Lunchtime Seminar L1-3

June 30 (Thu) 12:00-13:00 Room 3

The importance and trend in mechanism-integrated prediction of drug-induced liver injury

Speaker : Akinori Takemura (Laboratory of Biopharmaceutics, Graduate School of Pharmaceutical Sciences, Chiba University)

Chair : Shinsuke Aoyama (Drug Development Solutions Sales Office, SEKISUI MEDICAL CO., LTD.)

Sponsored by : SEKISUI MEDICAL CO., LTD.

Overview

Drug-induced liver injury (DILI) is the major reason for the discontinuation of new drug development and the withdrawal of drugs from the market. Several studies have been developed DILI prediction methods with high sensitivity and specificity by combining multiple targets (BSEP inhibition, mitochondrial toxicity, and metabolic activation). However, previous systems use cell-free system and hepatoma-derived cell, so it is insufficient to mimic in vivo condition. This seminar shows the present trends in DILI prediction systems including our laboratory data.

Lunchtime Seminar L1-4

June 30 (Thu) 12:00-13:00 Room 4

Modeling Neuroinflammation with iPSC-Derived Neurons, Astrocytes, Microglia, and Neural Organoid Systems

Speaker : Jason Hamlin, PhD (Product Manager - Neuroscience, STEMCELL Technologies Inc.)

Chair : Ikuro Suzuki (Graduate School of Engineering, Tohoku Institute of Technology)

Sponsored by : Veritas Corporation

Overview

Environmental toxicity and genetic factors contribute to neuroinflammation, which plays a central role in neurodegeneration. Microglia and astrocytes regulate neuronal connectivity and modulate inflammation within the CNS. We introduce human pluripotent stem cell (hPSC)-derived neurons, astrocytes, and microglia and how they may be used in vitro to model the toxic effects of neuroinflammatory processes. We will also provide an overview of tools in STEMCELL Technologies' STEMdiff™ Neural System for successful hPSC differentiation and experimental designs using multiple cell types.

Lunchtime Seminar L1-5 June 30 (Thu) 12:00-13:00 Room 5

When Gene Therapy Meets Regulatory Toxicology: From Strategies to Solutions & Applications

Speaker : Maggie Elorza (Senior Research Scientist, Lab Sciences, Charles River)
Audrey Saumure Di Fruscia (Research Scientist, Toxicology, Charles River)
Clotilde Lecrux-Leblond (Scientist, Study Management, Charles River)
Chair : Hiroyuki Minami, PhD (Charles River)
Sponsored by : Charles River

Overview

Gene therapy has emerged as a leading test article modality carrying high hopes for a wide range of diseases. Innovative gene delivery strategies need to address regulatory toxicology requirements across the development continuum. The session will present strategies and relevant regulatory considerations for the conduct of gene therapy toxicology programs.

Lunchtime Seminar L1-6 June 30 (Thu) 12:00-13:00 Room 6

Nonclinical species selection for biologics – why is it important and what are the options when no appropriate species exists?

Speaker : Robert Evans
Christopher Cooper
Chair : Sharon Tsai
Sponsored by : Labcorp Development Japan K.K.

Overview

Nonclinical species selection is a critical activity in the development process of biopharmaceutical candidates and forms the foundation of the nonclinical safety programme and regulatory strategy. It must be considered and initiated early in the drug development process. The ICH S6(R1) guideline describes the importance of species selection and the regulatory expectation to use pharmacologically relevant species. The use of "non-relevant species may be misleading and are discouraged." This luncheon seminar will start by exploring the process and important considerations for selecting a pharmacologically relevant species for the nonclinical development of biopharmaceuticals. The seminar will then further explore scenario's where a pharmacologically relevant species is not available, as is often the case for human specific targets. The potential alternative pathways that can be followed will be explored, including a focus on the utilisation of in vitro studies that can be useful in understanding the immunotoxicology of biotherapeutics and help understand the MABEL for translation to first-in-human dosing. Specific examples of how a suite of in-vitro cytokine release assays utilising human cells can be used to bridge the gap between pre-clinical toxicology assessment and setting first in-human dose will be discussed.

