Morning Seminar M2-2 July 4 (Thu) 8:00-8:45 Room 2

Extended One-Generation Reproductive Toxicity Study (EOGRTS - OECD Test Guideline No. 443). The ECHA study design review project, recommendations and the Future of ED Evaluations

Speaker : Steve Renaut (Associate Director, Developmental and Reproductive Toxicology (DART))
Chair : Kazushi Tajima (Sales Director, Crop Protection & Chemicals, Labcorp)
Sponsored by : Labcorp Laboratories Japan K.K.

Overview

A summary of the ECHA review project evaluating the performance of the EOGRTS in terms of design, conduct, analysis, and reporting, and how the results support hazard assessment in the EU regulatory context. Labcorp will guide you through ECHA critical recommendations, review project final report and subsequent industry workshop to illustrate how these regulatory milestones have impacted upon study design. Furthermore, our second topic will cover an overview of endocrine disruptor assessment in Europe with different endocrine modalities and how weight of evidence assessments are conducted and impact on classification and labeling.

Morning Seminar M2-4 July 4 (Thu) 8:00-8:45 Room 4

Regulatory Considerations for Nonclinical Safety Evaluation of New Drugs

Speaker : Dr. Yongbin (Robert) Zhang (Chief Technology Officer & VP, JOINN Laboratories)
Chair : Zheng Yao
Sponsored by : JOINN Laboratories

Overview

1. FDA regulation tips and considerations of new drugs
2. Nonclincial safety considerations of new drugs
3. Case study

Application of Image Analysis and Artificial Intelligence in the Histology of Pharmaceutical, Chemical and Medical Device Studies

Speaker : Dr. Nils Warfving (AnaPath Services GmbH)

Chair : Yoshimasa Okazaki (AnaPath Services GmbH)

Sponsored by : AnaPath Services GmbH

Overview

The history of analyzing images of histological slides is old, but with the rapid technological development of imaging systems, computing power, and artificial intelligence the applications have become more widespread, and the potential is still growing. In this seminar, I will highlight numerus examples of classical image analysis and image analysis using more novel approaches of machine learning and artificial intelligence, using an illustrative approach, in for both regulatory and exploratory studies in the fields of pharmaceuticals, chemicals and medical devices.

Profiling Genome Editing Outcomes in Human iPS Cell Clones by CELL HANDLER™

Speaker : Yuichiro Miyaoka (Regenerative Medicine Project, Tokyo Metropolitan Institute of Medical Science)

Chair : Yoshinori Utsumi (New Business Development Center, Medical Device Business Division, Yamaha Motor Co., Ltd.)

Sponsored by : Yamaha Motor Co., Ltd.

Overview

Grasping outcomes of genome editing in individual cells can be critical for its applications. Therefore, we analyzed more than 2,600 genome-edited single human cultured cell clones (Takahashi, iScience 25:105619 2022). However, we could not isolate human iPS cell clones due to their high mortality. Therefore, we have developed a method to efficiently isolate genome-edited iPS cell clones by CELL HANDLER™. With this method, we have been able to analyze genome editing outcomes in more than 1,000 iPS cell clones and found that identical editing tends to occur in individual human iPS cells.

Lunchtime Seminar

Lunchtime Seminar L1-1 July 3 (Wed) 12:00-13:00 Room 1

Current status and issues of pyrogenicity testing

Speaker : Yuji Haishima (Medical Equipment Business Promotion Management Center / Medical Yokohama Lab, MIURA CO.,LTD.)

Chair : Kazuo Miyazaki (CEO, MiCAN Technologies, Inc.)

Sponsored by : MiCAN Technologies, Inc.

Overview

Strict quality control is required for pyrogen contamination in medical products. Pyrogen test with rabbits, endotoxin test and HCPT can be used to evaluate pyrogenicity. Since each method has a different reaction mechanism, advantage and disadvantage, ISO/TR 21582:2021 recommends that appropriate method should be selected according to the purpose of the test. It is also required to understand the properties of test samples.
In this lecture, classification of pyrogens, characteristics of each test method, and the problems and solutions regarding current pyrogenicity testing will be outlined.

