

# Pharmco Laboratories Inc. 12/15/16



555 Winderley Place, Suite 200  
Maitland, Florida 32751

**VIA UPS NEXT DAY AIR  
w/ DELIVERY CONFIRMATION**

**WARNING LETTER  
FLA-17-03  
December 15, 2016**

Mr. Robert L. Cohn, President  
Pharmco Laboratories, Inc.  
3520 South Street  
Titusville, FL 32780-2918

Dear Mr. Cohn:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Pharmco Laboratories, Inc. at 3520 South Street, Titusville, Florida from November 9 to 30, 2015.

This warning letter summarizes significant violations of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals, 21 CFR Parts 210 and 211, and significant deviations from CGMP for active pharmaceutical ingredients (API).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drugs are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

In addition, you market over-the-counter (OTC) acne and sunscreen drug products that violate provisions of the FD&C Act. As described below, your OTC acne drug products are misbranded under section 502(c) of the FD&C Act, 21 U.S.C. 352(c). Micronized BPO 5% Scrub and Micronized BPO 5% Wash are also misbranded under section 502(f)(2) of the FD&C Act, 21 U.S.C. 352(f)(2). Additionally, your OTC sunscreen drug products are misbranded under section 502(a) and 502(f)(1) of the FD&C Act, 21 U.S.C. 352(a) and 21 U.S.C. 352(f)(1). Anti-Aging Day Protect SPF22

is also misbranded under section 502(f)(2) of the FD&C Act, 21 U.S.C. 352(f)(2). By introducing these drug products into interstate commerce, you are in violation of section 301(a) of the FD&C Act, 21 U.S.C 331(a).

We reviewed your December 18, 2015, response in detail.

During our inspection, our investigator observed specific violations and deviations including, but not limited to, the following:

### **Finished Drug Violations**

**1. Your firm failed to establish adequate written procedures for production and process control designed to assure that the drug products you manufacture have the identity, strength, quality, and purity they purport or are represented to possess. (21 CFR 211.100(a))**

You have not validated your topical over-the-counter (OTC) drug products' manufacturing processes. Manufacturing processes must be designed and controlled to assure that in-process materials and the finished products meet predetermined quality requirements and do so consistently and reliably. Furthermore, you have not validated your reverse osmosis purified water system to demonstrate that you can effectively control, maintain, sanitize, and monitor the system so it consistently produces pharmaceutical grade water that, at a minimum, meets the USP monograph for purified water.

**2. Your firm failed to establish and document the accuracy, sensitivity, specificity, and reproducibility of its test methods. (21 CFR 211.165(e))**

You have not validated the in-house assay methods that you developed for testing benzoyl peroxide and salicylic acid. You have not demonstrated that the methods your firm developed are equivalent to or better than the USP methods.

**3. Your firm failed to establish laboratory controls that include scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity. (21 CFR 211.160(b))**

With the exception of one product, you have no scientific data to demonstrate the antimicrobial effectiveness of the preservatives in your topical OTC drug products. Your owner told our investigator that you only had such data for CR98 Anti-Aging Day Protect SPF 22, and a contract laboratory performed the testing in April 2015.

**4. Your firm failed to establish and follow an adequate written testing program designed to assess the stability characteristics of drug products, and to use results of such stability testing to determine appropriate storage conditions and expiration dates. (21 CFR 211.166(a))**

The assay methods you use to evaluate the stability of your OTC drug products do not indicate stability. In addition, your quality unit did not assess the stability characteristics of your topical OTC drug products at various time intervals as specified by your stability program. For example, in 2014 and 2015 you failed to perform adequate stability testing. We note your firm acknowledges placing insufficient samples on stability.

## **API Deviations**

### **1. Failure to demonstrate that your manufacturing process can reproducibly manufacture an API meeting its predetermined quality attributes.**

You have not validated your manufacturing processes for dyclonine HCl or p-BUTAP. You failed to provide any validation documentation to demonstrate your processes are capable of operating within established parameters to assure batch uniformity, integrity, and consistent drug quality.

