Food and Drug Administration
Center for Drug Evaluation and Research

SUMMARY MINUTES
ARTHRITIS ADVISORY COMMITTEE

February 23, 1999
Holiday Inn Silver Spring
8777 Georgia Avenue, Silver Spring, MD

Members Present
Steven B. Abramson, M.D., Chair
Daniel J. Lovell, M.D., M.P.H.
E. Nigel Harris, M.D.
Leona Malone, MSW
Frank Pucino, Jr., Pharm.D.

Consultants
Matthew Liang, M.D., M.P.H.
Kevin R. McConnell, M.D.
Felix Fernandez-Madrid, M.D., Ph.D.
Harvinder Luthra, M.D.
Kenneth Brandt, M.D.
Leigh Callahan, Ph.D.
David Felson, M.D., M.P.H.
Ildy Katona, M.D.
Larry W. Moreland, M.D.
Barbara White, M.D.
Michele Petri, M.D., M.P.H.

Members Absent
David Yocum, M.D.

Executive Secretary
Kathleen R. Reedy

FDA Participants
Robert DeLap, M.D.
John Hyde, M.D.
William Schwieterman, M.D.
Jeffery N. Siegel, M.D.

Guest Experts
Earl Silverman, M.D.
Yvonne Sherrer, M.D.
David Isenberg, M.D.
Dafna Gladman, M.D.
Vibeke Strand, M.D.
Edmund Lewis, M.D.
Dimitrios Boumpas, M.D.
Ellen Ginzler, M.D.
James Balow, M.D.
Paul Fortin, M.D.
James Donadio, M.D.
Ken Kalunian, M.D.
Sterling West, M.D.
Jack Klippel, M.D.

These summary minutes for the February 23, 1999 meeting of the Arthritis Advisory Committee were approved on 6/4/99.

I certify that I attended the February 23, 1999 meeting of the Arthritis Advisory Committee and that these minutes accurately reflect what transpired.

Kathleen R. Reedy,
Executive Secretary

Steven B. Abramson, M.D.
Chairperson

The Arthritis Advisory Committee met at the Holiday Inn Silver Spring, 8777 Georgia Avenue, Silver Spring, MD at 8:00 am on February 23, 1999 to discuss issues to be considered in Design and assessment of clinical trials of drugs, biologics and devices that are being developed for treatment of systemic lupus erythematosus. The Committee and the guest speakers and expert panelists had been sent an outline of discussion topics. Approximately two hundred people attended the meeting.

The meeting was called to order by Steven Abramson, M.D., Acting Chair, of the Arthritis Advisory Committee and after introductions of the participants, the meeting statement was read by Kathleen Reedy, Executive Secretary of the Arthritis Advisory Committee. Introductory comments were given by Robert DeLap, M.D., Director of Office of Drug Evaluation V, Center for Drug Evaluation and Research, followed by William Schwieterman, M.D., Branch Chief, Division of Clinical Trial Design and Analysis, Center for Biologics Evaluation and Research.

Jeffrey N. Siegel, M.D., Medical Officer, Division of Clinical Trial Design and Analysis, CBER introduced the agenda for the day. The morning session was dedicated to presentations and discussion pertaining to Efficacy Assessment for Clinical Trials in SLE. The speakers and topics were:

Disease activity:
Health status: David Isenberg, M.D., FRCPC, University College London

Definition of flare:
Responder index: Michelle A. Petri, M.D., M.P.H., Johns Hopkins University

Damage:
Drug toxicity: Dafna Gladman, M.D., FRCPC, University of Toronto

OMERACT: Vibeke Strand, M.D., Stanford University

The Open Public Hearing included two speakers.
Marc Gurwith, M.D., J.D., Vice President, Drug Development and Chief Medical Officer of Genelabs Technologies, Inc. spoke of DHEA for SLE.
Jill Buyon, M.D., Professor of Medicine, NYU Medical Center, Hospital for Joint Diseases spoke of Guidelines for Usage of Activity, Flare, Responder and Damage Indices by Participating Investigators in Multi-Center Trials.

A panel of discussants, Paul Fortin, M.D., M.P.H., McGill University; Ellen Ginzler, M.D., M.P.H. , State University of New York at Brooklyn; Ken Kalunian, M.D., University of California Los Angeles; and Jack Klippel, M.D., National Institute of Arthritis and Musculoskeletal and Skin Disease addressed and discussed the following questions with participation with the speakers and the Advisory Committee members and consultants.

1. What claims would represent a clinically important benefit in SLE?
   Discuss the following as potential claims for novel therapeutic agents:
   a) Decreases disease activity;
   b) Decreases damage;
   c) Improves health related quality of life;
   d) Effective for organ specific disease (e.g. renal);
   e) Effective for fibromyalgia/ fatigue
2. Suggest acceptable endpoints for clinical trials.
   Which of the following represent potential endpoints:
   responder indices;
   flares;
   disease activity;
   damage;
   steroid-sparing effects;
   health status/QOL;
   drug toxicity.
   other
3. What is the appropriate duration of clinical trials in SLE?
4. What parameters should be measured in all clinical trials in SLE?
5. Discuss the importance of serologic and other laboratory markers in outcome assessment for SLE clinical trials.

Discussion ranged over the spectrum of responses to these topics with consensus not necessarily achieved. A verbatim transcript is available for monitoring the sense of the discussion.

The afternoon topic was Clinical Trials in Lupus Nephritis and other Organ-Specific Manifestations of SLE. The topics and speakers were:

Surrogate Markers: Susan Ellenberg, Ph.D., Division of Biostatistics and Epidemiology, CBER

Lupus nephritis: Dimitrios Boumpas, M.D., National Institute of Arthritis and MusculoSkeletal and Skin Disease, National Institutes of Health

Lupus nephritis: Edmund J. Lewis, MD, Rush-Presbyterian-St. Luke's Medical Center

A panel of discussants, James Balow, M.D., National Institute of Diabetes and Digestive and Kidney Disease; James Donadio, M.D., Mayo Clinic; and Sterling West, M.D., University of Colorado addressed and discussed the following questions with participation with the speakers and the Advisory Committee members and consultants.

1. What indicators of lupus nephritis can serve as surrogate markers of a clinical benefit?
   Discuss the following as potential surrogate markers in trials of lupus nephritis:
   doubling of serum creatinine;
   normalization of elevated serum creatinine;
   decrease in the frequency of renal flares;
   decrease in proteinuria.
2. Could a decrease in the use of toxic agents such as high doses of corticosteroids and cyclophosphamide serve as a valid outcome measure in a trial of lupus nephritis?
3. What would be an acceptable control regimen in a trial of renal lupus?
4. Discuss the design of clinical trials for other specific manifestations of lupus including:
   CNS lupus;
   anti-phospholipid antibody syndrome;
   cutaneous lupus;
   fatigue/arthralgias/malaise

The scope of the discussion extended over the spectrum of responses to these topics with consensus not necessarily achieved. A verbatim transcript is available for extracting the essence of the discussion.

The Chair, Steven Abramson, M.D., summarized the day's discussion in closing remarks and the meeting was adjourned at 4:45 pm.