Lunchtime Seminar L1-2 July 3 (Wed) 12:00-13:00 Room 2

①Frontiers in the evaluation of dependence liabilities and harmful effects of new psychoactive substances and their regulation

Speaker : Masahiko Funada, Professor, PhD (Shonan University of Medical Sciences, Department of Pharmacology)

②Comparison of Drug Dependency Testing Guidances in Japan, Europe and the United States

Speaker : Masahiko Iino (Research Administration Dept., Ina Research Inc.)

Chair : Kenichiro Hayashida (Nonclinical Company Drug Safety Research Laboratories, Pharmacology Department, Associate Director, Shin Nippon Biomedical Laboratories, Ltd.)

Sponsored by : Shin Nippon Biomedical Laboratories, Ltd.

Overview

① Health problems arising from abuse of new psychoactive substances (NPS) are an issue in Japan. In order to regulate NPSs, rapid evaluation of dependency and cytotoxicity is vital, and a comprehensive designation for NPSs with similar chemical structure can be an effective tool. In this seminar, we will introduce conditioned place preference and drug discrimination methods used to evaluate dependency in mice and a cell culture system used to evaluate cytotoxicity. We will also talk about the current status of NPS dependency and toxicity evaluation and the process of comprehensive designation.
② The Guidelines for Safety Pharmacology Studies (2001) recommend the consideration of "dependency potential" in a section under follow-up studies, and the ICH-M3(R2) Guidance (2010) states that evaluation of abuse potential should be considered for CNS-active drugs regardless of indication. Currently, the trilateral regions of Japan, Europe and the United States have each established their own non-clinical guidance for assessing the dependence/abuse potential of drugs. In this seminar, we will compare and explain the features of these 3 guidances for drug dependency testing.

Lunchtime Seminar L1-3 July 3 (Wed) 12:00-13:00 Room 3

Moving away from animal models: Organoids and MPS, the forefront of next-generation in vitro models

Speaker : Taro Nakazawa (Molecular Devices Japan KK)
Yoko Ejiri (Mimetas Japan KK)
C h a i r : Koji Udagawa (Molecular Devices Japan KK)
Sponsored by : Molecular Devices Japan KK / Mimetas Japan KK

Overview

Microphysiological Systems (MPS), such as Organ-on-Chip (OOC) and Organoids, are gaining increasing attention as a new research alternative to animal testing. These technologies can simulate the in vivo environment and reflect human physiological responses. Mimetas is a company with a proven history of working with many of the world's leading pharmaceutical companies over the last 10 years. Molecular Devices is working on revolutionary organoid automation with an AI system that can automatically determine the timing of passaging based on data. In our seminar, we will present our latest research and innovations in the use of organoids and OOC.

Lunchtime Seminar L1-4 July 3 (Wed) 12:00-13:00 Room 4

Sense and Nonsense of Bone Marrow Differentiation in Toxicology Studies

Speaker : Dr. Klaus Weber (AnaPath Services GmbH)
Dr. Kristel Kegler (AnaPath Services GmbH)
C h a i r : Yoshimasa Okazaki (AnaPath Services GmbH)
Sponsored by : AnaPath Services GmbH

Overview

Introduction: Bone marrow evaluation is a standard component of the toxicological investigation of routine studies. It involves mainly the routine evaluation of bone marrow sections. Bone marrow differentiation (BMD) is not specifically requested by the guidelines. It can, however, be a powerful tool in understanding mechanisms of pathogenesis and/or pharmacological actions.
Experimental Design: The evaluation of bone marrow (BM) sections and the sample preparation of smears are included in the standard protocols of every regulatory study. Evaluation of bone marrow smears is not mandatory, but if performed, there are different ways of evaluation including BMD.
Methods: Standard for BMD is the evaluation of smears stained by a May-Grünwald technique. The number of cells differentiated per smear impacts repeatedly the outcome of the results (i.e., 200 differentiated cells may cause a 50% variation when a BMD is repeated; whereas, 500 differentiated cells causes a 10% variation when a BMD is repeated). Species, age and sex-related differences might play a role and need to be known before conducting the BMD (i.e. control data are helpful in the interpretation of results).
Results: Age-related changes in adult animals are unusual, however, during pregnancy and lactation, females show different BMD values compared to other females of the same age. Side effects caused by the route of application need to be considered (e.g. inflammatory lesions due to emboli induced by liposomes). In studies performed with compounds that are previously known to affect BM (e.g., corticosteroids, platinum compounds, Doxorubicin), BMD could serve for the setting of thresholds for the applied doses. Similarly, in studies with colony stimulating

