FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Arthritis Advisory Committee (AAC)
November 16, 2010

Draft Questions to the Committee

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1. Discuss the efficacy data of belimumab considering the following:
   - **a.** Efficacy driven by contribution of musculoskeletal and mucocutaneous organ systems results
   - **b.** Lack of demonstrated efficacy in organ systems associated with poor outcome and mortality in systemic lupus erythematosus
   - **c.** Lack of demonstrated efficacy in patients of African American or African heritage
   - **d.** Numerically smaller efficacy results for patients from US and Canada compared to some other regions

2. Discuss the overall safety profile of belimumab considering the following:
   - **a.** Safety signals of infection, malignancy, suicidality, and mortality
   - **b.** Potential risk of using belimumab when combined with other immunosuppressive agents, which may be needed to treat more serious manifestations of systemic lupus erythematosus that are associated with poor outcome and mortality

3. Discuss the suicidality data and provide recommendations for further evaluation, if necessary.

4. Considering the totality of the data, has belimumab at a dose of 10 mg/kg at 2-week intervals for the first 3 doses and at 4-week intervals thereafter demonstrated substantial evidence of <u>efficacy</u> for reducing disease activity in adult patients with active, autoantibody-positive, systemic lupus erythematosus who are receiving standard therapy? **(Voting Question)**

   a. If not, what further efficacy data should be obtained?

5. Is the <u>safety</u> profile of belimumab sufficient for approval for reducing disease activity in adult patients with active, autoantibody-positive, systemic lupus erythematosus who are receiving standard therapy? **(Voting Question)**

   a. If not, what further safety data should be obtained?

6. Do the efficacy and safety data provide substantial evidence to support <u>approval</u> of belimumab at a dose of 10 mg/kg at 2-week intervals for the first 3 doses and at 4-week intervals thereafter for reducing disease activity in adult patients with active, autoantibody-positive, systemic lupus erythematosus who are receiving standard therapy? **(Voting Question)**