We also observed a lack of validation for your manufacturing processes during our May 2006 and August 2008 inspections.

### **2. Failure to establish and follow adequate written procedures for the cleaning and maintenance of equipment.**

Specifically, there is no assurance that your cleaning and sanitation methods are adequate for the non-dedicated equipment used in the manufacture of dyclonine HCl. This is particularly important because your dryer **(b)(4)** is also used in the manufacture of dietary supplements containing soy meal. Soy meal is derived from soybeans, which the FDA recognizes as a major food allergen. Dyclonine HCl is an API intended for use in throat lozenges. If contaminated with soybean, throat lozenges could potentially provoke an allergic response in sensitive individuals.

During our May 2006 and August 2008 inspections, we also observed inadequate cleaning and sanitation methods for equipment used to manufacture dyclonine HCl.

### **3. Failure to establish an impurity profile for identified and unidentified impurities.**

You failed to establish an impurity profile for dyclonine HCl that defines both known and unknown batch impurities. In addition, your batch specifications do not include appropriate controls for either impurity or degradant testing.

We also observed your failure to establish an impurity profile for dyclonine HCl during our May 2006 and August 2008 inspections.

### **4. Failure to verify the suitability of analytical methods.**

You have not verified and documented the suitability of the USP assay method for dyclonine HCl under actual conditions of use, and therefore have not demonstrated your ability to produce accurate and reliable results. For example, you do not record analytical calculations, HPLC mobile phase preparations, and sample weights.

## **Repeat Deficiencies**

Your quality unit released multiple batches of drugs for distribution, despite these deficiencies, which are the same or similar to the CGMP deficiencies documented during multiple FDA inspections of your facility since 2006. You proposed specific remediation for the deficiencies noted above, which is essentially the same as your commitments following previous FDA inspections. These repeated lapses demonstrate a failure of your executive management to exercise proper oversight and control over the manufacture of drugs.

Because of your failure to correct these repeat deficiencies, we are concerned about your firm's fundamental understanding of the regulatory expectations for your contract manufacturing facility. Firms acting as contract manufacturers for various aspects of drug manufacturing must comply with CGMP. FDA is aware that many pharmaceutical product manufacturers use independent contractors, such as production facilities, testing laboratories, packagers, and labelers. FDA regards contractors as extensions of the manufacturer.

You are responsible for the quality of drugs you produce, regardless of agreements in place with product owners. You are required to ensure that drugs are made in accordance with section 501(a)(2)(B) of the FD&C Act for safety, identity, strength, quality, and purity.

## **Misbranded Finished Drugs**

### **1. Acne Products**

According to the labeling, Micronized Benzoyl Peroxide Treatment 10%, Micronized Benzoyl Peroxide Treatment 5%, Micronized BPO 5% Scrub, and Micronized BPO 5% Wash contain the active ingredient benzoyl peroxide. The product labels state that the ingredient's purpose is to treat acne. Based upon the products' formulation and claims, Micronized Benzoyl Peroxide Treatment 10%, Micronized Benzoyl Peroxide Treatment 5%, Micronized BPO 5% Scrub, and Micronized BPO 5% Wash are drugs within the meaning of Section 201(g)(1)(B) of the FD&C Act, 21 U.S.C. 321(g)(1)(B), because they are intended for use in the diagnosis, treatment, or prevention of disease, and under section 201(g)(1)(C) of the FD&C Act, 21 U.S.C. 321(g)(1)(C), because they are intended to affect the structure or function of the body.

