Objectives of the CRA Workshop

• Despite the lessons learned from TGN1412 and other mAbs, the risk of cytokine release syndrome triggered by new biologic entities remains a significant safety concern in the clinic.

• The objective of this workshop is to bring together academic, industry and regulatory agency scientists to share information and gain a common understanding on current technologies, practices and scientific challenges and discuss critical issues.
CRA Workshop Organizing Committee

Raegan O’Lone (HESI)
Megan Harries (HESI)

Raffaella Faggioni (MedImmune)
Deborah Finco-Kent (Pfizer)
Madeline Fort (Amgen)
Christine Grimaldi (Boehringer Ingelheim)
Rodney Prell (Genentech)
Amy Schneider (MedImmune)
Mindi Walker (Janssen R&D)
Ronald Wange (FDA)
About HESI

- ILSI Health and Environmental Sciences Institute (HESI) (www.hesiglobal.org)
  - Non-profit scientific organization since 1989
  - Washington DC based with global reach
  - Collaborative approaches to drug and chemical safety, risk assessment, and innovation

- **Vision:** Creating science-based solutions for a sustainable, healthier world.

- **Mission:** Engage scientists from academia, government and industry to identify and resolve global health and environmental issues.
How HESI Operates

- 16 scientific committees
- 11 staff manage projects
- 30 scientists on Board of Trustees
  - Half from public sector, half from sponsor companies
- Tripartite scientific engagement (academic, government, and industry) at the core of all HESI scientific committees and governance
- HESI and committees are financially sustained by participating companies and in-kind contributions
HESI in 2013

90 Universities & Research Centers

From 14 Countries

33 Government Agencies

From 12 Countries

54 Corporate Sponsors

Across multiple sectors

16 Scientific Committees

77 Distinct Projects

IMPACT via Quality Science
Scientific Committees 2013
What HESI Committees Do

• Typical activities of HESI’s scientific committees:
  – Collaborative research programs
  – Workshops, conferences, and expert panels
  – Literature reviews and white papers
  – Development and analysis of databases
  – Development of accepted test guidelines
  – Dissemination of information through journals and other publications, including the HESI website.
The Immunotoxicology Technical Committee (ITC)

Mission:

- To identify and address scientific issues related to the development and application of immunotoxicology to public health and human health risk assessment

- To promote the understanding and appropriate use of immunotoxicologic data to protect human health

- To contribute substantively to the scientific decision-making processes relative to the development of guidelines and regulations for immunotoxicologic testing at the local, national, and international levels
Committee Leadership & Participants

**Leadership:**

Co-Chairs:
Dr. Ellen Evans, Pfizer Inc.
Dr. Hervé Lebrec, Amgen Inc.
Dr. Marc Pallardy, University of Paris-Sud

Scientific Advisors:
Dr. Hans Merk, University of Aachen
Dr. Jacques Descotes, Centre Antipoison-Centre de Pharmacovigilance

Staff:
Dr. Connie Chen
Dr. Raegan O’Lone
Ms. Megan Harries

**Participant affiliations:**

- AbbVie
- Amgen, Inc.
- Astra-Zeneca
- BASF
- Battelle
- Bayer AG
- Boehringer-Ingelheim
- Bristol-Myers Squibb
- Celgene
- Centre Antipoison-Centre de Pharmacovigilance
- Charles River Laboratories
- Covance
- Dow Chemical
- DuPont
- Eli Lilly and Company
- GlaxoSmithKline
- Hoffmann-La Roche
- Johnson & Johnson
- Merck & Co. Inc.
- Novartis Pharma AG
- Pfizer, Inc.
- sanofi aventis
- Stellar Biotechnologies
- Syngenta
- UCB
- UK NIBSC
- University of Aachen
- University of Paris-Sud
- University of Washington
- US EPA
- US NIEHS
- US FDA
ITC Projects

**New predictive itox assays & reduction of animal usage**
- In vitro platforms to predict immunotoxicity
- **Cytokine Release Assays**

**Developmental Immunotoxicology**
- Historical control data and species immune system development

**Harmonization of existing itox assays and data interpretation**
- Interpretation of alveolar macrophage responses
- TDAR good practices

**Testing strategies & risk assessment**
- In vivo itox models
- Approaches to assessment of itox for env chem
- Respiratory sensitizers

**Translational immunotoxicology**
- Clinical Immunotoxicology

**Predictive tools for immunogenicity, hypersensitivity and autoimmunity**
- Drug hypersensitivity reactions
WORKSHOP ON CYTOKINE RELEASE:
State-of-the-Science, Current Challenges and Future Directions

22 October 2013
Silver Spring, MD

Organized by the
ILSI Health and Environmental Sciences Institute
Immunotoxicology Technical Committee
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Key questions/Challenges

1. What are the scientific gaps in our understanding of cytokine release syndrome?

2. What are the criteria for performing CRA?

3. Consideration for CRA formats: Should PBMCs vs whole blood; soluble vs immobilized; single vs multiple formats be used?
   » Is there a standardized approach?

4. What is a “positive” result; how should companies respond?

5. How should CRA data be used: quantifiable risk assessment or hazard identification, clinical dose selection?

6. How well do the CRA results correlate with clinical results?