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**Plenary Session:**

**Update on emerging technologies for regulatory application — A global perspective**

Session Co-Chairs: [William Slikker, Jr.](#) (NCTR/FDA, USA) and Marta Hugas (EFSA-EU)

**Opening Remarks:**

- [Francis Collins](#) (Director, NIH, USA)
- [Bernhard Url](#) (Executive Director, EFSA-EU)
- [Elke Anklam](#) (Principal Advisor to the JRC-EC Director General (JRC-EC)
- [Masamitsu Honma](#) (Deputy Director General, National Institute of Health Sciences, Japan)
- [Margaret Hamburg](#) (Foreign Secretary, National Academy of Medicine, USA)

<p><b>Track A</b></p> <p><i>Artificial Intelligence for Drug Development and Risk Assessment</i></p> <p>Co-Chairs: <a href="#">Weida Tong</a> (NCTR/FDA, USA) and Arnd Hoeveler (JRC-EC)</p>	<p><b>Track B</b></p> <p><i>OMICS, Biomarkers, and Precision Medicine</i></p> <p>Co-Chairs: <a href="#">Neil Vary</a> (CFIA/ACIA) and <a href="#">Primal Silva</a> (CFIA/ACIA)</p>	<p><b>Track C</b></p> <p><i>Microphysiological Systems (MPS) and Stem Cells</i></p> <p>Co-Chairs: <a href="#">William Slikker, Jr.</a> (NCTR/FDA, USA) and Elke Anklam (JRC-EC)</p>
<p><a href="#">Henry Kautz</a> (NSF and U Rochester, USA): <i>Using AI to improve food and drug safety</i></p>	<p><a href="#">Mirko Rossi</a> (EFSA, EU): <i>Whole Genome Sequencing advances for biological risk assessment</i></p>	<p><a href="#">Hajime Kojima</a> (NIHS, Japan) <a href="#">Seiichi Ishida</a> (NIHS, Sojo University, Japan): <i>Challenge of standardization in the AMED-MPS project</i></p>
<p><a href="#">Akihiko Hirose</a> (NIHS, Japan): <i>Development of risk assessment support database system</i></p>	<p><a href="#">Sir Munir Pirmohamed</a> (Inst. of Translational Med, U of Liverpool, UK): <i>Pharmacogenomics &amp; precision medicine</i></p>	<p><a href="#">Alexandre Ribeiro</a> (CDER/FDA, USA): <i>Establishing strategies to evaluate micro-physiological Systems for drug development</i></p>
<p><a href="#">Blanka Halamoda Kenzaoui</a> (JRC, EU): <i>Automatic tools for systematic review of safety effects of nanomaterials</i></p>	<p><a href="#">Tim Mercer</a> (Garven Institute, Australia): <i>Liquid biopsy and SEQC2</i></p>	<p><a href="#">A.J.M. (Janny) van den Eijnden-van Raaij</a> (Institute for Human Organ and Disease Model Technologies): <i>Organ-on-chip in Europe</i></p>
<p><a href="#">Stefan Platz</a> (AstraZeneca, UK): <i>AI for safety in drug development</i></p>	<p><a href="#">Parastoo Azadi</a> (U of Georgia, USA): <i>Glycobiology of SARS-CoV-2 and its implications for therapeutics and vaccine development</i></p>	<p><a href="#">Suzanne Fitzpatrick</a> (CFSAN/FDA, USA): <i>Advancing alternatives at FDA</i></p>
<p><a href="#">Philippe Girard</a> (Switzerland, Swissmedic): <i>A pilot study to detect safety signals using artificial intelligence</i></p>	<p><a href="#">Paul Skipp</a> (U of Southampton, UK): <i>Pathway biomarkers for precision medicine</i></p>	<p><a href="#">Kit Parker</a> (Harvard University, USA): <i>Development of multi-scale in vitro models or studying engineered nanomaterial toxicity</i></p>

