MARRIOTT CRYSTAL GATEWAY • 1700 JEFFERSON DAVIS HIGHWAY • ARLINGTON, VA, USA

Co-sponsored by DIA ® & FDA

ARLINGTON, VA **FEBRUARY 14-16, 2005**

FDA/DIA Scientific Workshop on
Follow-on Protein Pharmaceuticals

COMMITTEE CHAIRPERSONS

CHI WAN CHEN, PHD, Deputy Director, Office of New Drug Chemistry, CDER/FDA

CHRISTOPHER JONECKIS, PHD, Senior Advisor to the Director, CBER/FDA

KEITH WEBBER, PHD, Acting Director, Office of Biotechnology Products, CDER/FDA

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JANICE BROWN, MS, Chemistry Reviewer, Office of New Drug Chemistry, CDER/FDA

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SARA RADCLIFFE, MPH, Managing Director, Scientific and Regulatory Affairs, Biotechnology Industry Organization

MARIE A. VODICKA, PHD, Senior Director, Biologics & Biotechnology, Pharmaceutical Research and Manufacturers of America

WORKSHOP SUMMARY

This workshop will examine the scientific basis (including chemistry, manufacturing, and controls (CMC), pharmacology-toxicology, clinical pharmacology, and clinical aspects) for the assessment of the quality, safety, and efficacy of follow-on protein products.

The focus will be on recombinant and natural protein products that are directly administered to humans. Synthetic peptides, *in vitro* diagnostics, and devices will not be covered.

Plenary sessions will present scientific and technical issues and provide the framework for discussions in the breakout sessions. Breakout sessions will be focused on identifying risks and recommending the appropriate scientific information needed for evaluating follow-on protein products.

FDA's findings from this workshop will contribute to the scientific foundation for the development of regulatory guidance.

GOALS & OBJECTIVES

At the conclusion of this meeting, participants should be able to:

- Evaluate relevant terminology, e.g., interchangeability/noninterchangeability, sameness, similarity, and comparability, as it applies to protein products
- Describe the types of data needed to ensure the safety and efficacy of follow-on protein products, including:
  - chemistry, manufacturing, and controls information
  - preclinical and clinical studies, and conditions under which such studies are needed

TARGET AUDIENCE

This program is designed for:

- professionals working in pharmacology/toxicology, clinical pharmacology, and safety
- individuals conducting clinical research
- pharmaceutical manufacturers
- regulatory authorities
- FDA regulators

Interested members of the public not specified above are also encouraged to attend.

DIA, 800 Enterprise Road, Suite 200, Horsham, PA 19044-3595, USA tel: +1 215 442 6100 fax: +1 215 442 6199 email: dia@diahome.org

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The Drug Information Association (DIA) has been reviewed and approved as an Authorized Provider by the International Association for Continuing Education and Training (IACET), 1620 I Street, NW, Suite 615, Washington, DC 20006. The DIA has awarded up to 1.7 continuing education units (CEUs) to participants who successfully complete this program.

If you would like to receive a statement of credit, you must attend the program and return the credit request and evaluation forms to the DIA. Statements of credit will be issued within 30 days of receipt of these forms.

Disclosure Policy: It is Drug Information Association policy that all faculty participating in continuing education activities must disclose to the program audience (1) any real or apparent conflict(s) of interest related to the content of their presentation and (2) discussions of unlabeled or unapproved uses of drugs or medical devices. Faculty disclosure will be included in the course materials.

Learning Objectives: At the conclusion of this meeting, participants should be able to:

- Evaluate relevant terminology, e.g., interchangeability/noninterchangeability, sameness, similarity, and comparability, as it applies to protein products
- Describe the types of data needed to ensure the safety and efficacy of follow-on protein products, including: chemistry, manufacturing, and controls information; preclinical and clinical studies, and conditions under which such studies are needed

This is a *preliminary* program. Speakers and agenda are subject to change without notice.

Updates will be available on DIA's website. Please monitor www.diahome.org for the most current information.

SUNDAY • FEBRUARY 13

6:00-8:00 PM REGISTRATION

MONDAY • FEBRUARY 14

7:00-8:00 AM REGISTRATION AND CONTINENTAL BREAKFAST

8:00-8:10 AM WELCOME AND OPENING REMARKS

Keith Webber, PhD
Acting Director, Office of Biotechnology Products
CDER/FDA

8:10-8:30 AM KEYNOTE ADDRESS

Charles Cooney, PhD
Professor of Chemical and Biochemical Engineering
Co-Director, Sloan Program on the Pharmaceutical Industry
Massachusetts Institute of Technology
Acting Chair, CDER Advisory Committee for Pharmaceutical Science

Statements made by speakers are their own opinion and not necessarily that of the organization they represent, or that of the Drug Information Association. Speakers and agenda are subject to change without notice. Audio/visual taping of any DIA workshop is prohibited without prior written consent from DIA.