factors (e.g., EPO, G-CSF), BMD can demonstrate dose-dependent pharmacological effects and can also explain adverse side effects at higher doses. For several compounds, BMD can reveal unique findings involved in the pathogenesis of adverse side effects (e.g., PPAR agonists, alpha-methylase inhibitors, lipopolysaccharide, propofol).
Conclusion: Generally, the entire spectrum of lesions recorded in the dose group of interest needs to be considered together with the BMD results. Every inflammatory or degenerative change, test item induced or technically related to study procedures, may affect the results. Further, lesions and measured values of the hematology profile requires consideration. BMD is expensive and time-consuming and should be well justified before being initiated.
Impact Statement: The isolated diagnostic on either bone marrow sections or bone marrow smears may cause misinterpretation or even misdiagnosis. BMD may be an interesting tool for threshold effects, and, for some compounds, it might explain the pathogenesis of side effects.

Lunchtime Seminar L1-5 July 3 (Wed) 12:00-13:00 Room 5

Use of virtual control groups in nonclinical developmental, reproductive, and juvenile toxicity studies: are we ready yet?

Speaker : Elise M. Lewis, Ph.D. (Principal Director, Toxicology, Charles River)
Chair : Sayaka Odagriri (DSA SCIENTIFIC)
Sponsored by : Charles River

Overview

As nonclinical scientist, we have a responsibility not only to align with the 3Rs in animal-based research, but we must exercise responsible use of animals in our research practices. Virtual control groups have emerged as a tool with the promise of reducing animal use by replacing control group animals with virtual counterparts in nonclinical studies, where feasible. For developmental, reproductive, and juvenile toxicology, the conversation starts today. How do we advance as a community towards 21st century thinking and reduce, eliminate, or consider alternative approaches to facilitate data comparisons and interpretation through other means such as historical control data warehouses?

Lunchtime Seminar L1-6 July 3 (Wed) 12:00-13:00 Room 6

Exploring the Potential Application of Natural Language Processing AI to the Field of Safety Evaluation

Speaker : Makoto Miyamoto (Director, Lifescience AI Research Team, FRONTEO, Inc.)
Chair : Hiroyoshi Totoshiba (Executive Officer CTO, FRONTEO, Inc.)
Sponsored by : FRONTEO, Inc.

Overview

FRONTEO has developed its own natural language processing (NLP) AI engine, "KIBIT," and has already used it for novel drug target discovery, drug repositioning, biomarker discovery, their hypothesis generation, etc. The use of NLP technology in the field of toxicity, as well as in target discovery, would be useful for predicting and understanding clinical safety. Currently, the use of NLP technology in safety prediction/evaluation is still progressing. Therefore, in this seminar, we focus on drug safety evaluation and explore the effectiveness of using KIBIT in the safety assessment process.

Lunchtime Seminar L1-7 July 3 (Wed) 12:00-13:00 Room 7

Best Practices and Challenges in Avian and Aquatic Toxicology Testing

Speaker : Suzanne Z. Schneider, Ph.D (Associate Director of Aquatic Toxicology, Eurofins-Easton)
Patrick Hubbard, B.S. (Senior Scientist Avian Toxicology, Eurofins-Easton)
C h a i r : Satoshi Furukawa, PhD, DVM, DJSOT, DJSTP, DJCVP, FIATP (Nissan Chemical Corporation)
Sponsored by : Eurofins EAG Agroscience

Overview

This seminar will cover the following topics that Eurofins Easton conducts.
1. Avian toxicology studies: overview including hen metabolism and residue studies, and challenges faced.
2. Endocrine disruptor screening program
   i. Tier 1 screening: best practice
   ii. Tier 2 assays: overview of MEOGRT and LAGDA and challenges faced.
3. Panel discussion: emerging technologies and regulatory updates that might impact testing for registration.

Lunchtime Seminar L2-2 July 4 (Thu) 12:00-13:00 Room 2

①Imitation of in-vivo environment using multi-organ MPS “HUMIMIC”

Speaker : Hideo Takeda (PHYSIO MCKINA Co., Ltd.)
C h a i r : Chihiro Imai (PHYSIO MCKINA Co., Ltd.)