<p style="text-align: center;"><b>Track A</b></p> <p><b>Artificial Intelligence for Public Health</b></p> <p>Co-Chairs:  <b>Arnd Hoeveler</b> (JRC-EC) and  <b>Weida Tong</b> (NCTR/FDA, USA)</p>	<p style="text-align: center;"><b>Track B</b></p> <p><b>OMICS, Biomarkers, and Precision Medicine</b></p> <p>Co-Chairs:  <b>Richard Beger</b> (NCTR/FDA, USA) and  <b>Susan Sumner</b> (UNC)</p>	<p style="text-align: center;"><b>Track C</b></p> <p><b>Microphysiological Systems (MPS) and Stem Cells</b></p> <p>Co-Chairs:  <b>Elke Anklam</b> (JRC-EC) and  <b>William Slikker, Jr.</b> (NCTR/FDA, USA)</p>
<p><b>Yinyin Yuan</b> (The Institute of Cancer Research, London, UK):  <i>AI for digital pathology</i></p>	<p><b>Richard Beger</b> (NCTR/FDA, USA):  <i>Current concepts in metabolomics: Quality control, biomarkers, and precision medicine</i></p>	<p><b>Uwe Marx</b> (CEO, TissUse):  <i>Microphysiological systems - Status of industrial adoption and regulatory acceptance for candidate decision making</i></p>
<p><b>Robert Ball</b> (CDER/FDA, USA):  <i>AI to enhance Sentinel</i></p>	<p><b>Susan Sumner</b> (UNC, USA):  <i>Metabolomics reveals biomarkers of opium use disorder, and informs nutritional intervention strategies</i></p>	<p><b>Kyung Sung</b> (CBER/FDA, USA):  <i>Microphysiological systems to assess the functional capacity of cellular therapy products</i></p>
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<p><b>Weida Tong</b> (NCTR/FDA, USA):  <i>Artificial intelligence for regulatory science research</i></p>	<p><b>Reza Salek</b> (IARC, France):  <i>Metabolomics and Exposomics applications in cancer epidemiological research</i></p>	<p><b>Clive Niels Svendsen</b> (Cedars-Sinai Medical Center, USA):  <i>Combining iPSC's and MPS technology to enhance regulatory decisions for neurological diseases</i></p>
<p><b>Liang Peng</b> (Center for Medical Device Evaluation, China):  <i>Regulatory science of medical device and new evaluation concept of artificial intelligence supervision in China</i></p>	<p><b>Hairuo Wen</b> (National Institutes for Food and Drug Control [NIFDC], China):  <i>Preclinical safety evaluation of chimeric antigen receptor-modified T cells against CD19 in NSG mice</i></p>	<p><b>Ivan Rusyn</b> (Texas A&amp;M, USA):  <i>Reproducibility of the MPS: Role of the cell sources</i></p>

## Plenary Session:

### *Update on emerging technologies for regulatory application — A global perspective*

Session Co-Chairs: [Marta Hugas](#) (EFSA-EU) and William Slikker, Jr. (NCTR/FDA, USA)

- [Steve Hahn](#) (Commissioner, US-FDA)
- [Chris Austin](#) (Director, NCATS/NIH, USA)
- [Denise Hinton](#) (Chief Scientist, US-FDA)
- [Primal Silva](#) (Chief Science Operating Officer, Science Branch, Canadian Food Inspection Agency)
- [Anand Shah](#) (Deputy Commissioner for Medical and Scientific Affairs, US-FDA)
- [George Kass](#) (EFSA-EU)

