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San Francisco District  
1431 Harbor Bay Parkway  
Alameda, CA 94502-7070  
Telephone: 510/337-6700

February 27, 2004

## WARNING LETTER

Via FEDEX

Mr. Mark A. Horne, President  
PharmPak, Inc.  
1221 Anderson Drive, Suite B  
San Rafael, CA 94901

Dear Mr. Horne:

During an inspection of your facility located at 1221 Anderson Drive, Suite B, San Rafael, CA on August 25 through September 3, 2003, we determined that you repack various drug products, which are human drugs within the meaning of section 201(g)(1)(B) of the Federal Food, Drug and Cosmetic Act (the Act).

The inspection revealed that the drugs repacked by your firm are adulterated within the meaning of section 501(a)(2)(B) of the Act in that they are human drugs and the methods used in, or the facilities or controls used for, their processing, packing or holding do not conform with current good manufacturing practice (cGMP) regulation for drugs specified in Title 21, Part 211 of the Code of Federal Regulations (21 CFR 211) as follows:

1. Failure to conduct repacking of penicillin and repacking of non-penicillin drugs in separate facilities. [21 CFR 211.42(c) and (d)]

Penicillin products, cephalosporin products, and non-beta-lactam drug products are processed in the same facility at your firm. Although penicillin and non-penicillin beta-lactam drug products are repacked in a dedicated room, the room is not designed to prevent air migration, nor have sufficient controls been established to prevent the exposure of non-beta-lactam drug products to cross-contamination. In addition, containment procedures have not been established to assure that employees, in moving about the plant, do not carry residue from penicillin/non-penicillin beta-lactams into non-penicillin areas. This separation (penicillin room) is ineffectual given the lack of containment procedures and practices observed by the investigator. For example, employees are allowed to repack non-penicillin and non-beta-lactam drug products after re-packing penicillin and/or non-penicillin beta-lactam drug products; employees do not change work apparel between packing penicillin drug products and non-penicillin drug products; employees move throughout the facility without restriction and share common areas, such as cafeterias and restrooms without re-gowning.

Cephalosporin products, like penicillin products, are beta-lactam drugs and present a health hazard to consumers with sensitivities to these compounds. The processing of beta-lactam drugs (e.g., penicillin and cephalosporin) must be separate from non-beta-lactam drugs (e.g., aspirin). Penicillin and non-penicillin beta-lactam drugs must also be separate from each other. In this case, there is no separation of the cephalosporin and penicillin drug products repackaging processes, which occur in the same penicillin repackaging area at the firm.

The agency has taken the position that all three of those drug products should be separated from each other. In order to reach the goal of no cross contamination, a system-based approach towards separation should be taken. This entails a complete separation of every aspect of the manufacturing operation. Adequate separation should include physical barriers, air handling systems, personnel, and equipment with well established written procedures and controls. The separation should be verified by testing, auditing, and continuous monitoring if necessary.

2. Failure to separate completely the air handling systems for the packing of penicillin products and non-penicillin beta-lactam drug products from non-penicillin drug products. [21 CFR 211.42(c) and 211.46(d)]

The same air handling system is used for the repackaging of penicillin and cephalosporins in violation of 21 CFR 211.42(c) and (d). In addition, the firm could not verify through blueprints or diagrams that the air handling system for the repackaging of penicillins is separate from the air handling system used for repackaging non-penicillin drug products that is required by 21 CFR 211.46(d). Your firm has not established minimal personnel, equipment, and material movement controls, minimal containment controls, and other control systems to prevent cross-contamination. These controls must also be applied to the re-packing of non-penicillin beta-lactam drug products (cephalosporin).

3. Failure to provide assurance through drug testing that non-penicillin drug products have not been exposed to cross-contamination with penicillin. [21 CFR 211.176]

The regulations require that non-penicillin drug products be tested for the presence of penicillin where a reasonable possibility of exposure to cross contamination exists. Such products may not be marketed if detectable levels of penicillin are found. Product testing does not have to be performed if your firm can demonstrate that the possibility of exposure to traces of penicillin does not exist in your non-penicillin drug products. However, the lack of containment procedures/practices observed by the investigator lead us to believe that the possibility of contamination exists at your facility; therefore, non-penicillin products must be tested according to 21 CFR 211.176.

4. Failure to conduct stability studies or to have such studies conducted for you to justify the expiration dates that you use on solid oral dosage forms repacked into unit-for-use

containers [21 CFR 211.166(a)], or to have data demonstrating the container/closure system used by your firm is equal to or better than that used by the manufacturer, allowing use of the manufacturer's expiration date, or two years, whichever is shorter.

During the inspection of your facility, your firm did not have any stability data for solid oral dosage forms repacked in container and closure systems that are different from the original containers and closures to support the use of the manufacturers' expiration dates on the repackaged drug products. Moreover, your firm has not evaluated the original and repackaged container and closure systems for equivalency, in lieu of performing stability testing.

The above deficiencies should not be construed as an all-inclusive list of violations which may exist at your facility. It is your responsibility to ensure that all requirements of the Act and regulations promulgated there under are being met. Federal agencies are advised of the issuance of all Warning Letters about drugs and services so that they may take this information into account when considering the award of contracts. Failure to promptly correct these deviations may result in regulatory action without further notice. This includes seizure and/or injunction.

We acknowledge receipt of your response dated October 10, 2003. While your response appears to adequately address several of the observations, our review found that your response fails to adequately address other observations listed on the Form FDA 483 issued to you on September 23, 2003. Your proposed corrective actions regarding the separation of operations for penicillin products, non-penicillin beta-lactam products and non-beta lactam products are not adequate.

We believe that a meeting between our office and you and your firm's representatives would be the best means to discuss your proposed corrective actions. Please contact Russell A. Campbell, Compliance Officer, U. S. Food and Drug Administration, San Francisco District, 1431 Harbor Bay Parkway, Alameda, CA 94502, tel. 510-337-6861, within 15 days of the receipt of this letter to schedule this meeting.

Sincerely,



Charles M. Breen  
Acting District Director