
The 11th Global Summit on Regulatory Science (GSR21)

Virtual Conference



Regulatory Sciences for Food/Drug Safety with Real-World Data and Artificial Intelligence (AI)

OCTOBER 4-6TH 2021 (7:00 – 10:00 AM CT)

Sponsored by: Global Coalition for Regulatory Science Research (GCRSR)

Co-hosted by:

National Center for Toxicological Research, U.S. Food & Drug Administration (FDA)

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About GCRSR

The Global Coalition for Regulatory Science Research (GCRSR) was established in 2013, under the leadership of the U.S. Food and Drug Administration (FDA). Its membership is comprised of regulatory bodies from various countries including the European Union (EU). GCRSR has forged international partnerships and collaborations that focus on adopting emerging technologies to improve regulatory-science research on the safety and efficacy of foods and drugs. To that end, it facilitates and promotes the development of regulatory science research as a tool for advancing regulatory science in a manner that is directly applicable to the public health goal of safe food and therapeutic products. GCRSR has sponsored and hosted the annual GSRS conference since 2013 as a platform for improved communication among international regulators.

About GSRS

The Global Summit on Regulatory Science (GSRS) is an international conference for discussion of innovative technologies and partnerships to enhance translation of basic science into regulatory applications within the global context. The conference provides an opportunity for scientists from government, industry, and academic-research communities to objectively assess the utility of emerging technologies (such as nanotechnology, imaging, omics for translational science, personalized medicine, medical product safety, and food safety) for addressing regulatory-research questions and to discuss the best way to translate these technologies into real-world applications. The conference provides a platform where regulators, policy makers, and bench scientists from various countries can exchange views on how to develop, apply, and implement innovative methodologies into regulatory assessments in their respective countries, as well as harmonizing strategy via global collaboration. To engage the global community to address regulatory-science research and training needs, GSRS is held in different countries on an annual basis.

GSRS21 Program at a Glance

**All times are in U.S. Central Standard Time*

Day 1 October 4 th	Day 2 October 5 th	Day 3 October 6 th
7:00 – 7:30 am Opening Remarks Keynote	7:00 – 7:20 am Keynote	7:00 – 10:00 am Workshop on Data Analytical Tools for drug and food review by global regulatory agencies
7:30 – 9:30 am Digital Health and Safety	7:20 – 9:20 am Artificial Intelligence and Machine Learning	
9:30 – 10:00 am Is Regulatory Science Ready for AI?	9:20 – 9:50 am Is Regulatory Science Ready for AI?	
	9:50 – 10:00 am Closing Remarks	

Day 1 Overview: The program starts with opening remarks by Janet Woodcock (U.S. FDA Acting Commissioner) and the keynote address by Frank Yiannas (U.S. FDA Deputy Commissioner), followed by six international speakers and a LIVE Q & A session. The program will end with a LIVE debate on the topic, “Is Regulatory Science Ready for AI?” where two debaters take one position of either “support” or “against” the motion and their position will be reversed in the next day’s debate on the same topic.

Day 2 Overview: The program starts with a keynote presentation by Stephen Quest (General Director at Joint Research Center, EU), followed by six international speakers and a LIVE Q & A session. The program will end with a LIVE debate on the same topic as Day One – “Is Regulatory Science Ready for AI?” – except both debaters will argue the reversed positions compared to Day One. The main event ends with closing remarks.

Day 3 Overview: The workshop will host the LIVE demonstration of data analytics tools by FDA, European Medicines Agency (EMA), and Swissmedic. These tools have been developed (or are being developed) to facilitate the regulatory application in the corresponding agencies.

**GCRSR Bioinformatics Working Group and GRS21 Scientific
Program Committee**
(not in a specific order)

USA	William Slikker, Jr.	FDA/NCTR
	Shraddha Thakkar (Exec Sec)	FDA/CDER
	Weida Tong (Chair)	FDA/NCTR
Canada	Burton Blais (Technical Team Lead)	CFIA
	Primal Silva (Co-Chair)	CFIA
Australia	Scott Crerar	FSANZ
	Ben Daughtry	FSANZ
EU	Guy Van den Eede	JRC, EC
	Arnd Hoeveler	JRC, EC
	Giovanni Lacono	EFSA, EU
	Mirko Rossi	EFSA, U Helsinki
	Maurice Whelan	JRC, EC
Japan	Kenichi Aisaki	NIHS
	Ayako Furuhashi	NIHS
	Toru Kawanishi	FSCJ
	Takashi Yamada	NIHS
Switzerland	Michael Renaudin	Swissmedic