<b>Track D</b> <b>Bioimaging</b> Co-Chairs: <a href="#">Serguei Liachenko</a> (NCTR/FDA, USA) and <a href="#">John Waterton</a> (U. of Manchester)	<b>Track E</b> <b>Microbiome</b> Co-Chairs: <a href="#">Reinhilde Schoonjans</a> (EFSA-EU) and <a href="#">George Kass</a> (EFSA-EU)
<a href="#">Serguei Liachenko</a> (Director of Bioimaging, Division of Neurotoxicology, NCTR/FDA, USA): <i>MRI biomarkers of neurotoxicity</i>	<a href="#">Martin Iain Bahl</a> (Technical University of Denmark, DK): <i>The needs to consider human microbiome in chemical risk assessment</i>
<a href="#">Ira Krefting</a> (Division of Imaging and Radiation Medicine, CDER/FDA, USA): <i>FDA's approach to gadolinium-based contrast agent safety</i>	<a href="#">Paul Carlson</a> (CBER/FDA, USA): <i>The functioning and variability of the healthy human microbiome at the systems level and study its alteration in disease</i>
<a href="#">John Waterton</a> (Professor of Translational Imaging, University of Manchester/Bioxydyn Ltd): <i>The development and validation of translational imaging biomarkers of harm or lack-of-harm</i>	<a href="#">Joseph V Rodricks</a> (Ramboll): <i>Food additives and their impact on the gut microbiota</i>
<a href="#">Timothy McCarty</a> (VP & Head, Digital Medicine & Translational Imaging, Pfizer, Inc.): <i>What is the role of imaging to assess drug safety?</i>	<a href="#">Carmen Peláez</a> (Spanish Council for Scientific Research, CSIC, Spain): <i>Models to study the gut microbiome in risk assessment</i>
<a href="#">Yan Liu</a> (CMO, Median Technologies): <i>Next generation AI-based imaging biomarkers for precision medicine</i>	<a href="#">Chris Mason</a> (Cornell Medical School, USA): <i>Developing MetSub consortium to survey detect disease early based on the microbial data collected from subway</i>

## Workshop 1

### *Artificial Intelligence (AI)/Machine Learning (ML)*

Co-Chairs:

**Shraddha Thakkar** (CDER/FDA, USA) and Weida Tong (NCTR/FDA, USA)

**Jae Kim** (NCTR/FDA, USA):

*AI for natural language processing*

**Russ Wolfinger** (SAS):

*Statistical consideration for reproducible AI*

**Viswanath Devanarayan** (GSK):

*Actionable biomarker signatures for drug development*

**Shraddha Thakkar** (CDER/FDA, USA):

*AI/ML for predicting drug-induced liver injury (DILI)*

## Workshop 2

### *Nanotechnology/Nanoplastics*

Co-Chairs:

**Anil Patri** (NCTR/FDA, USA) and **Arnd Hoeveler** (JRC-EC)

**Co-Chairs Anil Patri and Arnd Hoeveler**

**RADM Denise Hinton** (Chief Scientist, OC, US-FDA): *Nanotechnology at FDA; Unveiling of Nanotechnology Task Force Report*

**Mihail C. Roco** (NSF): *Global outlook in nanotechnology*

**Lisa Friedersdorf** (NNCO): *Nanotechnology in the US*

**Piotr Grodzinski** (National Cancer Institute): *Cancer Nanotechnology*

**Denise Mitrano** (ETH Zurich, Swiss): *Nanoplastics*

**Nizar Benismail** (Nestle, France): *Microplastics analyses in clean environmental waters and drinking waters: Analytical challenges for methodology and opportunities for standardization*

**Arnd Hoeveler** (JRC-EC): *Microplastics and nanoplastics*

**Anil Patri** (NCTR/FDA, USA): *US Interagency efforts on microplastics and nanoplastics*

### *Conclusions and Appreciation*

GSR20 Co-chairs: Marta Hugas (EFSA-EU) and **William Slikker, Jr.** (NCTR/FDA, USA)



**\*\*VIEW RECORDED Q&A SESSION\*\***

<b>8:00-8:40 am CST</b>	<b>Track A – Artificial Intelligence</b>
<b>8:40-9:20 am CST</b>	<b>Track B – OMICS, Biomarkers, and Precision Medicine</b>
<b>9:20-10:00 am CST</b>	<b>Track C – Microphysiological Systems (MPS) and Stem Cells</b>
<b>10:00-10:20 am CST</b>	<b>Track D – Bioimaging</b>
<b>10:20-10:40 am CST</b>	<b>Track E – Microbiome</b>
<b>10:40-11:00 am CST</b>	<b>Workshop 1 – Artificial Intelligence (AI)/Machine Learning</b>
<b>11:00-11:20 am CST</b>	<b>Workshop 2 – Nanotechnology/Nanoplastics</b>



