FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
ENDOCRINOLOGIC AND METABOLIC DRUGS
ADVISORY COMMITTEE MEETING

QUESTIONS TO THE COMMITTEE
JUNE 10, 2003

Holiday Inn, Versailles Ballroom, Bethesda, Maryland

sNDA 19-640/S-033, Humatrope® (somatropin [rDNA origin] for injection),
Eli Lilly and Company. Proposed for the indication of non-growth hormone deficient short stature (NGHDSS).

1. Has the efficacy of Humatrope in NGHDSS been sufficiently characterized?
   a. Is the dose regimen proposed supported by the results of the studies presented?

   b. Please comment on the discussion by the sponsor of the importance of height augmentation in the target population and on the conclusion that the expected effects are clinically meaningful.

2. Has the safety of Humatrope in NGHDSS been sufficiently characterized?
   a. Do the results of the trials and the current knowledge of the safety profile of GH in children support a favorable balance of risk and benefit in NGHDSS?

   b. Please comment on the proposal for long-term follow up of these children as part of the Genetics and Neuroendocrinology of Short Stature International Study (GeNeSIS). What other surveillance of the safety of this intervention, if any, do you recommend?

3. Are the available data from the studies presented sufficient to guide the safe and effective use of Humatrope in patients with NGHDSS?
   a. The sponsor has proposed a restrictive height criterion for treatment eligibility. Is this proposal satisfactorily rationalized?

   b. Are additional criteria needed, such as pre-treatment height velocity, bone age, chronological age, serum IGF-1 level.

   c. The range of responses observed in the trials (and thus expected in the clinic) is broad. Additionally, a dose-response is evident. Please discuss the following:
      i. the need for information on effect of individualization of dose, age at initiation of therapy, and duration of therapy on growth response and on safety
      ii. the need for information on potentially useful predictors of response, both pre-treatment and on-treatment (e.g., early growth or biomarker effects), again to enhance safe and effective use

4. Please comment on the sponsors risk management proposals?

5. Please comment on additional concerns regarding safety and efficacy.

6. Do you recommend that the use of GH in NGHDSS as proposed by the sponsor be approved by FDA?