### *Misbranding Violations*

Absent an FDA-approved application, in order for OTC topical acne drug products to be legally marketed, they must conform to the conditions set forth in the final monograph for topical acne drug products set forth in 21 CFR Part 333, Subpart D. We have determined that Micronized Benzoyl Peroxide Treatment 10%, Micronized Benzoyl Peroxide Treatment 5%, Micronized BPO 5% Scrub, and Micronized BPO 5% Wash do not fully comply with this final monograph. Specifically, 21 CFR 330.1 describes general conditions for which OTC drug products are generally recognized as safe and effective, and not misbranded. This regulation states that the "Uses"

section of the label and labeling of the product shall contain the labeling describing the “Indications” that have been established in an applicable OTC drug monograph. 21 CFR Part 330.1(c)(2). However, the product labeling for your Micronized Benzoyl Peroxide Treatment 10%, Micronized Benzoyl Peroxide Treatment 5%, Micronized BPO 5% Scrub, and Micronized BPO 5% Wash does not include a “Uses” section that includes the products’ indications described in the applicable topical acne drug products monograph, as required under 21 CFR 333.350(b). Therefore, these products are misbranded under section 502(c) of the FD&C Act, 21 U.S.C. 352(c), because the information that is required to appear on the labeling is not prominently placed thereon with such conspicuousness and in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.

In addition, Micronized BPO 5% Scrub and Micronized BPO 5% Wash are misbranded under section 502(f)(2) of the FD&C Act, 21 U.S.C. 352(f)(2), because the products’ Drug Facts panels fail to include all of the warnings required per 21 CFR 333.350(c). For example, the products’ Drug Facts panels fail to disclose important warnings such as, “When using this product, skin irritation and dryness are more likely to occur if you use another topical acne medication at the same time. If irritation occurs, only use one topical acne medication at a time.”

## **2. Sunscreen Products**

The labels for Pharmco Skincare Labs Daily Facial Moisturizer Broad Spectrum SPF30+ and Pharmco Skincare Labs Anti-Aging Day Protect SPF22 state that they are intended to prevent sunburn. Therefore, these products are drugs within the meaning of section 201(g)(1)(B) of the FD&C Act, 21 U.S.C. 321(g)(1)(B), because they are intended for use in the diagnosis, treatment, or prevention of disease, and under section 201(g)(1)(C) of the FD&C Act, 21 U.S.C. 321(g)(1)(C), because they are intended to affect the structure or function of the body.

Over-the-Counter (OTC) sunscreen drugs, such as Daily Facial Moisturizer Broad Spectrum SPF30+ and Anti-Aging Day Protect SPF22 are subject to, among other regulations, the OTC Sunscreen Drug Products; Final Rule Labeling and Effectiveness Testing; Sunscreen Drug Products for Over-the-Counter Human Use, 21 CFR 201.327. Pending the finalization of the Sunscreen Drug Products for Over-the-Counter Human Use [Stayed Indefinitely] monograph, 21 CFR 352, the Agency does not object to the marketing of sunscreen products that meet the formulation requirements under 21 CFR 352.10 and 352.20 in addition to all applicable final rules such as 21 CFR 201.327.

### *Misbranding Violations*

Daily Facial Moisturizer Broad Spectrum SPF30+ and Anti-Aging Day Protect SPF22 are misbranded under section 502(a) of the FD&C Act, 21 U.S.C. 352(a) because the labeling is false and misleading. The “Uses” section of the Drug Facts panel states “Higher SPF gives more sunburn protection” and “Provides high protection for skin highly sensitive to sunburn.” As explained in the final rule *Labeling and Effectiveness Testing, Sunscreen Drug Products for Over-the-Counter Human Use*, 76 FR 35642 (June 17, 2011), these statements are misleading since characterizations such as

“low,” “medium,” “high,” or “highest” are no longer used or permitted by the Agency, and therefore, would confuse the consumer. The statement, “Higher SPF products give more sun protection, but are not intended to extend the time spent in the sun,” is a truthful and non-misleading statement that may appear outside of Drug Facts. 76 FR 35642 (June 17, 2011).