②Confocal Imaging of 3D Biological Tissue Using the HUMIMIC Chip

Speaker : Tetsuomi Takasaki (Nikon Solutions Co., Ltd.)
C h a i r : Kenji Miyamoto (Nikon Solutions Co., Ltd.)

Sponsored by : PHYSIO MCKINA Co., Ltd. / NIKON SOLUTIONS CO., LTD.

Overview

① When I talked to researchers who wanted to use MPS to imitate the in-vivo environment, I realized that their goals varied greatly depending on the researcher.Therefore, in this seminar, I will provide an overview of why MPS is attracting attention, what MPS can do, and global trends, using TissUse's multi-organ MPS ""HUMIMIC"" as an example.
② An observation example of TissUse’ s HUMIMIC Chip with Nikon’ s confocal microscope Eclipse Ti2E-AX will be introduced in this seminar. The HUMIMIC Chip has the characteristic of being able to co-culture multiple organoids. As an example, results of image acquisition regarding 3D culture samples of the intestine and bone marrow will be introduced. The cells’ polarity was confirmed by observation of the tight junction marker ZO-1 with the intestine model, and then, growth of the elongated MSCs expressing F-actin and circular HSCs was observed in the confocal images of the bone marrow model. In addition, the tissue-specific three-dimensional morphology and localization of markers were successfully observed with Ti2E-AX. The bone marrow model is expected to be used in Toxicity assessment of long-term administration of anticancer drugs, then contribute to drug discovery research as one of the alternative tools to animals.

Lunchtime Seminar L2-3 July 4 (Thu) 12:00-13:00 Room 3

Validation of a Zebrafish Developmental/Teratogenic Assay as a Qualified New Alternative Method (NAM) for its Regulatory use following the ICH S5(R3) Guideline

Speaker : Arantza Muriana (Co-founder, R&D Director, and CEO of USA, BBD BioPhenix S.L.U (Biobide))

Chair : Kazuhiro Shimomura, PhD (DAIICHI SANKYO CO., LTD. Vaccine Research Laboratories Group II, R&D Division)

Sponsored by : BioBide (BBD BIOPHENIX S.L.U.) / BioSafety Research Center Inc.

Overview

The ICH S5 (R3) Guideline on detection of reproductive and developmental toxicity of human pharmaceuticals, in its 2020 review proposes the use of new alternative methods (NAMs) as part of an integrated testing strategy to minimize the use of animals. The guideline provides a list that contains 29 positive compounds that have been shown to induce specific malformations or embryo-fetal lethality, plus 3 negative compounds to be used to support the qualification of an alternative assay.

Our research was focused on the predictivity of the zebrafish developmental toxicity assay. The Zebrafish embryo model is highly popular in toxicology and provides an ethically acceptable small-scale analysis system with the complexity of a complete organism. This model enables continuous developmental monitoring and has been widely used for the generation of relevant answers on mammalian developmental hazards. Our goal was to validate this model for its regulatory use by testing the 32 compounds indicated in the ICH S5(R3) Guideline. To determine the teratogenic risk of these pharmaceuticals, the presence of morphological alterations was analyzed at two different stages and the Teratogenic Indexes established as the ratio between LC50 and EC50 for each stage.

The 32 compounds were screened in the zebrafish developmental toxicity assay. 23 out of the 29 reference compounds were classified as teratogenic in zebrafish, 6 of them were false negatives initially, 4 were classified as inconclusive, 1 was classified as not toxic, and 1 compound resulted toxic for zebrafish embryos under the testing conditions.

The bioavailability analysis performed after the teratogenicity assay allowed the classifying properly several of the inconclusive compounds, increasing accuracy of the assay to 89.66%, sensitivity to 88.46%, and specificity and repeatability being 100%, compared to rodents and rabbits. Therefore, this is a well-integrated approach using New Alternative Methods to minimize the use of animals in developmental toxicity studies.

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

Case study of IND enabling toxicity study in KI animals and recent topic of FDA/CBER

Speaker : Hideo Fukui (Science Strategy & Planning, Axcelead Drug Discovery Partners, Inc.)

