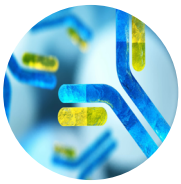
Immuno-Safety



Our Mission

The mission of the HESI Immuno-Safety Technical Committee (ITC) is to identify and address scientific issues related to immune safety and translation to human health risk assessment.

Chairs

Public Chair
Dr. Marc Pallardy (Université Paris-Saclay)

Private Chairs
Dr. Herve Lebrec (Sonoma Biotherapeutics)
Dr. Curtis Maier (GlaxoSmithKline)

HESI Staff

Dr. E'Lissa Flores (eflores@hesiglobal.org)
Dr. Shermaine Mitchell-Ryan
(smitchell-ryan@hesiglobal.org)

Webpage

https://hesiglobal.org/immuno-safety/

2022 Committee Highlights

Participating Organizations
8 government/regulatory agencies,
9 academic/research institutes, 30 industry

Publications
2 submitted, 4 in progress

Web Tools, Assays and Resources
- Immuno-Safety Resource Site
- Virtual On-Demand Training Course

Collaborations
1 internal, 2 external

- HESI DART Committee
- The American Association of Pharmaceutical Scientists (AAPS)
- Society of Toxicology (SOT)

Scientific Meetings and Trainings
3 meetings

- ITC 2022 Spring Business Meeting (virtual; 120 attendees)
- ITC 2022 Fall Business Meeting (hybrid; 127 virtual & 14 in-person attendees)
- Immuno-safety Mentorship Program (virtual; 20 attendees)

Outreach
1 networking event

American Association of Immunologist
- *Roundtable Mentoring Event*. E'Lissa Flores (HESI).

Geographic Representation
Belgium, Canada, Denmark, England, France, Germany, Japan, Norway, Switzerland, United States

Working Groups

- **Regulatory Gaps.** Workstream generating exercise that summarizes and contrasts available guidelines and/or key documents used to direct immune safety assessments to support follow-up discussions on perceived gaps as they relate to current and emerging modalities. Depending on the nature of the gap(s) identified, the appropriate ITC WG may choose to develop a white paper, host a workshop, or develop best practices for an assay in question.
- **Immunomodulation and Pregnancy Risk Assessment.** Evaluate and incorporate learnings on preclinical immune-safety assessment of pregnancy risk in the presence of immunomodulatory therapy.
- **Immunogenicity Assay – Standards Study.** To address the lack of availability of standard positive and negative control therapeutic proteins used for *in vitro* T cell immunogenicity assays, the project team will develop a reference panel of lyophilized mAbs known to elicit ADA response in clinic, as well as a negative control, in a cross-site evaluation of the reagents. A multi-lab pilot will be conducted in Q1 2023. Pending the results of the evaluation, the validated reagent will be available for distribution, broadening the impact and contributions of this study.
- **CTL Assays.** Manuscript outlines the tools and assays available to assess Cytotoxic T-Lymphocyte function.
- **Examining the Use of Humanized Mice as Preclinical Model in Drug Development.** This project is designed to identify gaps/issues highlighted from case studies and manuscripts regarding the use of the model and to design specific projects to resolve important issues identified. The group continued their webinar series to showcase and provide information on a variety of humanized mouse models that are currently available or are in the development phase. The group has since formed a subgroup and is discussing preliminary study design ideas to test and improve current models to increase confidence in translational applications and immuno-safety assessments.
- **IgG Fc-containing Biotherapeutics: Translation, Pharmacological and Toxicological Effects from Animals to Humans to Support Human Risk Assessment.** Case-study informed white paper on nonclinical safety testing approaches used for characterizing potential risks of Fc-modifications engineered into antibody-based molecules. This manuscript will investigate the impact of receptor modification on the binding and activation profiles to some or all of the receptors and complement between species.
- **Cytokine Release Assay –** ***In vivo*** **cytokine release.** Evaluating parameters that may contribute to the variability of cytokine levels in cynomolgus monkey control animals.

HESI ITC Translational Immune Safety Clinician Roundtable Series. A series of one-hour. webinars that center on topics to bridge translational gaps in immune safety. This effort will result in (1) a paper that highlights the key discussion points from each roundtable discussion, recommendations, and future directions as well as (2) the development of an actionable workstream that identifies new projects that is in congruence with the needs of the clinicians while capturing the gaps and limitations in preclinical studies.

- **FIH Dose Selection for Immunomodulators.** This group is focusing on how to determine a suitable course of action for establishing a FIH dose for various types of immunomodulators. They continue to compile publicly available FIH data and collect additional survey responses from respective organizations to confirm their compound data collected, as well as inquiry about their key decision-making factors in selecting FIH doses. This year, the group also launched an FIH Dose case study webinar series with over 11 case studies across seven organizations. The group is currently drafting two papers based on survey responses and case study insights will be published in 2023.
- **Drug Hypersensitivity Reaction.** Initially started as an internal compendium guidance on how to assess and test for drug hypersensitivity reactions in both pre-clinical and clinical settings. The information was converted to a manuscript and submitted for publication.
- **Scientific Outreach – Mentor Webinar & Mentorship Program.** The Scientific Outreach group is developing resources and activities for outreach at select scientific meetings and to create a platform to advocate and educate the next generation of immuno-safety scientist. This year, the group launched an inaugural Mentorship Program that allowed one-on-one interactions between trainees and mentors to give insight on career pathways and discuss mentees' long-term career goals. The group is currently working on collaborating with the SOT ITSS specialty group to conduct a mentor networking event for trainees to gain insights on various non-academic immuno-safety careers.
- **ITC Clearinghouse Database.** To create and utilize a clearinghouse/database that contains resources and relevant information that include literature, events, emerging topics and experts in immune safety for both internal and external audiences.
- **ITC Website Development.** Development of an ITC-centric website where both scientists and the public can find information on the field of immuno-safety.