**\*\*VIEW RECORDED Q&A SESSION\*\***

## **Track A: Artificial Intelligence and Machine Learning**

(Co-Chairs: Weida Tong and Arnd Hoeveler)

Artificial Intelligence (AI) is the training of machines to think and behave like humans, consisting of a wide range of statistical and machinal learning approaches used to learn from existing data/information to predict future outcomes. A new AI methodology, deep learning, is even capable of extracting complex patterns from a new data stream and format (e.g., treat the chemical structure as graphic input and image data) which has been increasingly used in the regulatory context. The concept of AI was introduced in the 1950s and its critical role in a broad range of applications—particularly in regulatory science concerning food and drug safety—has yet to be realized. Besides the possibilities that AI offers in automating current regulatory science workflows, 21<sup>st</sup> century regulatory science has increasingly used new tools, particularly alternative methodologies. Alternative methodologies generate information beyond conventional tabular “data”—such as imaging data—where AI offers both opportunities and challenges. This track will discuss the basic concept and methodologies of AI applied in regulatory science and will include real-world examples. In addition, the AI guiding principle and best practice regarding regulatory research will be discussed, including how to assess and evaluate AI-based products and how to develop and implement AI-based application to improve the agencies’ functions. Therefore, the current thinking and ongoing efforts with various stakeholders in applying AI in regulatory science research will be discussed with respect to the areas of:

- Drug and food safety
- Clinical application (e.g., prognosis and diagnosis)
- Precision medicine
- Biomarker development
- Natural language processing
- Omics and imaging data analysis
- Regulatory science application
- Methodologies: validation and interoperability
- AI regulation, ethics, and policy

## **Track B: Omics, Biomarkers, and Precision Medicine in Regulatory Science**

(Co-Chairs: Neil Vary and Rick Beger)

Molecular biology specializations in “omics” (genomics, proteomics, and metabolomics) is being incorporated into regulatory science laboratories, such as food production and precision medicine, as these scientific fields continue to evolve. These specializations are being used to identify specific biomarkers of interest, such as antibiotic resistance in foodborne pathogens or targeted genetic sequences and metabolites used in precision medicine. The adoption of genomics analyses of pathogens in microbiological laboratories, including regulatory

laboratories, is becoming common. Genomics is now being used to confirm the identify of pathogens, characterizing them by matching clinical isolates to foodborne isolates and identifying specific genetic sequences of interest (e.g., toxin genes, antimicrobial resistance [AMR] genes, and serotypes). Genomics is also used to detect genetic disorders in precision medicine. Similarly, proteomic approaches are beginning to be explored and integrated in regulatory laboratories. Proteomics can be used for food traceability and quality, as well as food safety to screen for foodborne pathogens or allergens with high sensitivity and specificity. Currently, metabolomics is used to diagnose complex metabolic diseases, and the field is growing rapidly. This track will focus on the evolving “omics” fields and how they are being used by regulatory bodies through incorporation into regulatory science laboratories, and how they can be further exploited as these fields continue to mature.

### **Track C: Microphysiological Systems and Stem Cells as Predictive Tools**

(Co-Chairs: William Slikker, Jr. and Elke Anklam)

Emerging technologies are playing a major role in the creation of new approaches to assess the safety of both foods and drugs. However, the integration of emerging technologies in the regulatory decision-making process requires rigorous assessment and consensus amongst national and international partners in various research communities. The need for advanced approaches to allow for faster, less expensive, and more predictive methodologies is becoming increasingly clear. In addition, the strengths and weaknesses of each new approach needs to be systematically examined. In pursuit of the goal to simulate a human—at least in terms of chemical effects, safety evaluation, and the practice of regulatory science—a system of cells or tissue may be examined under strict criteria to reflect the human condition. These “human-on-a-chip” and “human organ construct” microphysiological systems (MPS) are an emerging technology that has the potential to correlate in vivo with in vitro and simulate human organ systems. Even though the use of human cells may be an enormous advantage because there is no need to extrapolate across species, there is the requirement that different cell types be characterized in terms of developmental stage and functional capacity.