For questions, please contact:
Weida Tong, Ph.D. (Chair)
Email: Weida.Tong@fda.hhs.gov

GSRs21 Program

Day 1—Monday, October 4, 2021

Digital Health and Safety

**All times are in U.S. Central Standard Time*

7:00 – 7:30 am (Recorded session)	Chair: William Slikker, Jr., Director of FDA/NCTR (US) <ul style="list-style-type: none">• Opening remarks: Janet Woodcock, FDA Acting Commissioner (US)• Keynote Presentation:<ul style="list-style-type: none">○ Real World Data and its Role in FDA’s New Era of Smarter Food Safety Frank Yiannas, Deputy Commissioner for Food Policy and Response, FDA (US)
7:30 – 9:00 am (Recorded session with LIVE Q/A)	Chair: Primal Silva, Canada Food Inspection Agency (CFIA) (Canada) <ol style="list-style-type: none">1. Food Safety Genomics, Burton Blais, CFIA (Canada)2. To Unpack a Bag of Genomes: Metagenome Analytics for Rapid Detection and Genomic Characterization of Individual Pathogens in Mixed Microbial Communities, Kern Rei Chng, National Centre for Food Science, Singapore Food Agency (Singapore)3. National Policy Guidelines on NanoAgri and Food Products Technologies: India’s Step Towards Encouraging Translational Research and Industry Engagements, Alok Adholeya, TERI Deakin Nanobiotechnology Centre, The Energy and Resources Institute (TERI) (India)4. From <i>in silico</i> Medicine to <i>in silico</i> Toxicology: Applying the Universal Immune System Simulator, Francesco Pappalardo, University of Catania (Italy)5. ANVISA Open Data: The Way to Build Evidence for Health Decision Making, Mônica da Luz Carvalho Soares, General Manager of Knowledge, Innovation and Research, Brazilian Health Regulatory Agency – ANVISA (Brazil)6. The Potential of Nationwide Administrative Hospital Data for Post-Marketing Surveillance, Patrick Beeler, Swissmedic, Bern (Switzerland)
9:00 – 9:20 am	Q&A (20 Min)
9:20 – 9:30 am	Break (10 Min)
9:30 – 10:00 am (LIVE session)	Debate (30 Min): Is Regulatory Science Ready for AI? Moderators: Weida Tong, FDA/NCTR (US) and Maurice Whelan, JRC (EU) Debaters: Ruth Roberts, Apconix (UK) supports the motion while Jurgen Borlak, Hannover Medical School (Germany) is against the motion

Day 2—Tuesday, October 5, 2021

Artificial Intelligence and Machine Learning

**All times are in U.S. Central Standard Time*

7:00 – 7:20 am (Recorded session)	Chair: Marta Hugas, Chief Scientist of EFSA (EU) <ul style="list-style-type: none">• Keynote Presentation:<ul style="list-style-type: none">○ AI and Real-World Data for Regulatory Consideration – A Europe Perspective, Stephen Quest, General Director at JRC (EU)
7:20 – 8:50 am (Recorded session with LIVE Q/A)	Chair: Philippe Girard, Swissmedic (Switzerland) <ol style="list-style-type: none">1. Tailoring FDA's Regulatory Framework to Encourage Responsible Innovation in AI/ML, Matthew Diamond, FDA/CDRH (US)2. Human-Centric AI in Regulatory Science: Who is Needed Where, Didier Verloo, Head of the Assessment Methodologies Unit in EFSA (EU)3. The Future of Machine Learning in Identifying Actionable Biomarkers in Cancer: An Example from Head and Neck Oncology, Binay Panda, Jawaharlal Nehru University, New Delhi (India)4. Technology Innovations in Regulatory Science for Equitable Clinical Outcomes, Kelly Rose, Burroughs Wellcome Fund (US)5. AI and Machine Learning in European Medicine Agencies, Joaquim Berenguer Jornet, Digital Strategy Solution in the Digital Business Transformation Task Force & Lead Data Scientist of the Analytics Centre of Excellence, EMA (EU)6. Bigdata Analysis: Outcome of the 2nd AMES/QSAR International Challenge Project, