Immuno-Safety

Our Mission

The committee's mission is to identify and address scientific issues related to immune safety and translation to human health risk assessment. The committee's key objectives are (i) to leverage technical and scientific expertise from industry, academic, and regulatory organizations to advance immuno-safety science, (ii) to contribute to the scientific decision-making processes relative to the development of guidelines and regulations for immune safety testing, and (iii) to educate stakeholders in safety sciences and promote the understanding and appropriate use of immune safety data.

Chairs

Public Chair

Dr. Marc Pallardy (Université Paris-Saclay)

Private Chairs

Dr. Hervé Lebrec (Sonoma Biotherapeutics)
Dr. Curtis Maier (GlaxoSmithKline)

HESI Staff

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

Webpage

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

2021 Committee Highlights

Participating Organizations

7 government/regulatory agencies, **8** academic/research institutes, **23** industry, and **1** clinical

Publications

1 published and **4** in progress

Scientific Meetings and Trainings

2 meetings and **2** leadership retreats

- Spring and Fall Committee Meetings (virtual; 68 attendees and 74 attendees, respectively)
- Spring and Fall Leadership Retreats (virtual; 13 attendees)

Outreach

1 oral presentation and **1** webinar

- **1** oral presentation at the EUROTOX 2021 Congress on the preclinical immune-safety evaluation of immuno-oncology therapies (September 2021, virtual)
- **1** Immuno-Safety Career Webinar targeting graduate students, postdocs, and early career scientists with the intent to increase awareness about careers in the immuno-safety and immuno-pharmacology fields (September 2021, virtual)

Collaborations

2 internal and **1** external

- HESI Cell Therapy - TRAcking, Circulation, & Safety (CT-TRACS) Committee: continued development of the HESI Engineered Cell Safety Advisory Core, a cross-committee initiative that identifies existing synergies and optimizes intra-committee communication and collaboration by connecting the relevant technical expertise in the engineered cell space. The Advisory Core is expanding participation to other committees and has extended invitations to committees of interest.
- HESI Developmental and Reproductive Toxicology (DART) Committee: collaborating on immunomodulation and pregnancy risk assessment project
- American Association of Pharmaceutical Scientists (AAPS): collaborating on immunogenicity assay project

Geographic Representation

Belgium, Canada, France, Germany, Japan, Sweden, Switzerland, United Kingdom, and United States

Working Groups

- **Regulatory Gaps.** This workstream generating exercise summarizes and contrasts available guidelines or key documents used to direct immune safety assessments and 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 committee working group may choose to develop a white paper, host a workshop, or develop best practices for an assay in question.
- **Immunomodulation and Pregnancy Risk Assessment.** This working group aims to evaluate and incorporate learnings on preclinical immune safety assessment of pregnancy risk in the presence of immunomodulatory therapy.
- **Immunogenicity Assay Standards Study.** This project was initiated to address the lack of available 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 and conduct a cross-site evaluation of the reagents. Pending the results of the evaluation, the validated reagents will be available for distribution, broadening the impact and value of this study.
- **CTL Assays.** This project team is developing a manuscript that outlines the tools and assays available to assess Cytotoxic T-Lymphocyte (CTL) function.
- **Examining the Use of Humanized Mice as a Preclinical Model in Drug Development.** This project is designed to identify gaps/issues highlighted from a committee-wide survey regarding the use of the model and to design specific recommendations to resolve important issues identified. A new webinar series was launched to showcase and provide information on a variety of humanized mouse models that are currently available or are in the case study phase.
- **IgG Fc-Containing Biotherapeutics: Translation, Pharmacological, and Toxicological Effects From Animals to Humans to Support Human Risk Assessment.** This group is developing a 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.** This project is identifying and evaluating the parameters that contribute to the variability in cyno control animals.
- **ITC Translational Immune Safety Clinician Roundtable Series.** This working group will organize and host a series of one-hour webinars that center on topics related to bridging translational gaps in immune safety. This effort will result in (1) a paper that highlights the key discussion points from the roundtable discussion, recommendations, and future directions as well as (2) the development of an actionable workstream that identifies new projects that match the needs of the clinicians while capturing the gaps and limitations in preclinical studies.
- **FIH Dose Selection for Immunomodulators.** This group is determining a suitable course of action for establishing a FIH dose for various types of immunomodulators. Currently, the group is compiling FIH data and developing a survey to outreach to respective organizations to confirm their compound data collected, as well as inquiry about their key decision-making factors in selecting FIH doses.
- **Drug Hypersensitivity Reaction.** This group is developing a compendium for internal use on how to assess and test for drug hypersensitivity reactions in both pre-clinical and clinical settings. The compendium will be converted to a manuscript and submitted for publication.
- **Science Outreach Career Webinar and Mentor Program.** The Science Outreach group is developing resources and activities for outreach to create a platform to advocate and educate the next generation of immuno-safety scientists. The group has recently created an outreach career flyer and webinar that highlighted multi-sector immune safety careers. Future 2022 plans include developing a mentor-mentee program.
- **Immuno-Safety Training Course.** An on-demand virtual training course that will cover various topics in immuno-safety science is in development. The current course contains 45 distinct lectures that cover six different modules including: immune safety tools, therapeutic modalities, toxicities, regulatory considerations, and advanced/specialty topics.
- **ITC Clearinghouse Database.** This work aims to create a clearinghouse/database that contains resources, relevant information, related literature, events, emerging topics, and experts in immune safety for both internal and external audiences.
- **ITC Website Development.** An ITC-centric website where both scientists and the public can find information on the field of immuno-safety is being developed.

