded under Section 502(c) of the Act, [21 U.S.C. § 352(c)] because its label does not comply with the drug labeling format requirements under 21 C.F.R. § 201.66.

**(b)(4) Progesterone Crème**

Statements found on the label:

• "NATURAL PROGESTERONE . . . Because Change Is The Only Constant In A Woman's Life . . . **(b)(4)** . . . ."

• "SUGGESTED USE: . . Twice a day, morning and night with a heavier dose at night to help induce sleep. Apply to inner thigh & arms, face, neck, upper chest or abdomen. Rotate site with every application . . . Each pump of the dispenser contains approximately 32 MG of natural progesterone . . . ."

• "INGREDIENTS: . . . 2,625 MG. USP natural progesterone powder, aloe vera gel in distilled water, vitamin E, glyceryl stearate, Isopropyl alcohol, avocado oil, vitamin B complex factor, amino acids, emulsifying wax, fragrance . . . ."

Statements found on website **(b)(4)**

• "Natural progesterone's most important and powerful role in the woman's body is to balance or oppose estrogen.

•"Estrogen dominance leads to dangerous side effects, severe PMS and menopausal symptoms, and the promotion of cancer . . . ."

• "**PROGESTERONE** . . . Protects against breast fibrocysts . . .Natural anti-depressant . . . Prevents endometrical (sic) cancer . . . Helps prevent breast cancer. . . ."

• "Low progesterone levels in women results in estrogen dominance, PMS, early perimenopause onset, low libido, excessively heavy bleeding during a period, weight-gain, migraine like headaches, primary dysmenorrheal or cramps, increases the risk of endometrial cancer . . . ."

• "Failing to apply **(b)(4)** when a woman is estrogen dominant will simply lead to greater estrogen dominance . . . Apply **(b)(4)** as often as necessary to rid yourself of symptoms . . . ."

• "Taken orally progesterone is transported to the liver where 80 to 90% of it is removed from the body. . . Transdermal creams are the safest and effective way to get the proper physiologic dose of progesterone . . . ."

• "**(b)(4) ENCAPSULATION** . . . ."

• "Liposomes are microscopic vesicles composed of membrane-like lipid bilayers separated by an aqueous layers. By encapsulating active ingredients within multilayers of lipid spheres, liposomes penetrate 25-30 layers deep in the skin.

Increasing the concentration in the epidermis and dermis, proving a prolonged time-release action throughout the entire day . . . ."

• "**(b)(4)** is the one and only progesterone cream on the market that contains 100% pure micronzied (sic) USP progesterone powder in a topical cream using **(b)(4)** encapsulation . . . **(b)(4)** natural progesterone cream corrects low progesterone levels and counters the negative effects of estrogen dominance, relieving and preventing symptoms of PMS, perimenopause, and menopause . . . ."
Based on the above labeling claims, **(b)(4)**Progesterone Crème is a "drug" as defined by section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 321(g)(1)), because it is intended to prevent disease and to affect the structure or function of the body of man.

Furthermore, based on the labeling claims noted above, **(b)(4)** Progesterone Crème is subject to the final rule for over-the-counter (OTC) topical hormone-containing products labeled or promoted for use as drugs under 21 C.F.R. § 310.530. This rule states that any OTC drug product, other than hydrocortisone, that is labeled, represented, or promoted as a topically applied hormone-containing product for drug use is regarded as a new drug. **(b)(4)** Progesterone Crème falls within this rule because its labeling describes it as containing a hormone ingredient (progesterone) and promotes it as a topical hormone-containing product for drug use (see the website labeling claims discussed above). Moreover, OTC topical hormone creams are new drugs as defined in section 201(p) of the Act [21 U.S.C. § 201(p)] because there is no evidence that they are generally recognized by qualified scientific experts as safe and effective for their labeled uses. (See 21 CFR § 310.530.) Since **(b)(4)** Progesterone Crème is not the subject of an approved new drug application, its marketing in the United States violates sections 301(d) and 505(a) of the Act [21 U.S.C. §§ 331(d) and 355(a)].

FDA's regulations state that a drug may be considered a new drug because of the newness of its dosage form or the method or duration of administration or application suggested in its labeling [21 CFR § 310.3(h)(5)]. Based on the above claims, **(b)(4)** Progesterone Crème is administered by a transdermal delivery system using **(b)(4)** encapsulation. A transdermal delivery system for a drug is a novel dosage form. None of these delivery systems is covered under FDA's OTC Drug Review and we are not aware of any data to show that **(b)(4)** Progesterone Crème is generally recognized as safe and effective in this dosage form. Accordingly, FDA considers this transdermal drug delivery product to be a new drug under § 201(p) of the Act [21 U.S.C. § 321(p)] and under 21 CFR § 310.3(h)(5).

Regarding the claims/representations that this product provides a timed-release dosage (extended) of the active ingredient, FDA has, through rule making procedures, accorded new drug status to such drugs. 21 C.F.R. § 310.502. Included among these are timed-release dosage forms. 21 C.F.R. § 310.502(a)(14). Thus, **(b)(4)** Progesterone Crème is also a new drug within the meaning of section 201(p) of the Act, 21 U.S.C. § 201(p) pursuant to the rule governing this dosage form.