Lunchtime Seminar L1-7 June 30 (Thu) 12:00-13:00 Room 7

Elsevier Lifesciences Solutions

Speaker : Takahiro Ohyama (Life Science Solutions, Elsevier)
Toshikazu Dewa (Life Science Solutions, Elsevier)
C h a i r : Naoko Suzuki (Life Science Solutions, Elsevier)
Sponsored by : Elsevier Japan K. K.

Overview

Elsevier is a leader in for customers information and analytics across the global research and health ecosystems.
PharmaPendium provides comparative regulatory-based evidence in a single database, informing critical drug development activities. Users gain access to almost 2.5 million searchable FDA and EMA regulatory documents, including reports from the FDA Advisory Committee and FDA Adverse Event Reports, and to extracted pharmacokinetic, efficacy, safety and metabolizing enzyme and transporter data.

In this session, We will present the following topics:
1) Some useful search techniques of PharmaPendium
2) Examples of custom projects using PharmaPendium data and our other datasets.

We are looking forward to meeting you.

Lunchtime Seminar L1-8 June 30 (Thu) 12:00-13:00 Room 8

Automated safety study by image analysis AI

Speaker : Kazumi Hakamada (LPIXEL Inc. CTO)
C h a i r : Yuki Shimahara (LPIXEL Inc. COO)
Sponsored by : LPIXEL Inc.

Overview

LPIXEL has been addressing to accelerate drug discovery by image analysis technology. We are working on automating preclinical trials through our drug discovery AI, "IMACEL TOX".
Since last December, by using Deep Learning, we have started providing service for in vitro micronucleus test for genotoxicity evaluation.
Micronucleus test is time-consuming and dependent on the skill of each researcher, so the contribution of AI to research efficiency is significant.
In this seminar, we would like to discuss details of the technology for automating micronucleus test and future AI application to other preclinical studies.

Lunchtime Seminar L2-2

July 1 (Fri) 12:00-13:00 Room 2

Application of novel high quality *in vitro* human hepatocytes for safety study.

Speaker : Hiroshi Suemizu (Central Institute for Experimental Animals)
Seiichi Ishida (Graduate School of Engineering, Department of Life Science, Sojo University)
Chair : Hiroshi Suemizu (Central Institute for Experimental Animals)
Sponsored by : Central Institute for Experimental Animals

Overview

Since 1952, CIEA has contributed to the realization of "Scientific and Reproducible Animal Experiments" by aiming to establish quality standards for laboratory animals. We believe that cells obtained from experimental animals developed based on this philosophy, will also enable "Scientific and Reproducible Experiments *in vitro*". The Hu-liver cell is a standardized human hepatocyte produced in a planned manner using the experimental animal. In this seminar, Dr. Suemizu from CIEA will talk about the characteristics of the Hu-liver cell, and Dr. Ishida of Sojo University will talk about its utilization.

Lunchtime Seminar L2-3

July 1 (Fri) 12:00-13:00 Room 3

Photosafety Evaluation Strategy for Small Molecule Drug Development

Speaker : Hirofumi Nagai (Axcelead Drug Discovery Partners, Inc.)
Sponsored by : Axcelead Drug Discovery Partners, Inc.

Overview

ICH M3 (R2) and S10 guidelines describing the timing and testing items for the photosafety assessment of small molecule pharmaceuticals in general; However, it may be difficult to adopt in practice during the actual drug development process. In this seminar, a practical photosafety evaluation strategy will be presented with real world examples based on the presenter's nonclinical drug development experiences in past 20 years.

Lunchtime Seminar L2-4 July 1 (Fri) 12:00-13:00 Room 4

Realities of Safety Studies Using Juvenile Animals

Speaker : Akihiro Arima, PhD. (Shin Nippon Biomedical Laboratories, Ltd.)