Chair : Hisaharu Yamada (Corporate Strategy Div., Mediford Corporation / Faculty of Pharmaceutical Sciences, Tokyo University of Science)

Sponsored by : Axcelead Drug Discovery Partners, Inc / Mediford Corporation

Overview

Regulatory authorities require non-clinical safety studies of new modality drugs and small molecule drugs to evaluate on-target and off-target toxicity. In particular, monkeys are often

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selected as a non-clinical animal species in new modality medicines. However, due to the high price of monkeys and import restrictions, it is difficult to conduct non-clinical studies, and it seems that the progress of many projects in Japan and overseas has been affected. Recently, successful cases of switching to toxicity studies using KI animals have begun to be disclosed. The case study and the recent topic of the FDA/CBER will be introduced.

Lunchtime Seminar L2-5 July 4 (Thu) 12:00-13:00 Room 5

Early de-risking and prediction of human safety in drug discovery

Speaker : Paul Walker Ph.D. (VP Head of Toxicology and Innovation Efficiency)
Chair : Masaaki Yatsu (Authorized Agent, Cyprotex Discovery Limited)
Sponsored by : Cyprotex Discovery Limited

Overview

We present *in vitro* approaches and associated safety cascades to de-risk small chemical entities (NCEs) in early drug discovery. Using *in vitro* models of human relevance such as human liver microtissues (hLiMTs) and cardiac tri-culture organoids. Human safety prediction is determined with combining these *in vitro* models with 3D high content imaging (HCI) and full genome transcriptomics (Tx). AI/ML models are utilised to determine a human safety risk profile.

Lunchtime Seminar L2-6 July 4 (Thu) 12:00-13:00 Room 6

Unlocking the Power of AI and Advanced Analytics for Data-Driven Decision Making in Drug Safety: A Case Study with Unstructured and Structured Safety Data in PharmaPendium

Speaker : Thomas Vargues (Elsevier)
Chair : Takahiro Ohyama (Elsevier Japan)
Sponsored by : Elsevier Japan K. K.

Overview

The pharmaceutical industry generates vast amounts of safety data from various sources, including clinical trials, post-marketing surveillance, and regulatory submission (FDA, EMA, PMDA) documents. However, much of this data is unstructured (labels, full packages, advisory committee reports etc…) and difficult to analyze, making it challenging to identify potential safety issues and make informed decisions. In this talk, we will explore how AI and advanced analytics can be used to unlock the power of unstructured and structured safety data in PharmaPendium for data-driven decision making in drug safety. We will discuss how AI techniques, such as natural language processing (NLP) and retrieval augmented generation (RAG), can be used to analyze unstructured regulatory documents and extract safety-related information to improve safety monitoring and compliance with regulatory requirements. Additionally, we will explore how structured safety data in PharmaPendium, such as safety related adverse drug reactions (ADRs) data and pharmacokinetic data, can be analyzed using advanced analytics and visualization to optimize drug development strategies and prioritize safety testing efforts.

1. The New Approach for Carcinogenic Evaluation — Accumulate More Information for Weight of Evidence in Early Stage of Drug Discovery

Speaker : Chun-Yao Lee, Ph.D. (Director of Molecular Pharmacology, Managing Director, Eurofins Discovery Taiwan)

2. Can We Better Predict Potential Drug Toxicity Using the BioMAP® Translational Biology Platform to Help Reduce Attrition or Withdrawal?

Speaker : Alastair J. King, Ph.D. (Head of Biology, Eurofins Discovery)

Chair : Makoto Imatachi (Regional Director of Business Development Japan/Korea, Eurofins Discovery)

Sponsored by : Eurofins Discovery

Overview

1. ICH S1B (R1) guidance introduces a Weight of Evidence (WoE) approach using varieties of evidence—in vitro, in vivo, and clinical data to assess carcinogenic potential. Oncogenic responses are triggered by chemical exposure via inflammation, immune modulation, and cellular damage, which led Eurofins Discovery to develop a panel integrating 30 key targets to assess mechanisms and identify non-genotoxic carcinogens. In addition to this, a Cell Transformation Assay has been developed to evaluate carcinogen-induced malignant phenotypes, incorporating an AI-based image analysis module to improve objectivity. In vitro assays as alternatives to animal modeling remain crucial tools for understanding and mitigating carcinogenic risk.
2. Despite the availability of many robust, well-qualified in vitro safety and toxicity assays, drug failure in clinical testing due to unanticipated toxicity is still disappointingly high. However, these assays do not sufficiently model the human body's intricate biology well enough to more reliably predict such adverse outcomes. We will discuss the use of complex cell co-culture models and data analytics to identify potential toxicity signatures in a translational and clinically relevant in vitro platform. This will be highlighted using case studies with approved and withdrawn drugs, to illustrate how a reduction in the occurrence of unforeseen toxicities could lower attrition and withdrawal.

