

Workshop on Protein Aggregation

**September 26-27, 2006
Great Divide Lodge, Breckenridge, Colorado**

Presented by

University of Colorado Center for Pharmaceutical Biotechnology

AAPS Focus Group on Protein Aggregation and Immunogenicity

U.S. Food and Drug Administration

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Organizing Committee

John Carpenter, Univ. of Colorado

Mary Cromwell, Genentech

Allen Minton, NIH

Anthony Mire-Sluis, Amgen

John Philo, Alliance Protein Labs

Valerie Quarmby, Genentech

Theodore Randolph, Univ. of Colorado

Amy Rosenberg, FDA

Steve Shire, Genentech

Phil Wyatt, Wyatt Technology Corp.

Rationale for Workshop

Aggregation is a common phenomenon that occurs during bioprocessing and storage of proteins. The understanding of the qualitative and quantitative aspects of aggregation of therapeutic protein products in engendering various types of immune responses to product is critical. Such immune responses can be a major stumbling block to product development and have plagued even licensed protein therapeutics. To understand the impact of protein aggregation on immunogenicity, the specific questions to address must be defined, including the appropriate methods for measuring, quantifying, and characterizing aggregates; the models to meaningfully study immunogenicity; and the methods for predicting immunogenicity. In addition, it is critical to gain insight into the formation and removal of aggregates during bioprocessing and into the causes and inhibition of aggregates in formulations of therapeutic proteins.

Workshop Agenda

This Workshop will focus on each of these key issues through the presentation of plenary lectures in four sessions:

- Immunological Consequences of Protein Aggregates
- Analytical Methods for Aggregates
- Process Engineering: Formation and Removal of Aggregates
- Formulation: Causes and Inhibition of Aggregation

After each session, there will be a panel discussion. At the end of each day there will be breakout discussions for each topic covered that day. These discussions will provide an opportunity for all participants to contribute to an effort to discern what is known in each topic area, what critical questions remain unanswered and how to go about getting the needed answers.

There will be a poster session and reception on the first evening for contributed papers. This session will allow for further discussions of the critical issues.

The Workshop will conclude with a summary of outcomes of the four breakout sessions and a discussion of these outcomes. It is planned that the overall summary for the Workshop will be published as a white paper in an appropriate journal.

Abstract Submission for Poster Session

Abstracts should be prepared on a single page with one-inch margins. Abstracts will be reproduced as received for in the proceedings booklet of the Workshop. Abstracts should be submitted by August 15 to:

Dr. John F. Carpenter
School of Pharmacy, Box C238
University of Colorado Health Sciences Center
4200 E. Ninth Ave.
Denver, CO 80262

Registration for Workshop

Register for the Workshop online at <http://aggregationworkshop.webregpro.com>

Early Registration Fee (before August 1):	\$600
Government rate (before August 1):	\$400
Late Registration Fee (after August 1):	\$800
Government rate (after August 1):	\$600

The fee includes workshop registration, proceedings booklet, refreshments at the three receptions, and continental breakfast and lunch each day of the Workshop.

Workshop attendance will be limited to the first 200 registrants.

Cancellation: Only requests for cancellation received prior to September 1, 2006 will receive a refund, minus a \$100 processing fee. If cancellation is not received by September 1, 2006, the registration fee will be forfeited.

Hotel Room Reservation

Hotel rooms at the Great Divide Lodge can be reserved by calling the hotel directly:

Toll Free Reservations: (888) 906-5698
Local/International Reservations: (970) 547-5725

Please indicate that you will be attending the **Aggregation Workshop** to receive a discounted rate.

A block of rooms for the Workshop with a special discounted rate of \$104/night will be held until August 26, 2006. After that date, room availability cannot be assured.