Chair : Hirofumi Minomo, PhD. (Shin Nippon Biomedical Laboratories, Ltd.)

Sponsored by : Shin Nippon Biomedical Laboratories, Ltd.

Overview

The ICH-S11 Guideline on Nonclinical Safety Testing in Support of Development of Paediatric Medicine reached Step 4 in April 2020. This guideline recommends international standards for determining the availabilities of juvenile animal studies (JAS), and its timing and designs. However, JAS are not necessarily required before conducting clinical trials that have a paediatric component. The necessity of conducting a JAS is judged comprehensively based on factors such as the target patient group age, dosing period, existing clinical or nonclinical data, pharmacological properties, pharmacokinetics data, using a weight-of-evidence approach. The final decision on whether to conduct a JAS and the details of the study design are left to the pharmaceutical company developing the drug, and these decisions must be dealt with on a case-by-case basis. Furthermore, at the laboratory performing the nonclinical safety study, there are limits on the age at which dosing can start, dosing route, and volume for blood collection, and these can often lead to difficulties in conducting the study as envisaged by the pharmaceutical company. In this seminar, I would like to provide SNBL's experience in JAS in light of these realities.

Lunchtime Seminar L2-5 July 1 (Fri) 12:00-13:00 Room 5

ICH S5 (R3) and ICH S11 Guidance – Conducting DART and Juvenile Studies Based on the Latest Guidance

Speaker : Alan M. Hoberman, Ph.D., DABT, Fellow ATS
(Executive Director, Global Developmental, Reproductive and Juvenile Toxicology, Charles River)

Chair : Masamichi Kaminishi, PhD (Charles River)

Sponsored by : Charles River

Overview

This presentation will focus on the most recent revisions to ICH S5 including alignment with other ICH guidelines, exposure margins in dose selection, risk assessment, vaccines, biopharmaceuticals, alternative assays, and options for deferral of studies. ICH S11 Juvenile toxicity study guidance will include the need for a case-by-case approach. The use of information gained from non-clinical adult toxicity studies, the intended use of the pharmaceutical in the clinic, the age of the population and target organs and the duration of use in the population all affect the final juvenile study design.

Nikon's drug discovery support business

Speaker : Yasujiro Kiyota (Fellow, Department Manager, Stem Cell Business Department HealthCare Business Unit, NIKON CORPORATION)

Chair : Kenji Miyamoto (Department Manager, Drug Discovery Research Support Department Bioscience Sales Division, NIKON SOLUTIONS CO., LTD.)

Sponsored by : NIKON CORPORATION

Overview

In recent years, evaluations of effects and toxicities of drug candidate compounds in vitro have been advanced, by applying human stem cell technologies. As various evaluation systems are being developed and used, cell observation devices are becoming more diverse. Nikon has been supporting our customers to solve problems in this field.
In this seminar, we will introduce a wide range of Nikon technologies such as observation devices / image analysis softwere & service / AI technologies / Microphysiological System (MPS) / single-cell assay & sorting (Beacon) / Signal Pathways Analysis service.

①Development of CiPA panel assay by using automated whole cell patch-clamp (Qube 384) technique

Speaker : Muthukrishnan Renganathan, Ph.D (Eurofins Panlabs Inc.)

②ICH S1B(R1): ADDENDUM TO THE GUIDELINE ON TESTING FOR CARCINOGENICITY OF PHARMACEUTICALS - Suggestion of *in vitro* molecular targeted panel assay approach -

Speaker : Masami Tamaoka (Eurofins Discovery - Japan)

③Novel Multiple Targeting Monitoring by Label-Free Binding by Mass Spectrometry Directly in Tissue

Speaker : Manilduth Ramnath, Ph.D (Eurofins Cerep SA)

Chair : Makoto Imatachi (Eurofins Discovery - Japan)

Sponsored by : Eurofins Discovery

Overview

① The objective of the CIPA initiative is to facilitate the adoption of a new paradigm for assessment of clinical potential of TdP that is not measured exclusively by potency of hERG block and not at all by QT prolongation.
The automated whole cell patch-clamp (Qube 384) technique is used to record depolarizing currents, hNav1.5 and hCav1.2, and repolarizing potassium currents, hKv4.3/KChIP2, KCNQ1, and hERG in multihole mode.
In this JSOT seminar, we will show the validation data of the automated whole cell patch-clamp assay and present usefulness of this assay system.

