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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

DEC 29 2004

Peter Gertas  
Technical Director  
D'ARCY Skincare  
1100 S.W. 12<sup>th</sup> Avenue  
Pompano Beach, Florida 33069

RE: Docket No. 2004P-0271  
Comment No. CP1

Dear Mr. Gertas:

This letter is in response to your citizen petition dated June 24, 2004, on over-the-counter (OTC) acne drug products. Your petition is filed as CP1 under Docket No. 2004P-0271 in the Division of Dockets Management.

In your petition, you request that the Food and Drug Administration (FDA) amend the monograph for OTC topical acne drug products (21 CFR Part 333) to include the combination of sulfur (10.0%) and salicylic acid (2.0%) as generally recognized as safe and effective (GRASE). Currently, under 21 CFR 333.310 (c) and (d), respectively, 0.5 to 2% salicylic acid and 3 to 10% sulfur are GRASE active ingredients for the treatment of acne, but this combination of active ingredients is not GRASE. To support your request, you assert that you have marketed Drying Lotion™ acne treatment, which contains this combination of active ingredients, for over 20 years without any reported adverse events. In addition, you submit a repeat insult patch test to demonstrate the safety of the combination. To support the effectiveness of the combination, you provide numerous customer testimonials describing customer satisfaction with your product.

FDA denies your petition because we are unaware of any clinical studies demonstrating that both sulfur and salicylic acid contribute to the overall effectiveness of the combination, as required by 21 CFR 330.10(a)(4)(iv). You do not include any effectiveness data in your petition. Furthermore, the Advisory Review Panel on OTC Antimicrobial (II) Drug Products (the Panel) reviewed two clinical studies involving products containing sulfur and salicylic acid, but neither of these studies demonstrated the contribution of each active ingredient to the overall effectiveness of the products (47 FR 12430 at 12466-7). Thus, in the advance notice of proposed rulemaking (ANPR) published in the *Federal Register* on February 23, 1982, the Panel concluded that there was inadequate effectiveness data to classify the combination of sulfur and salicylic acid as GRASE (47 FR 12430 at 12471).

In the tentative final monograph (TFM) for OTC topical acne drug products, published in the *Federal Register* on January 15, 1985, FDA discussed a comment submitted to FDA in response to the Panel's recommendation that the combination is not GRASE (50 FR 2172 at 2176). Because FDA was not aware of any effectiveness data demonstrating the contribution of sulfur and salicylic acid in the combination product, FDA agreed with the Panel's recommendation. FDA explained that studies had to be conducted in accordance with FDA's general guidelines for OTC drug combination products, which supplement the combination policy in 21 CFR 330.10(a)(4)(iv) (50 FR 2172 at 2176). As

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stated in the TFM, the guidelines discuss the following two situations that apply to combination products:

- “. . . ingredients from the same therapeutic category that have different mechanisms of action may be combined to treat the same symptoms or conditions if the combination meets the OTC combination policy in 21 CFR 330.10(a)(4)(iv) in all respects and the combination is, on a benefit-to-risk basis, equal to or better than each of the active ingredients used alone at its therapeutic dose.”
- “. . . ingredients from the same therapeutic category that have the same mechanism of action should not ordinarily be combined unless there is some advantage over the single ingredient in terms of enhancing effectiveness, safety, patient acceptance, or quality of formulation.”

FDA stated that the mechanisms of action for salicylic acid and sulfur are unknown. Therefore, either situation described above must comply with the combination policy. To view the referenced *Federal Register* documents, please go to [http://www.fda.gov/cder/otcmonographs/acne/new\\_acne.htm](http://www.fda.gov/cder/otcmonographs/acne/new_acne.htm).

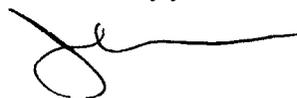
Although you submitted customer testimonials, these do not represent scientific data on which FDA can conclude that the combination of sulfur and salicylic acid is GRASE in the treatment of acne. FDA's definition for effectiveness in the procedures for classifying OTC drugs as GRASE (see 21 CFR 330.10(a)(4)(ii)) includes the following statements:

Isolated case reports, random experience, and reports lacking the details which permit scientific evaluation will not be considered. General recognition of effectiveness shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data.

Because FDA is still unaware of such studies, there is no basis to classify the combination of sulfur and salicylic acid as GRASE for the treatment of acne.

For the foregoing reasons, FDA denies your petition. If you have any questions regarding this matter, please refer to the docket and comment numbers shown at the beginning of this letter and submit all inquiries in triplicate to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, Maryland 20852.

Sincerely yours,



John M. Taylor, III  
Associate Commissioner  
for Regulatory Affairs