New Method for Calculating Safety Margin in Cardiovascular Safety Evaluation per New ICH S7B Guideline Q&As

Speaker : Atsushi Sugiyama (Department of Pharmacology, Faculty of Medicine, Toho University; Yamanashi Research Center of Clinical Pharmacology)

Hiroshi Matsukawa (Kashima laboratories, Mediford Corporation)

Chair : Hideomi Uchida (Kashima laboratories, Mediford Corporation)

Sponsored by : Mediford Corporation

Overview

Drug-induced cardiotoxicity is a major concern in drug development, necessitating reliable data for appropriate cardiovascular safety assessment. In recent years, the newly developed ICH S7B Guideline Q&As, which address the evaluation of adverse effects of drugs on the cardiovascular system critical for life support, have provided best practices for integrated clinical and non-clinical risk assessment, significantly transforming the ways of conducting

cardiovascular assessment. In the first half of the seminar, we will explain the evolution from the latest ICH S7B Q&As Stage 1 to Stage 2 and the evaluation of anticancer agents. In the second half, we focus on the hERG assay, which plays a central role in in vitro assessments, and present the work we have been conducting. In addition to actual methods for data acquisition and analysis with reference drugs (moxifloxacin, ondansetron and dofetilide), we provide details on how to calculate the hERG safety margin associated with a 10 ms QTc prolongation and pooled safety margin, both of which have attracted considerable interest (submitted).

Lunchtime Seminar L3-2

July 5 (Fri) 12:00-13:00 Room 2

①Human hepatocytes usable for the industrial implementation of microphysiological systems

Speaker : Seiichi Ishida (Division of Applied Life Science, Graduate School of Engineering, Sojo University)

②Mitigation strategy of drug-induced liver toxicity by utilizing PXB-cells in lead optimization stage

Speaker : Tomoya Yukawa (Takeda pharmaceutical company limited, Research, Drug Safety Research and Evaluation)

Chair : Tatsuya Matsumi (PhoenixBio Co., Ltd.)

Sponsored by : PhoenixBio Co., Ltd.

Overview

Dr. Seiichi Ishida, Sojo University, and Dr. Tomoya Yukawa, Takeda Pharmaceutical Company will present examples of hepatotoxicity evaluation using fresh human hepatocytes (PXB-cells) isolated from the chimeric mice with humanized liver.

Lunchtime Seminar L3-3

July 5 (Fri) 12:00-13:00 Room 3

Collaborating with CROs: The Prospects of Novel Medical Research Enabled by Bio 3D Printing

Speaker : Shizuka Akieda (CEO, Cyfuse Biomedical K.K.)

Chair : Mayumi Kano (Sales Planning Department, Nihon Bioresearch Inc.)

Sponsored by : Nihon Bioresearch Inc.

Overview

In recent years, regenerative medicine and drug discovery research has accelerated using Bio 3D printing technology. In the field of regenerative medicine, 3D tissue is being used in transplantation, and in the field of drug discovery, its use as a tool for evaluating the kinetics and efficacy of drugs is accelerating.

3D tissues of Cyfuse are created using only cells, and clinical trials for nerve, cartilage, blood vessel regeneration, etc. are being conducted. Additionally, Cyfuse has initiated the sale of human 3D mini livers for drug discovery.

We would like to introduce our partnership strategy and product development with NBR, from basic research to clinical development to commercialization.

Lunchtime Seminar L3-4 July 5 (Fri) 12:00-13:00 Room 4

Mycobacterium caprae infection in imported laboratory Cynomolgus macaques (*Macaca fascicularis*): what have we learned from diagnosis and management from an outbreak caused by an emerging mycobacterial species?