② The ICH S1B (R1) guideline addendum for carcinogenicity testing is gathering opinions toward reaching Step 3, and it will be integrated with the S1B guideline at Step 4 stage. As molecular targets involved in carcinogenicity, 2 targets in drug metabolizing enzyme-related, 2 in DNA repair-related, 5 in reactive oxygen species-related, 13 in inflammation-related, 11 in apoptosis-related, 13 in receptor-related and 12 in cell proliferation-related, in total of 58 molecular targets were selected for in vitro panel assay. Such comprehensive *in vitro* molecular targets panel assay data would be useful & supportive to determine the significance of conducting carcinogenicity study in rodents.

③ Polypharmacology describes the activity of compounds at multiple targets. The "gold standard" for binding assays remains the use of radioligands. However, this approach does not allow for the monitoring of multiple targets simultaneously.
Our aim was to determine the feasibility of using label-free multiple target monitoring (MTM) to monitor 10 receptors simultaneously located in the rat brain cerebral cortex.
This work clearly demonstrates that using MTM label-free binding by mass spectrometry does allow for multiple target monitoring in complex biological matrices, and might be an attractive approach for safety/toxicology studies related to polypharmacology issues.

Lunchtime Seminar L3-3 July 2 (Sat) 12:00-13:00 Room 3

High-throughput 3D imaging analysis using microphysiological systems (MPS) for toxic assesment and disease model studies

Speaker : Yoko Ejiri (MIMETAS Japan KK)
Koji Udagawa (Molecular Devices Japan KK)
Chair : Yoko Ejiri (MIMETAS Japan KK)
Sponsored by : MIMETAS Japan K.K. / Molecular Devices Japan KK

Overview

ImageXpress® high-content imaging systems from Molecular Devices features unique confocal technology that enables to acquire high-quality images of thicker tissues, biological models, and intra- and intercellular events in three dimensions. With water immersion lenses and autofocus function suitable for specialized plate designs such as MIMETAS OrganoPlate®, the system can play an important role in the development and analysis of assays using complex 3D tissue models. In this seminar, we will present actual cases of analysis of 3D tissue and cell samples performed using with our high-content imaging systems.

Lunchtime Seminar L3-4 July 2 (Sat) 12:00-13:00 Room 4

Leveraging Target Safety Assessment (TSA) and visualization of non-clinical data controlled by CDISC SEND -Instem's solution helps to building the foundation of non-clinical data repository for Digital Transformation-

Speaker : Jonathan Sparkes (Instem LSS Limited)
Terukazu Kitahara (Instem Japan K.K.)
Chair : Takayuki Anzai (Showa University School of Medicine)
Sponsored by : Instem Japan K.K.

Overview

Instem's KnowledgeScan™ Target Safety Assessment (TSA) service sets new standards in biological target profiling. We understand the challenges and opportunities associated with target modulation. Join us to learn how our pioneering, technology-enabled service is transforming the TSA process, driving quality, pace, and insight in R&D.
Powered by the latest technology, SEND Explorer® leverages controlled SEND data to enable visualization of nonclinical data, review the analysis process of nonclinical data, and transform the way you work. In addition, we will introduce solutions that efficiently build controlled SEND data.