Ground Transportation

Shuttle service from Denver International Airport to the Great Divide Lodge can be reserved through Colorado Mountain Express:

<http://www.ridecme.com/>
Toll Free: 800-525-6363.
Local/International: 970-926-9800

For further information contact:

John Carpenter
303-315-6075
john.carpenter@uchsc.edu

Workshop Schedule

September 25

7:00-9:00 pm **Opening Reception**

September 26

7:00 am **Continental Breakfast**

7:45 **Welcome and Overview**
Mary Cromwell, Genentech

Immunological Consequences of Protein Aggregates

Chairs: Amy Rosenberg, FDA and Anthony Mire-Sluis, Amgen

8:00 **Suzanne Hermeling**, Octopus Development BV
Aggregation Increases Immunogenicity of Therapeutic Proteins

8:35 **Martin Bachmann**, Cytos Biotechnology, Switzerland
Proposed Mechanisms for Aggregate Induced Immunogenicity

9:10 **TBA**
Clinical Consequences of Protein Aggregates: Breaking Tolerance, Hypersensitivity, etc.

9:45 **Amy Rosenberg**, FDA
The Need to Gain Better Understanding of Aggregates and the Immune System – Experimental Plans and Formation of Consortium

10:20 **Panel Discussion**

10:35 **Coffee Break**

Analytical Methods for Aggregates

Chairs: John Philo, Alliance Protein Labs and Phil Wyatt, Wyatt Technology Corp.

11:00 **Chulani Karuntilake**, Chiron Inc.
Oligomeric Structure Analytical Technologies: SEC-MALS, FFF-MALS, and Native-PAGE

11:35 **Steven Berkowitz**, Biogen Idec

Assessing the Aggregation of Biopharmaceuticals: Capabilities and Limitations of Analytical Ultracentrifugation in Comparison to Other Techniques

12:10 pm **Lunch**

1:30 **Natalia Markova**, Biovitrum
Screening for Protein Aggregates with a DLS Plate Reader: A General Tool for Evaluation and Optimization of Protein Homogeneity

2:05 **Tudor Arvinte**, University of Geneva
Characterization of Protein Aggregation Using Field Flow Fractionation, Light Scattering, Optical Spectroscopy and Electron Microscopy Methods: Case Studies

2:40 **Hanns-Christian Mahler**, Hoffmann-La Roche
Complimentary Methods for Particulate Testing of Biopharmaceuticals

3:15 **Panel Discussion**

3:30 **Coffee Break**

3:45 **Breakout sessions**

6:00 **Reception and Poster Session**

September 27

7:00 am **Continental Breakfast**

Process Engineering: Formation and Removal of Aggregates

Chairs: Mary Cromwell, Genentech and Ted Randolph, Univ. of Colorado

8:00 **Alois Jungbauer**, University of Natural Resources and Applied Life Sciences, Vienna
Aggregation during Chromatographic Separations

8:35 **Chris Allen**, Medimmune
Aggregation of Monoclonal Antibodies

9:10 **Zhanfeng Cui**, Oxford University
Removal of Protein Aggregates by Ultrafiltration

9:45 **Ted Randolph**, University of Colorado
High Pressure Processing for Aggregate Removal

10:20 **Panel Discussion**

10:35 **Coffee Break**

Formulation: Causes and Inhibition of Aggregation

Chairs: Steve Shire, Genentech and John Carpenter, Univ. of Colorado

11:00 **John Carpenter**, University of Colorado

Protein Aggregation and Particle Formation Induced by Foreign Nanoparticles

11:35 **Shouvik Roy**, Amgen

Light Induced Aggregation of Type I Soluble Tumor Necrosis Factor Receptor

12:10 pm **Lunch**

1:30 **Frank Ferrone**, Drexel University

Physical Principles in Protein Assembly: Lessons from Sickle Hemoglobin Polymerization

2:05 **Mike Pikal**, University of Connecticut

The Role of Molecular Mobility in Optimization of Protein Stability in the Solid State: Fast Dynamics vs. Global Relaxation Dynamics

2:40 **Panel Discussion**

2:55 **Coffee Break**

3:30 **Breakout sessions**

5:30 **Final discussion of outcomes from four breakout sessions**

6:30 **Closing Reception**