Speaker : Dr. Kristel Kegler (AnaPath Services GmbH)
Dr. Klaus Weber (AnaPath Services GmbH)
Chair : Yoshimasa Okazaki (AnaPath Services GmbH)
Sponsored by : AnaPath Services GmbH

Overview

Emerging mycobacterial species causing tuberculosis (TB) are a major challenge for diagnosis and surveillance. Here we present a natural outbreak caused by *Mycobacterium caprae* in imported cynomolgus macaques (*Macaca fascicularis*) occurring at AnaPath Research S.A.U. (APR). Despite repetitive Intradermal Tuberculin Test (IDT) at the breeding farm and European quarantine station, 10 out of 114 animals had gross and histologic findings compatible with TB confirmed by PCR and culture, and 4 animals had early infection diagnosed only by histopathology. Affected were three regulatory toxicity studies and stock animals, and one worker had positive IDT reaction. *M. caprae* spoligotype SB1622 was identified tracing the infection to Asia. Diagnostic approaches used at APR including IDT, Interferon-γ release assay, and ultrasound were sensitive in detecting chronic-active cases but failed to identify early infection. Histologically, *M. caprae* induces a distinctive type of granuloma characterized by lack of capsule with high rate of rupturing into airways, and presence of a specific population of spindle cells forming glomeruloid-like structures at the periphery of the granuloma. Metagenomics used to identify possible co-infection with bacteria or viruses aiming to explain these characteristic features failed to demonstrate any concomitant microorganism. Hence, solely infection with *M. caprae* elicits a distinctive type of granuloma with high transmission potential. Nonetheless, all sanitary measures implemented were effective in eradicating the disease at the facility.

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

Addressing Unmet Needs for Reproductive, Developmental, and Juvenile Toxicology Testing using Advanced Therapies and Technologies

Speaker : Elise M. Lewis, Ph.D. (Principal Director, Toxicology, Charles River)
Chair : Hiroyuki Minami, Ph.D. (DSA SCIENTIFIC)
Sponsored by : Charles River

Overview

The field of developmental, reproductive, and juvenile toxicology have evolved over decades to allow scientists and clinicians to address unmet needs that stem from inborne errors in development. Though the ICH guidelines pertaining to reproductive, developmental, and juvenile toxicity explicitly excludes cellular therapies, gene therapies, and tissue-engineered products from the testing guidelines, the safety of these products must be addressed in nonclinical settings to ensure efficacy and patient safety. To meet future needs we are realizing that the understanding the molecular basis of drug interactions with the developing embryo will allow us to better predict the hazard from exposure.

Lunchtime Seminar L3-6 July 5 (Fri) 12:00-13:00 Room 6

The cynomolgus macaque in nonclinical safety testing: Relevance of animal origin and insights into intrathecal dosing of antisense-oligonucleotides

Speaker : Lars Mecklenburg, DVM, PhD, DACVP, FIATP (Executive Director,Global Safety Assessment, Labcorp Early Development)

Chair : Michiko Fukuda (Business Development Director / Early Development, Labcorp)

Sponsored by : Labcorp Laboratories Japan K.K.

Overview

Cynomolgus macaques are the predominant species for nonclinical safety testing of biopharmaceuticals. The recent shortage in animal supply urges to optimize their use. This presentation reviews the impact of geographical animal origin in relation to selected endpoints that are relevant in nonclinical safety testing. The presentation will also discuss intrathecal dosing in macaques as an increasingly common route of administration for antisense oligonucleotides that target central nervous system diseases. We present typical clinical observations and pathology findings in such studies and explain their relevance in preclinical safety testing.

Lunchtime Seminar L3-7 July 5 (Fri) 12:00-13:00 Room 7

Support for Life Science and Drug Discovery Research by AMED BINDS and Utilization of Incucyte® at the Center for Supporting Drug Discovery and Life Science, Osaka University

Speaker : Kazutake Tsujikawa (Graduate School of Pharmaceutical Sciences, Osaka University)

Chair : Shohei Shimonishi (Sartorius Japan K.K.)

Sponsored by : Sartorius Japan K.K.

Overview

AMED Basis for Supporting Innovative Drug discovery and life Science research (BINDS) is a research support program that aims to link the results of Japan's outstanding life science research to drug discovery research. The Center for Supporting Drug Discovery and Life Science. Grad. Sch. Pharm. Sci., Osaka University has been selected for BINDS and has established a system to seamlessly support life science and drug discovery research. In this seminar, I will introduce our BINDS support system as well as examples of Incucyte®'s utilization in toxicity evaluation using spheroids and organoids.