Lunchtime Seminar L3-5 July 2 (Sat) 12:00-13:00 Room 5

Trends and developments in Environmental (Risk) Assessment of human drugs

Speaker : Daphne de Roode, PhD, ERT (Section Head Regulatory Environmental Toxicology and Chemistry, Charles River Den Bosch)

Chair : Sayaka Odagiri (Charles River)

Sponsored by : Charles River

Overview

Environmental (risk) assessment is a mandatory part of NDAs and MAAs in the USA and Europe. The existing guidance documents date back to 1998 for the USA and to 2006 for Europe, but both have been supplemented by additional guidance or amended by Q&A documents. An updated version of the European guideline has been drafted in 2018.
This presentation gives an overview of the tiered approach of environmental risk assessment in Europe and the US, discussing the basis and principles of each step. Trends and developments will be included, focusing on the consequences for the testing approach. The presentation will also highlight some recurring questions from pharma companies and feedback from authorities.

Lunchtime Seminar L3-6 July 2 (Sat) 12:00-13:00 Room 6

Recent Initiatives in Social Housing and Animal Welfare

Speaker : Ryosuke Kawashima, DVM. (Shin Nippon Biomedical Laboratories, Ltd.)

Chair : Akihiro Arima, PhD. (Shin Nippon Biomedical Laboratories, Ltd.)

Sponsored by : Shin Nippon Biomedical Laboratories, Ltd.

Overview

Public scrutiny of laboratory animals is becoming increasingly severe. One criteria when considering laboratory animal welfare is social housing. The Guidelines for the Management and Use of Laboratory Animals, 8th Edition state that social animals should be kept in pairs or groups unless there is a specific reason. Shin Nippon Biomedical Laboratories, Ltd., fully accredited by AAALAC International since 2011, is actively implementing social housing, including for sexually mature cynomolgus monkeys and male ICR mice. This seminar will introduce our social housing and animal welfare initiatives.

FUJIFILM Wako Pure Chemical Corporation Seminar at JSOT 2022 What is "Liver-ness" ? Comparison of in vitro Testing System using Various Hepatocytes

Speaker : Seiichi Ishida, Ph. D. (Professor of Division of Applied Life Science, Graduate School of Engineering, Sojo University / Biological Safety Research Center, National Institute of Health Sciences)
Shiori Yamada (Bio One Stop Solutions Department, FUJIFILM Wako Pure Chemical Corporation, Japan)
Albert P. Li, Ph. D. (Chief Scientific Officer of Pharmacology and Toxicology, Discovery Life Sciences LLC, Columbia MD, USA)
Chair : Takashi Torashima (Director of Bio One Stop Solutions Department, FUJIFILM Wako Pure Chemical Corporation, Japan)

Sponsored by : FUJIFILM Wako Pure Chemical Corporation

Overview

Human frozen hepatocytes are widely used as the gold standard for the evaluation of drug properties such as drug metabolism, drug-drug interactions, hepatotoxicity, and pharmacology, though they also have functional issues. In this seminar, we invite Professor Ishida of Sojo University, he has been comparing various in vitro evaluation systems such as primary cells, iPSC-derived cells, and chimeric mouse-derived cells, to explain their position in vitro testing. Another topic is MPS (Microphysiological Systems), he talks the latest findings regarding the evaluation in an environment that will reproduce the real liver in vitro. In addition, Discovery Life Sciences, a supplier of frozen hepatocytes, will introduce the capacity for frozen hepatocytes.

①Introduction of imaging mass spectrometry (IMS)

Speaker : Hiroaki Aikawa (LSI Medience Corporation)

②Drug discovery support service using PDX (Patient-Derived Xenograft) model

Speaker : Shigenori Enoki (LSIM Safety Institute Corporation)
Chair : Hideomi Uchida (LSIM Safety Institute Corporation)

Sponsored by : LSIM Safety Institute Corporation

Overview

① IMS enables fine visualization of localization of administered drugs, their metabolites, and biological compounds in tissues as a two-dimensional image.
At this seminar, we introduce a part of our IMS technology using the MALDI FT-ICR mass spectrometry imaging system with an example of the pigmented rat eyeball administered with chloroquine.

② In collaboration with the National Cancer Center, we have established a PDX library derived from Japanese cancer patients (J-PDX) and developed a technological platform to utilize PDX in drug development and cancer treatment.
At this seminar, we introduce various services using J-PDX.