Areas of Focus for 2022

- Through intentional and thoughtful engagement with graduate students, postdocs, and early career scientists, the Science Outreach group will continue to heighten the awareness of careers in immuno-safety by complimenting the recently established career webinar series with mentor-mentee networking sessions that will connect trainees with mentors in their field of interest to learn more about the immuno-safety career path.
- The virtual Immuno-Safety Training Crouse 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 immune-safety in public health and human health risk assessment. The on-demand nature 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.

- To keep pace with the rapid development of technologies and novel methodologies used for immune profiling and pathway analysis, the Method Development group will actively recruit assay developers and experts in identified technologies or methodologies of interest to provide informational presentations on the science and application of the novel tool or method to help the committee properly assess the opportunities and challenges associated its with use.
- The committee will leverage technical expertise from the ITC membership to advocate for modern immune safety–related best practices and also to help inform current immune safety regulatory and risk assessment gaps.
- The evaluation of regulatory guidance documents, in particular the modality specific assessments conducted, in addition to elucidating deficiencies and or ambiguities, provides an opportunity for the committee to advocate for up-to-date best practices related to immune safety and risk assessment

Strategic Impact Areas

Enhanced Efficiency and Accuracy in Safety Assessment Practice

The ITC 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 career webinar series welcomes an audience of student, postdoc, and early career scientist by developing programming that is tailored to their interests and needs and appropriate for their respective career stages. Similarly, the Immuno-Safety Resource website and Clearinghouse Database will be a public-facing resources that will engage stakeholders and a community of learners with resources and information on immune safety science, as well as providing a list of upcoming related events and educational opportunities.

Development of Scientists Skilled in Translational Science

The Science Outreach group aims to increase awareness about careers in the immuno-safety and immuno-pharmacology fields, with the target audience of graduate students, postdocs, and early career scientists. The newly launched career webinar series allowed for meaningful discussions that gave insight on the immuno-safety field and multi-sector career pathways. The virtual Immuno-Safety Training Course will also provide an opportunity to expand scientific knowledge in immune biology (both the normal and disease states), toxicities associated with immune modulation, and tools/methods and modalities that integrate the latest science in the field. The newly re-designed training course offers introductory and advanced topic modules to ensure engagement from a wide range of scientists.

Publications

Published

Green S, Maier CC, Maki K, Ponce R, Shenton J (2021). The nonclinical safety assessment of engineered T-cell therapies. *Regulatory Toxicology and Pharmacology*. doi: 10.1016/j.yrtph.2021.105064.

In Progress

Assessing the impact and risk of immunomodulatory compounds on pregnancy. In preparation.

Drug hypersensitivity reactions: review of the state of the science for diagnosis and prediction. In preparation.

Current approaches to evaluate the function of cytotoxic T-cells in nonclinical studies. In preparation.

Beyond the Minimal Anticipated Biological Effect Level (MABEL): strategies for selection of first-in-human starting dose for novel modalities. In preparation.

Participating Organizations

Government/Regulatory Agencies

Medicines and Healthcare Products Regulatory Agency (UK)
National Institute for Biological Standards and Control (UK)
National Institute of Environmental Health Sciences
Pharmaceuticals and Medical Devices Agency (Japan)
Swissmedic
US Environmental Protection Agency
US Food and Drug Administration

Academic/Research Institutes

Michigan State University
RISE Research Institutes of Sweden
The Jackson Laboratory
Université Claude Bernard Lyon
Université Paris-Saclay
University of Aachen
University of Kitasato
University of Wisconsin

Industry

Amgen, Inc.
AstraZeneca
Bayer
Boehringer Ingelheim
Bristol-Myers Squibb Company
Burleson Research Technologies
Charles River Laboratories
Eli Lilly and Company
Genentech
genOway
GlaxoSmithKline
Janssen Pharmaceuticals
Kyowa Kirin
Labcorp Drug Development
Merck & Co.
Merck Healthcare KGaA
Novartis
Pfizer, Inc.
Roche
Sanofi
Taconic Biosciences
Takeda Pharmaceutical Company, Ltd.
UCB Biopharma

Clinical

Rosalind Franklin University Health System