

**Food and Drug Administration
Center for Drug Evaluation and Research**

Arthritis Advisory Committee

**CDER Advisory Committee Conference Room
5630 Fishers Lane, Room 1066, Rockville, MD**

**Questions
April 19, 2001**

NDA # 21-239 ASLERA™ (prasterone, Genelabs Technologies, Inc.)

1. Please comment on the use of a SLEDAI >2 as a criterion to define a clinically meaningful population for study. Can a physician use such a disease activity index to identify patients appropriate for therapy if a study were to show a clinical benefit only for such a subgroup of patients?
2.
 - a. When assessing steroid sparing ability, would it be important to show efficacy at reduction of steroid dose prior to considering a “responder” analysis such as that proposed by the sponsor?
 - b. Please comment on the differing trends seen for the two primary endpoints of “responder” and “mean reduction in steroid dose” in study 94-01.
 - c. Please comment on the trend seen for the subpopulation of SLEDAI >2 for the “responder analysis” and the apparent absence of a trend for the mean steroid dose analysis (see page 14-15 medical officer’s review).
3. In study 95-02 the sponsor amended the original protocol and defined the “per-protocol” analysis to include only those patients who completed 60 days of treatment and had measurements recorded after that time. Such a definition may exclude information regarding drug effect (informative censoring), particularly related to toxicity/safety. **Please comment on the clinical interpretation of the results that were obtained using this per-protocol definition. (See statistician review section IV.2.i).**
4. Please discuss the study 95-02 efficacy findings, including the results of the originally specified primary analysis plan as well as the findings obtained using the amended analytic plans (using the 60 day window and SLEDAI >2 analyses and the change in “responder definition). Please discuss from statistical and clinical viewpoints the amendments to the original analytic plan.
5. Please comment on the differences between placebo and DHEA in study GL95-02 in discontinuations for any cause and discontinuation due to adverse events (see appendix table 20 in medical officer’s review). Do higher withdrawal rates in the DHEA treated group impact interpretation of efficacy signals as per the sponsor’s subpopulation analyses (see medical officer’s review pages 35,36 and 37 and statistician’s review section IV.2.iii)?
6. Please discuss the safety findings in both studies. Please include comment on proteinuria, hematuria, and complement levels.