8:30-9:00 AM BACKGROUND FOR WORKSHOP: TERMINOLOGY AND CONCEPTS

Steve Kozlowski, MD
Acting Director, Division of Monoclonal Antibodies, Office of Biotechnology Products, CDER/FDA

9:00-10:30 AM **SESSION 1**

Approaches to Product Quality Issues: Physical, Chemical and Biological Characterization

CHAIRPERSON

Blair Fraser, PhD
Deputy Division Director, Office of New Drug Chemistry, CDER/FDA

SPEAKERS

William Hancock, PhD
Bradstreet Chair, Barnett Institute of Chemical and Biological Analysis

Ram Sasisekharan, PhD
Professor of Biological Engineering, Massachusetts Institute of Technology

Joerg Windisch, PhD
Global Head, Technical Development, Novartis

10:30-11:00 AM **REFRESHMENT BREAK**

11:00 AM-12:30 PM **SESSION 2**

Approaches to Pharmacokinetics/ Pharmacodynamics (PK/PD) Studies

CHAIRPERSON

Dena Hixon, MD
Associate Director for Medical Affairs, Office of Generic Drugs, CDER/FDA

SPEAKERS

Hae-Young Ahn, PhD
Pharmacologist, CDER/FDA

Raja B. Velagapudi, PhD
Director, Scientific Affairs, Barr Laboratories, Inc.

Mark Rogge, PhD
Vice President of Development, ZymoGenetics

12:30-1:30 PM **LUNCHEON**

1:30 -3:00 PM **SESSION 3**

BREAKOUT SESSIONS

The four concurrent breakout sessions listed below will be offered from 1:30-3:00 pm and again from 3:15-4:45 pm. This will enable participants to choose their preferred session topic in each time block.

■ BREAKOUT SESSION A

Physical Chemical Characterization and Impurities

- Which product attributes should be evaluated?
- What are the capabilities and limitations of the available analytical tools to evaluate those identified product attributes?
- What are the appropriate standard(s) for the comparison of those identified product attributes.

MODERATORS

Barry Cherney, PhD
Deputy Director, Division of Therapeutic Proteins, Office of Biotechnology Products, CDER/FDA

Stephen Moore, PhD
Chemistry Team Leader, Office of New Drug Chemistry, CDER/FDA

Andrew Chang, PhD
Acting Deputy Director, Division of Hematology, CBER/FDA

Charles Diliberti, PhD
Vice President, Scientific Affairs, Barr Laboratories, Inc.

Reed Harris, PhD
Director, Late Stages Analytical Development, Genentech, Inc.

■ BREAKOUT SESSION B

Biological Characterization and Impurities

- How can the clinical relevance of functional biological characterization studies (e.g., animal, cellular, binding assay) be established?
  - Under what circumstances can biological characterization studies be predictive of efficacy in humans and can this be used to justify limited clinical efficacy studies?
- What are the appropriate standard(s) for the comparison of biological activities?
- Based on biological characteristics, how can product-related impurities be distinguished from product-related substances and from the desired product? If a products-related substance can be identified/distinguished, can the acceptance criteria be wider for the follow-on product than that observed for the reference product.

MODERATORS

Janice Brown, MS
Chemistry Reviewer, Office of New Drug Chemistry, CDER/FDA

Steve Kozlowski, MD
Acting Director, Division of Monoclonal Antibodies, Office of Biotechnology Products, CDER/FDA

Christopher Joneckis, PhD
Senior Advisor to the Director, CBER/FDA

Robin Thorpe, PhD
Head, Division of Immunology and Endocrinology, NIBSC

Inger Mollerup, PhD
Vice President, Novo Nordisk A/S, Denmark

■ BREAKOUT SESSION C

Pharmacology-Toxicology Studies

- In which situation would animal studies be needed and why?

MODERATORS

Jeri El-Hage, PhD
Supervisory Pharmacologist, Division of Metabolic and Endocrine Drugs, CDER/FDA

Mercedes Serabian, MS
Toxicologist, CBER/FDA

Joy Cavagnaro, PhD
President, Access BIO

James D. Green, PhD, DABT
Senior Vice President of Preclinical and Clinical Development Sciences, Biogen Idec, Inc.

Andrea Weir, PhD
Pharmacologist, CDER/FDA

■ BREAKOUT SESSION D

Clinical Pharmacology Studies

- What information does a PK study provide?
- What additional information of value would a PD study provide?
- What factors affect study design and establishment of acceptable limits for PK/PD comparison?

MODERATORS

Dena Hixon, MD
Associate Director for Medical Affairs, Office of Generic Drugs, CDER/FDA

Hae-Young Ahn, PhD
Pharmacologist, CDER/FDA

Hong Zhao, PhD
Pharmacology Reviewer, CDER/FDA

Dave Parkinson, MD
Vice President, Global Development Head, Amgen Inc.

William Schwieterman, MD
Founder, Tekgenics, Inc.

3:00-3:30 PM **REFRESHMENT BREAK**

3:30-5:00 PM SESSION 4

BREAKOUT SESSIONS

The four concurrent breakout sessions listed previously will be repeated in this time block.

