

# **Dermatologic and Ophthalmic Drugs Advisory Committee**

**November 4 and 5, 2002**

## **Executive Summary**

Nearly 50 million people in the United States have acne (vulgaris), and it is especially common in adolescents and young adults. The significant physical and psychological burden of acne impels the public health need for safe and effective drug products for acne. The approval of such products requires evidence for effectiveness, among other informational needs, such as an adequate safety profile. FDA recognizes the need for a guidance document that describes how the evidence for effectiveness of drug products for mild to moderate acne vulgaris may be obtained and analyzed. Such major guidelines that will have significant impacts are appropriate topics to come before the advisory committee. Accordingly, the DODAC is asked to consider the science and societal values of specific issues related to both the evidence for effectiveness of drug products for mild to moderate acne and how the efficacy outcomes may be best presented in product labeling.

Since the Division was established in 1994, drugs products for mild to moderate acne have been approved based on dual primary efficacy endpoints: statistically significant superiority on a physician's global severity scale and statistically significant superiority on changes in two lesion counts, viz., total lesion counts and either inflammatory or noninflammatory lesion counts. Success has been demonstrated in two clinical trials that have compared the drug product against an oral placebo or topical vehicle. The physicians' global severity scale has generally included 5 or 6 grades of severity, one of which is completely clear. Those subjects in the "almost clear" and "clear" categories at the predesignated time for efficacy evaluation have been considered as "successes". Thus, the preferred global severity scale did not refer to improvement or change from baseline but instead described the severity at the predesignated time.

In contrast, the three lesion counts, total, inflammatory, and noninflammatory, did refer to change from baseline lesion counts. Lesion counts were analyzed as absolute change, percent change, or as a transformed value of change. Small absolute changes in lesion counts have driven significant p - values.

Even before the establishment of the Division, the review teams in CDER requested that evidence for effectiveness be based on both the lesion counts and the physicians' global severity scale. The global severity scale was regarded as having a more direct clinical meaning, and the lesion counts were regarded as having greater objectivity and precision. Subjects with less severe acne at baseline may contribute more to success as assessed by the physicians' global severity scale, and subjects with more severe acne (but still within the mild to moderate range), who began with greater lesion counts, may contribute more to success as assessed by changes in lesion counts.

The DODAC will be asked to consider the following issues:

1. Should the current success criteria using the co-primary endpoints be retained?
2. How should lesion counts be analyzed?
3. What physicians' global severity scale should be used? At what level should it be dichotomized into success and non-success?
4. Should acne lesion types (inflammatory or noninflammatory) be medically acceptable indications?
5. Should lesion counts be assessed at multiple time-points late in the study and averaged to increase power?
6. How should the efficacy outcomes of clinical trials be portrayed in labeling to be maximally useful to clinicians and patients? What graphics and tables should be provided?