Committee leaders:
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This scientific program is committed to:

• Identifying and addressing scientific issues related to the development and application of immunotoxicology to public health and human health risk assessment.
• Promoting the understanding and appropriate use of immunotoxicology data to protect human health.
• Contributing substantively to the scientific decision-making processes relative to the development of guidelines and regulations for immunotoxicology testing at the local, national, and international levels.

Areas of scientific focus:

• Harmonization of existing immunotoxicology assays and data interpretation
• Developmental and juvenile immunotoxicology best practices
• New predictive immunotoxicology assays and reduction of animal usage
• Predictive tools for immunogenicity, hypersensitivity, and autoimmunity
• Testing strategies and risk assessment
• Application of immunotoxicology for clinical application

Why get involved?
The Immunotoxicology Technical Committee (ITC) is a unique forum for generating scientific dialogue, fostering research, and developing practical approaches to assessing adverse effects of chemicals and pharmaceutical entities on the immune system and understanding human risk potential.

Key accomplishments:

• Cytokine Release Assays. The Cytokine Release Assay (CRA) working group, in collaboration with the UK National Institute for Biological Standards and Control (NIBSC), recently completed the experimental phase of a multi-site ring trial to test a repository of positive and negative control capabilities in a CRA. A manuscript detailing the results from this collaborative study is in progress. In addition, the group has been discussing other workstreams that look to establish, through the sharing of cross-company data, which criteria are important in control cyno cytokine studies.

• Developmental Immunotoxicology. This working group has completed a draft (currently in final review) of a comprehensive review document on the key time points of development of the immune system across several preclinical species and their predictability to humans.

• Drug Hypersensitivity Reactions. This working group has drafted a comprehensive manuscript that outlines the available tools and assays for diagnosing and characterizing drug hypersensitivity reactions (DHRs) in both preclinical and clinical settings.

• Immunomodulators and Cancer Risk Assessment. Through the gaps and opportunities outlined in the working group’s published position paper in Regulatory Toxicology and Pharmacology, the participants are carrying out a second phase to create a compendium that outlines the available models, tools, and approaches used to assess immune function. Specifically, the group is looking at those tools/assays that assess cytotoxic T lymphocyte (CTL) and natural killer (NK) cell function, and the goal is to publish this compendium before the end of 2018.

• In Vitro Immunotoxicology Models. The working group is nearly finished drafting a manuscript that highlights the cross-laboratory study using the human lymphocyte activation (HuLA) assay, which evaluates recall responses to influenza virus as an in vitro model to assess immune function. In addition to highlighting the results from that assay, the manuscript will also provide best practices and learnings for consideration when running future in vitro-based studies.
Clinical/Translational Immunotoxicology. The committee has been holding a series of webinars on clinically relevant topics throughout the past year. Topics that have been discussed, or are planned, include host cell proteins/impurities in biologics, keyhole limpet hemocyanin (KLH) and other vaccines used to measure immunocompetence, and risks of developing autoimmune disorders with immunomodulators.

T-Dependent Antigen Response (TDAR): Evaluation of Fit-for-Purpose KLH Attributes. This working group has been collecting, collating, and working toward publishing methods, challenges, results, and discussion on implementing immune responses to KLH to detect immunostimulation as a pharmacodynamic endpoint assessment on nonclinical toxicity studies.

Immunotoxicology Training Course. Following the success of the inaugural 2-day training course on “T-cell Biology and Application to Immunopharmacology and Immunotoxicology” in April 2017, an encore course was held in April 2018 in Munich, Germany. This maximum capacity–attended course was designed to provide an understanding of the foundational science and its application in drug development. Future topics are currently under discussion for 2019 and beyond.

Immunomodulation and Pregnancy Risk Assessment. Following a presentation at an ITC scientific meeting on the topic, the committee recently launched this working group in partnership with DART. Following a brief survey of members to assess how various institutions assess pregnancy risk using various models and literature support, the goal is to broaden the understanding in the field by holding a workshop in 2019. In addition, a position paper is being drafted that highlights the initial thoughts and current assessment strategies employed within the field.

Scientific Meetings. The committee began holding a bi-annual in-person scientific meeting in conjunction with their business meeting. During this time, issues relevant to the immunotoxicology committee are presented by inviting outside experts, presenting case studies, and holding a general discussion on the topic. Over the past year, topics have included nanomedicine, first-in-human dose selection, and immunomodulation and pregnancy risk.

The Committee’s focus for May 2018–May 2019:
- Launch and begin drafting a position paper on how to address nanomedicines and immunotoxicological risk assessment.
- Convene a workshop on CD3 bi-specifics and safety risk assessment in partnership with the US FDA.
- Work toward drafting a position paper on nanomedicines and immunotoxicologic risk assessment.
- Publish the CRA-NIBSC Ring Trial study, the HuLA manuscript, the compendium on tools and assays to assess CTL and NK function, the developmental immunotoxicology review, the KLH administration results, and the DHR compendium.
- Conduct regular webinars in clinical immunotoxicology, with the goals to increase dialogue between preclinical toxicologists and clinicians and identify gaps and needs between these two communities.
- Continue the discussion on potential areas for future projects relevant to the ITC through the scientific meeting format (e.g., immuno-oncology, immunogenicity, etc.).
- Continue the immunotoxicology training course to train the next generation of immunotoxicologists.

2017–2018 Participating organizations

Amgen Inc.  MedImmune  Sanofi
Boehringer Ingelheim GmbH  Merck & Co., Inc.  Stellar Biotechnologies
Bristol-Myers Squibb Company  Merck KGaA  Swedish Toxicology Sciences
Celgene Corporation  Michigan State University  Research Center (Swetrox)
Charles River Laboratories  MPI Research  Takeda Pharmaceutical Company Limited
Covance  National Institute for Biological Standards and Control (UK)
Eli Lilly and Company  National Institute of Environmental Health Sciences  UCB
Genentech  University of Aachen
GlaxoSmithKline  National Institutes of Health  University of Paris-Sud
Hoffmann-La Roche Ltd.  Novartis Pharma AG  US Environmental Protection Agency
Ions Pharmaceuticals  Pfizer Inc.  US Food and Drug Administration
Janssen Pharmaceuticals  Pharmaceuticals and Medical Devices Agency (Japan)
Medicines and Healthcare Products Regulatory Agency (UK)

For more information, contact the Committee’s manager, Dr. Stan Parish, sparish@hesiglobal.org.