Areas of Focus for 2023

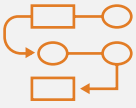
- Immuno-safety education and scientific outreach will remain a focus area of the committee. The Science Outreach subgroup will continue to expand their mentorship program and networking events to connect trainees with mentors in their field of interest to learn more about the immuno-safety career path. The committee will also establish a new professional development award for trainees, as well as present a CE training course at the SOT 2023 conference.
- The virtual training course will allow the committee to fulfill its commitment to educating and communicating to the public and scientific community on the scientific issues related to the development and application of immuno-safety in public health and human health risk assessment. The on-demand nature of these courses will improve the accessibility and reach to prospective participants by allowing "any time" paid access to the expanded course catalog. This system also allows greater flexibility with course offerings; heightening our ability to be responsive to new and emerging science as it develops.
- The Method Development WG will continue to actively recruit speakers for the "New Methods and Technologies" webinar series. The invitees will include assay developers and experts with demonstrated knowledge in the use of emerging technologies or methodologies employed for immune profiling and pathway analysis. While serving as a form of continuing education for committee members, the informational presentations will allow for expanded the discussion and help the committee properly assess the opportunities and challenges associated it's with use.
- The evaluation of regulatory guidance documents, in particular the modality specific assessments driven by a specific immuno-safety concern, will elucidate deficiencies and or ambiguities across modalities while providing an opportunity for the committee to advocate for up-to-date best practices related to immune safety and risk assessment informed by the science.
- The committee will expand its focus to include new topics of interest: (1) Inflam-aging, immuno-senescence and the evolving immune system, and (2) Immunomodulatory Oligonucleotides. The committee has invited two subject matter experts to present science talks highlighting the promise, opportunities, and current regulatory landscape for each topic.

Strategic Impact Areas

Enhanced efficiency and accuracy in safety assessment practice
Regulatory gaps project will help to identify current gaps and ambiguities that may exist in current regulatory guidance documents and encourage the development of revised or updated guidelines, enhance clarity in interpretation and offer best practices for assay used in immune safety assessments.

Increasing the audiences for collaborative safety science
The Science Outreach mentor and networking events welcome an audience of student, postdoc, and early career scientists by developing programing that is tailored to their interest and needs and appropriate for their respective career stages. Routine engagement with this population will assist in the conversion to regular and frequent attendees of ITC sponsored/hosted events. The mentor-mentee network provides the much-needed non-academic career exposure and resources consistent with the recommendations issued from the National academies of science report on Graduate Education Reform.

Development of scientists skilled in translational science
The Scientific Outreach group aims to increase awareness about careers in the immuno-safety and immunopharmacology field. Moreover, the training course and webinar series provide professional development opportunities for those interested in taking a deeper dive into the foundational principles of immuno-safety science.



Publications

Submitted

Drug Hypersensitivity Reactions: Review of the State of the Science for Diagnosis and Prediction.

Current Approaches to Evaluate the Function of Cytotoxic T Cells in Non-Clinical Studies.

In Progress

Assessing the Impact and Risk of Immunomodulatory Compounds on Pregnancy.

Beyond the Minimal Anticipated Biological Effect Level (MABEL): Strategies for Selection of First-in-Human Starting Dose for Novel Modalities.

Recommendation for the Selection of First-in-Human Dose of Immunomodulators by the Health and Environmental Sciences Institute (HESI) Immuno-Safety Technical Committee (ITC).

Impact of Antibody Fc Engineering on Translational Pharmacology, Safety and Immunogenicity.

Participating Organizations

Government/Regulatory Agencies

Medicines and Healthcare Products Regulatory Agency (MHRA)
National Institutes of Health (NIH), National Institute of Environmental Health Sciences (NIEHS)
Pharmaceutical and Medical Devices Agency (Japan)
Swissmedic
The Medicines and Healthcare Products Regulatory Agency
US Environmental Protection Agency (EPA)
US Food and Drug Administration (FDA)
US National Institutes of Health (NIH)

Academic/Research Institutes

Michigan State University
Research Institute of Sweden
Rosalind Franklin University
Swedish Toxicology Sciences Research Center
University of Aachen
University of Kitasato
University of Oslo
Université Paris-Sarclay
University of Wisconsin

Industry

Amgen
AstraZeneca
ApconiX
Axion BioSystems
Bayer
Boehringer Ingelheim
Bristol-Myers Squibb
Burleson Research Labs
Charles River Laboratories
Eli Lilly and Company
Genentech/Roche
Hoffmann-La Roche, Inc.
GenOway
Gilead
GSK
Janssen Pharmaceuticals
Kyowa Kirin
Labcorp Drug Development
LEO Pharma
Merck & Co., Inc.
Merck Healthcare KGaA
Novartis Pharmaceuticals
Pfizer, Inc.
Sanofi
Sonoma Biotherapuetics, Inc.
Stage Bio
Taconic Biosciences
Takeda Pharmaceutical Company, Ltd.
UCB Biopharma SPRL
Wave Life Sciences