Daily Facial Moisturizer Broad Spectrum SPF30+ and Anti-Aging Day Protect SPF22 are also misbranded under section 502(f)(1) of the FD&C Act, 21 U.S.C. 352(f)(1) because the product labels do not include all of the applicable directions for use as required under 21 CFR 201.327(e). For example, 21 CFR 201.327(e)(1)(ii), (e)(2) and (e)(4) require the following on your Daily Facial Moisturizer Broad Spectrum SPF30+ product label:

- apply liberally 15 minutes before sun exposure
  - use a water resistant sunscreen if swimming or sweating
  - reapply at least every 2 hours
- Sun Protection Measures [in bold font]. Spending time in the sun increases your risk of skin cancer and early skin aging. To decrease this risk, regularly use a sunscreen with a Broad Spectrum SPF value of 15 or higher and other sun protection measures including:

- limit time in the sun, especially 10 a.m.-2 p.m.
  - wear long –sleeved shirts, pants, hats, and sunglasses
- 21 CFR 201.327(e)(1)(ii) and (e)(4) also require the following on your Anti-Aging Day Protect SPF22 product label:

- apply liberally 15 minutes before sun exposure
- use a water resistant sunscreen if swimming or sweating
- reapply at least every 2 hours

Anti-Aging Day Protect SPF22 is further misbranded under section 502(f)(2) of the FD&C Act, 21 U.S.C. 352(f)(2), because the product label does not include the warning, “Skin Cancer/Skin Aging Alert [in bold font]; Spending time in the sun increases your risk of skin cancer and early skin aging. This product has been shown only to help prevent sunburn, not [in bold font] skin cancer or early skin aging,” as required by 21 CFR 201.327(d)(2).

We note that both product labels contain a “Sun Alert” warning in the “Other Information” section of the Drug Facts panel. As explained in the final rule, 76 FR 35642 (June 17, 2011), the “Sun Alert” statement has been removed as an option from the “Other Information” section and revised to the “Skin Cancer/Skin Aging Alert” warning as referenced above. 21 CFR 201.327(d)(2).

## **Conclusion**

We recommend that you work with your consultant with appropriate CGMP expertise to comprehensively assess your firm’s facility, procedures, processes, laboratory controls, and quality management systems to ensure that the drug products you manufacture are consistently of appropriate identity, strength, quality, and purity.

Violations and deviations cited in this letter are not intended as an all-inclusive list. You are responsible for investigating these violations and deviations, for determining the causes, for preventing their recurrence and for preventing other violations and deviations.

If you are considering an action that is likely to lead to a disruption in the supply of drugs produced at your facility, FDA requests that you contact CDER's Drug Shortages Staff immediately, at [drugshortages@fda.hhs.gov](mailto:drugshortages@fda.hhs.gov), so that FDA can work with you on the most effective way to bring your operations into compliance with the law. Contacting the Drug Shortages Staff also allows you to meet any obligations you may have to report discontinuances or interruptions in your drug manufacture under 21 U.S.C. 356C(b) and allows FDA to consider, as soon as possible, what actions, if any, may be needed to avoid shortages and protect the health of patients who depend on your products.

Correct the violations and deviations cited in this letter promptly. Failure to promptly correct these violations and deviations may result in legal action without further notice including, without limitation, seizure and injunction. Unresolved violations and deviations in this warning letter may also prevent other Federal agencies from awarding contracts.

Until these violations and deviations are corrected, we may withhold approval of pending drug applications listing your facility. We may re-inspect to verify that you have completed your corrective actions. We may also refuse your requests for export certificates.

After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done since our inspection to correct your violations and deviations and to prevent their recurrence. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Send your reply to:

Andrea Norwood, Compliance Officer  
U.S. Food and Drug Administration  
555 Winderley Place Suite 200  
Maitland, FL 32751

Please identify your response with FEI 1048788.

If you have questions regarding any issues in this letter, please contact Ms. Norwood via email at [andrea.norwood@fda.hhs.gov](mailto:andrea.norwood@fda.hhs.gov) or by phone at (407) 475-4724.

Sincerely,  
/S/  
Susan Turcovski  
District Director  
Florida District