The following draft questions are the

probable areas of discussion

for the meeting

VIII. PRELIMINARY QUESTIONS FOR YOUR CONSIDERATION

The following questions are draft questions only. They are included only to indicate some of the potential areas of concern of the agency for comment by the advisory committee:

1) Please comment on the design of the clinical trial with respect to the assessment of the safety and efficacy of Enbrel for use in patients with early rheumatoid arthritis, including:

   A The number of patients exposed
   B The use of ACR-N area under the curve to assess signs & symptoms
   C The use of total Sharp score vs. erosion score to assess radiographic progression. Would the same considerations apply to measures of radiographic progression in a trial of rheumatoid arthritis patients with longer duration of disease?
   D The methotrexate dosing regimen chosen. How closely does this reflect current clinical practice?

2) Please comment on the time course of x-ray progression observed in this study.

3) To what extent can the results regarding x-ray progression be generalized to rheumatoid arthritis patients with more long-standing disease?

4) The differences between Enbrel and methotrexate with respect to signs and symptoms were more marked when assessed using the area under the curve than when assessed using the landmark analyses at 6 and 12 months. If approved, what information should be included in the package insert regarding the signs & symptoms data?

5) Please comment on the adequacy of the completed and planned studies to assess the safety of long-term use of Enbrel in rheumatoid arthritis.

6) Do the data submitted indicate a favorable risk: benefit ratio to support extending the use of Enbrel to rheumatoid arthritis patients with early, active RA who have not yet received treatment with a DMARD?