ILSI Health and Environmental Sciences Institute

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Takahiko Yoshida, MD., PhD.
Asahikawa Medical University

June 30, 2015

Dear Dr. Yoshida,

On behalf of the Health and Environmental Sciences Institute (HESI) Immunotoxicology Technical Committee (ITC) leadership, we would like to extend an invitation to you and the members of the Japanese Society of Immunotoxicology to participate in this committee. HESI is a global branch of the International Life Sciences Institute (ILSI), a public, non-profit scientific foundation with branches throughout the world. HESI provides an international forum to advance the understanding and application of scientific issues related to human health, toxicology, risk assessment and the environment. HESI is widely recognized among scientists from government, industry and academia as an objective, science-based organization within which important issues of mutual concern can be discussed and resolved in the interest of improving public health. As part of its public benefit mandate, HESI's activities are carried out in the public domain, generate data and other information for broad scientific use and application, and include participation from government, industry and academic scientists. HESI's programs are supported primarily by its industry membership.

HESI's scientific programs are carried out by multi-sector technical committees. The ITC led by Dr. Hervé Lebrec (Amgen), Dr. Ellen Evans (Pfizer), and Dr. Marc Pallardy (University of Paris, Sud), was established in 1992 with the mission of identifying and addressing scientific issues related to the development and application of immunotoxicology to public health and human health risk assessment. Through a collection of projects, the goal is to promote the understanding and appropriate use of immunotoxicity data to protect human health, and contribute substantively to the scientific decision-making processes relative to the development of guidelines and regulations for immunotoxicity testing at the local, national, and international levels. The current portfolio includes the following areas under investigation:

- New predictive immunotoxicity assays and reduction of animal usage
- Harmonization of existing immunotoxicity assays and data interpretation
- Testing strategies and risk assessment
- Predictive tools for immunogenicity, hypersensitivity and autoimmunity
- Translational immunotoxicology

Please find attached an activities report that highlight the goals and accomplishments of the ITC during the past year for your reference. We look forward to the opportunity to speak to you, or any other members of the society, further about HESI and the ITC.

On behalf of the entire HESI ITC leadership,

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2014–2015 Activities and Accomplishments

Committee leaders:

Dr. Marc Pallardy
University of Paris-Sud

Dr. Ellen Evans
Pfizer Inc.

Dr. Hervé Lebrec
Amgen Inc.

HESI managers:

Dr. Connie Chen
Dr. Stan Parish

HESI associate:

Mr. Oscar Bermudez

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; and
- 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
- Translational immunotoxicology

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.* Building from the ITC October 2013 cytokine release assays (CRA) workshop, the working group has begun to develop a repository of standards, which will be held at the National Institute for Biological Standards and Control and will be tested at multiple sites for their positive and negative control capabilities in a CRA. In addition, the group continues to share their data on the *in vitro* to *in vivo* translatability of a CRA in order to build consensus around methodology.
- *Developmental Immunotoxicology.* The DART and ITC committees have successfully initiated collaboration on a comprehensive review document on the key time points of development of the immune system across several preclinical species and in humans.
- *Drug Hypersensitivity Reactions.* This working group has been working on developing a reference document of the available tools and assays for diagnosing and characterizing drug hypersensitivity reactions (DHRs) in both preclinical and clinical settings.
- *Immunomodulators and Cancer Risk Assessment.* The committee, in collaboration with the US FDA, convened a workshop with over 200 attendees (in-person and via webinar) in October 2014, at the FDA White Oak campus, in Silver Spring, Maryland. There were presentations outlining the current knowledge related to human cancer risk associated with altered immunity and the available models, tools, and approaches available to conduct weight-of-evidence–based

assessments of cancer risk associated with new immunomodulatory therapies. The discussions at the workshop helped to identify knowledge gaps and opportunities for research efforts to improve the conduct of such risk assessments. A manuscript is being prepared, which will summarize the workshop highlights and the points to consider in risk assessment and further research.

- *In Vitro Immunotoxicology Models.* The committee is currently conducting a cross-laboratory study to explore the use of a human lymphocyte activation (HuLA) assay, which evaluates recall responses to influenza virus as an *in vitro* model to assess immune function. Data are still being generated across the laboratories and analysis is ongoing.
- *Respiratory Sensitization.* The committee organized a workshop in May 2014 in Alexandria, Virginia, which discussed the current state of the science for identification and characterization of respiratory sensitizer hazards and identify the requirements for developing validated standard methods and frameworks. Workshop proceedings highlighting the regulatory and practical needs regarding hazard identification are currently in preparation.

The Committee's focus for May 2015–May 2016:

- Completing the manuscript proceedings and findings of the 2014 spring workshop entitled "Assessment of Respiratory Sensitization" and the 2014 fall workshop entitled "Immunomodulation and Cancer Risk Assessment."
- Completing the cross-laboratory evaluation of the *in vitro* HuLA assay and identifying the next *in vitro* assay to be evaluated.
- Completing the DHR reference manuscript, identifying knowledge gaps and challenges, and assessing how those could be addressed.
- Conducting regular webinars in the area of clinical immunotoxicology toward increasing dialogue between preclinical toxicologists and clinicians, and identifying gaps and needs between these two communities.
- Publishing the proceedings from the October 2013 CRA workshop and continuing to move forward with the development and validation of reference standards.

2014–2015 Participating organizations:

Amgen Inc.
Boehringer Ingelheim GmbH
Bristol-Myers Squibb Company
Celgene Corporation
Charles River Laboratories
Covance
Dow Chemical Company
Eli Lilly and Company
ExxonMobil Biomedical Sciences, Inc.
GlaxoSmithKline
Hoffmann-La Roche Inc.
Janssen Pharmaceuticals
MedImmune
Merck & Co., Inc.
National Institute for Biological Standards and Control (UK)
National Institute for Public Health and the Environment (RIVM, The Netherlands)
National Institute of Environmental Health Sciences
Novartis Pharma AG
Pfizer Inc.
Sanofi
Stellar Biotechnologies
Syngenta
Swedish Toxicology Sciences Research Center (Swetox)
UCB
Université Claude Bernard Lyon
University of Aachen
University of Manchester
University of Paris-Sud
US Environmental Protection Agency
US Food and Drug Administration

For more information, contact the Committee's managers, Dr. Connie Chen, cchen@hesiglobal.org, or Dr. Stan Parish, sparish@hesiglobal.org.