These microphysiological systems have the potential to be used to 1) assess basic biology and physiology, 2) assess the pharmacology and toxicology of drugs and chemicals, 3) study organ–organ interactions, and/or, 4) be used as a human disease model. With the use of human cells there is no need to extrapolate across species, but even so, there may be the requirement that different cell types interact in a three-dimensional relationship to provide prediction of the intact human. Another important consideration for simulating human outcome is the quantification of chemical exposure. Absorption, distribution, metabolism, and elimination are features that need to be considered. The linking together of several organs-on-a-chip to simulate an intact human-on-a-chip is a possibility with well-constructed and well-tuned fluid dynamic systems. Microfluidic control of multiple organ systems is possible, and models envisioned by bioengineers have been developed. The challenges include the requirement for each organ type to have its own specialized media while also being connected so that the human circulatory system can be replicated.

## **Track D: Bioimaging in Regulatory Science**

(Co-Chairs: Serguei Liachenko and John Waterton)

In-vivo imaging techniques have become powerful tools in drug development. They can help 1) investigate distribution of labeled compounds throughout the body, 2) determine pre-existing pathologies in subjects selected for toxicity or efficacy studies, or 3) monitor pathologies throughout the in-life phase of such studies. This session will give an overview of the potential and actual use of techniques—such as magnetic resonance imaging (MRI), positron emission tomography (PET), computed tomography (CT), and others—in drug research and development and other regulatory-science applications across multiple therapeutic areas and various settings. A panel of leading experts from the pharmaceutical industry, contract research organizations, academia, and government agencies will outline examples on how such technologies have supported or may support regulatory decision-making and have assisted in addressing specific efficacies, toxicities, or background lesions. Knowledge of the above technologies and their applicability in preclinical and clinical studies will help investigators to develop improved study designs and to refine existing approaches according to the principles of the 3 Rs.

## **Track E: Microbiome**

(Co-Chairs: Reinhilde Schoonjans and George Kass)

Microbiome refers collectively to communities of microorganisms and their genomes in a defined environment, such as in humans, plants, animals, soils and aquatic environments. Microbiomes include many life forms like bacteria, archaea, viruses, or eukaryotic microorganisms (such as protists, fungi, and algae). Because of their ubiquitous presence, microbiomes occupy a central position in the “One Health” framework, which approaches human, animal, and plant health from a new integrated perspective.

Many recent research projects have offered new insights into the associations between microbiomes and a wide range of diseases. Ongoing studies demonstrate that microbiome structures and dynamics across the food system (from soils and marine habitats to plants, animals, and the foods produced from them) can have both direct and indirect effects on human/animal microbiomes and health, in addition to their obvious impact on food quality, safety, and sustainability (CNBBSV concept paper, 2019).

The microbial ecosystem most explored is the microbiome of the human gut. This microbial community interacts with the host and the intestinal mucosa. There is mounting evidence on the role of gut microbiome in several enteric and systemic disorders in humans. Interactions between the microbiome and an environmental chemical modulator might influence host health through direct chemical-induced changes. The capacity of chemical modulators to induce

microbiome changes in animals has been demonstrated with a variety of pesticides, metals, artificial sweeteners, and drugs.

In the absence of explicit legal requirements to account for microbiome in risk assessment, there is no guidance nor methodology in place to systematically account for possible effects on/by microbiome on human/animal/plant health in risk assessments of regulated substances. The main objective of this session is to discuss with regulatory scientists around the world the risk assessment questions to be asked and the appropriate starting points for meaningful action in this field.

Speakers will share their insights about the impact on/by microbiomes when exposed to chemicals or biologicals. Furthermore, the strengths and weaknesses of methodologies that may be useful for risk or benefit assessment need to be discussed. As microbiome assessment lies at the intersection of chemical and biological risk assessment, it will provide opportunities for these two disciplines to collaborate and foster mutual understanding on their respective risk evaluations.