5:00-6:00 PM RECEPTION

TUESDAY • FEBRUARY 15

7:00-8:00 AM REGISTRATION AND CONTINENTAL BREAKFAST

8:00-9:30 AM OPENING REMARKS: REPORTS OF DAY 1 BREAKOUT SESSIONS A, B AND C

Christopher Joneckis, PhD
Senior Advisor to the Director, CBER/FDA

9:30-10:45 AM SESSION 5

APPROACHES TO IMMUNOGENICITY STUDIES

CHAIRPERSON

Amy Rosenberg, MD
Director, Division of Therapeutic Proteins, Office of Biotechnology Products, CDER/FDA

SPEAKERS

Robin Thorpe, PhD
Head, Division of Immunology and Endocrinology, NIBSC

Huub Schellekens
UTRECHT UNIVERSITY, NETHERLANDS

10:45-11:15 AM REFRESHMENT BREAK

11:15-12:30 PM SESSION 6

APPROACHES TO CLINICAL SAFETY AND EFFICACY STUDIES

CHAIRPERSON

David Orloff, MD
Director, Division of Metabolic and Endocrine Drug Products, CDER/FDA

SPEAKERS

Jay P. Siegel, MD
President, Research & Development, CENTOCOR, INC.

Carole Ben-Maimon, MD
President and COO, DURAMED RESEARCH INC.

12:30-1:30 PM LUNCHEON

1:30-3:00 PM SESSION 7

BREAKOUT SESSIONS

The two concurrent breakout sessions listed below will be offered from 1:30-3:00 pm and again from 3:30-5:00 pm. This will enable participants to choose their preferred session topic in each time block.

BREAKOUT SESSION E

IMMUNOGENICITY STUDIES

- Can we define specific circumstances in which animal studies would be useful for predicting immunogenicity (including hypersensitivity) of protein therapeutics in humans? Are immunogenicity studies in animals useful in determining whether there are meaningful differences between two similar products?
- Follow on products must be similar to innovator products in terms of product safety, including immunogenicity. What clinical immunogenicity studies should be performed pre-approval and what studies should be done post-approval to ensure the similarity of the follow on to innovator in terms of immunogenicity?
  - What trial designs are appropriate for assessing immunogenicity of the follow on and how does risk, as defined below, factor into such designs?
    - For high risk products (i.e., life saving products, or products with endogenous counterparts that mediate unique biological functions?
    - For lower risk products (i.e., ameliorative products or products with endogenous counterparts that are biologically redundant)?
    - For products with a high probability of inducing hypersensitivity responses (i.e., foreign proteins)?

MODERATORS

Amy Rosenberg, MD
Director, Division of Therapeutic Proteins, Office of Biotechnology Products, CDER/FDA

Alexandra Worobec, MD
Medical Officer, CDER/FDA

Jay Lozier, MD, PhD
Senior Staff Fellow, CBER/FDA

Kathryn Stein, PhD
Vice President, Product Development and Regulatory Affairs, MACROGENICS

Theresa L. Gerrard, PhD
President, TLG CONSULTING, INC.

BREAKOUT SESSION F

CLINICAL SAFETY AND EFFICACY STUDIES

- In which situation would safety and/or clinical studies be needed and why?
- What factors should be considered in designing appropriate/relevant clinical studies?
- What concerns can be addressed via postmarketing surveillance as part of risk management?

MODERATORS

David Orloff, MD
Director, Division of Metabolic and Endocrine Drug Products, CDER/FDA

Marc Walton, MD
Director, Division of Therapeutic Internal Medicine Products, CBER/FDA

■ BREAKOUT SESSION F *continued*

Dorothy Scott, MD
Branch Chief, Laboratory of Plasma Derivatives, Division of Hematology, CBER/FDA

Dawn Viveash
Vice President, Regulatory Affairs, AMGEN INC.

Yafit Stark, PhD
Senior Director, Global Clinical Research, TEVA PHARMACEUTICAL INDUSTRIES LTD.

3:00-3:30 PM REFRESHMENT BREAK

3:30-5:00 PM SESSION 8
BREAKOUT SESSIONS

The two concurrent breakout sessions listed previously will be repeated in this time block.

WEDNESDAY • FEBRUARY 16

7:30-8:30 AM REGISTRATION AND CONTINENTAL BREAKFAST

8:30-10:00 AM OPENING REMARKS: REPORTS OF DAY 2 BREAKOUT SESSIONS D, E AND F

Chi-Wan Chen, PhD
Deputy Director, Office of New Drug Chemistry, CDER/FDA

10:00-10:30 AM REFRESHMENT BREAK

10:30-10:45 AM BIO/PHRMA PERSPECTIVE

10:45-11:00 AM GPHA PERSPECTIVE

11:00-11:30 AM SUMMATION AND NEXT STEPS

Keith Webber, PhD
Acting Director, Office of Biotechnology Products, CDER/FDA

11:30 AM-12:00 PM CLOSING REMARKS

Ajaz Hussain, PhD
Deputy Director Office of Pharmaceutical Science, CDER/FDA

12:00 PM WORKSHOP ADJOURNED