In addition to new drug charges, **(b)(4)** Progesterone Crème is misbranded under Sections 502(f)(1) and 503(b)(4) of the Act, [21 U.S.C. § 352(f)(1) and 353(b)(4)], because some of the indications for use found in the product labeling, such as preventing endometrial and breast cancer, are not amenable to self-diagnosis and treatment by the lay consumer as described in 21 CFR 201.5 and thus adequate directions cannot be written. In addition, claims that are described on the website are not included in the package labeling, therefore the package labeling violates section 502(f)(1) of the Act, [21 U.S.C. § 352(f)(1)] because it does not bear any directions covering the uses described on the website.

Further, as discussed earlier, **(b)(4)** Progesterone Crème is marketed as an OTC drug and therefore must list active and inactive ingredients separately, as required by 21 U.S.C. § 352(e)(1)(A)(ii) and (iii). The labeling provided for **(b)(4)** Progesterone Crème does not differentiate between active and inactive ingredients as required.
Therefore, this product is misbranded under section 502(e)(1)(A) of the Act [21 U.S.C. § 352(e)(1)(A).

Lastly, **(b)(4)** Progesterone Crème is further misbranded under Section 502(c) of the Act, [21 U.S.C. § 352(c)] because its label does not comply with the drug labeling format requirements under 21 C.F.R. § 201.66.

**Unapproved New Drugs Positioned as Cosmetics**

Your firm also manufactures and distributes several eyelash products including "**(b)(4)** Lashes," "**(b)(4)** Lash Conditioner," "**(b)(4)** lash,""**(b)(4)** Mascara," and "**(b)(4)** Lash Colors" with claims to affect the structure or function of the body or for use in the diagnosis, cure, mitigation, treatment, or prevention of disease. Examples of these claims include, but are not limited to, the following:

**(b)(4) Lashes**

• *(product label)* "This eyelash enhancer . . . stimulates follicle growth and strength."

• *(www.* **(b)(4)***.com)* "[N]ourish lash follicles and promote fuller, longer, healthier eyelashes."

• *(www.* **(b)(4)***.com)* "Prevents alopecia from progressing"

**(b)(4) Lash Conditioner**

• *(product label)* "Stimulates eyelash follicles which can improve the length and strength of lashes"

**(b)(4) Lash**

• *(product label)* "Stimulates hair follicles resulting in longer, fuller and more youthful eyelashes."

• *(pamphlet)* "Eyelash Growth Promoter Complex stimulates hair follicles to improve the length and thickness of eyelashes."

• *(www.* **(b)(4)***.com)* "One of the main complaints he had was his hair had thinned and his eye lashes had also thinned and fallen out. I thought I would try **(b)(4)** on him. I started applying the **(b)(4)** every night on the top and bottom eye line. Within 2 weeks his lashes were visible again. Within 4 weeks his eyelashes had come back thicker and longer."

• *(www.* **(b)(4)***.com)* "**(b)(4)** is amazing. . . My lashes grew longer and thicker!"

• *(www.* **(b)(4)***.com)* "**(b)(4)** (I cut my lashes to see how much it grows and its grown!!)"

**(b)(4) Mascara**

• (*pamphlet)* "Stimulate hair follicles for full and lengthy lashes. . .."

**(b)(4) Colors**

• *(pamphlet)* "STIMULATES FOLLICLES Eyelash Growth Promoter Complex stimulates hair follicles to improve the length and thickness of eyelashes."

Therefore, "**(b)(4)** Lashes," "**(b)(4)** Lash Conditioner,"" **(b)(4)**," "**(b)(4)** Mascara," and "**(b)(4)** Colors" are drugs under sections 201(g)(1)(B) and (C) of the Act (21 U.S.C. §§ 321(g)(l)(B) and (C)) because they are articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, or articles (other than food) intended to affect the structure or function of the body.

Moreover, "**(b)(4)** Lashes," "**(b)(4)** Conditioner,"" **(b)(4)**," "**(b)(4)** Mascara," and "**(b)(4)** Colors" are new drugs, as defined by Section 201(p) of the Act, 21 U.S.C. § 321(p), because they are not generally recognized as safe and effective under the conditions prescribed, recommended, or suggested in its labeling. Under Sections 301(d) and 505(a) of the Act (21 U.S.C. §§ 331(d) and 355(a)), a new drug may not be introduced or delivered for introduction into interstate commerce unless an FDA approved application is in effect for it.

The violations cited in this letter are not intended to be an all-inclusive statement of violations that exist at your facility. You are responsible for investigating and determining the causes of the violations identified above and for preventing their recurrence and the occurrence of other violations. It is your responsibility to assure compliance with all requirements of federal law and FDA regulations.

You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in legal action without further notice including, without limitation, seizure and injunction. Other federal agencies may take this Warning Letter into account when considering the award of contracts. Additionally, FDA may withhold approval of requests for export certificates, or approval of pending drug applications listing your facility, until the above violations are corrected. FDA may re-inspect to verify corrective actions have been completed.

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct violations. Include an explanation of each step being taken to prevent the recurrence of violations and copies of supporting documentation. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the date by which you will have completed the correction. Additionally, your response should state if you no longer manufacture or distribute products, and provide the date(s) and reason(s) you ceased production.

Please send your reply to the attention:

Darlene Almogela
Director, Compliance Branch
U.S. Food and Drug Administration
San Francisco District
1431 Harbor Bay Parkway
Alameda, CA 94502

If you have any questions regarding any issue in this letter, please contact Carl Lee, Compliance Officer at 510-337-6737, or by fax at (510) 337-6703.

Sincerely,

/S/

Barbara Cassens
District Director

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**Links on this page:**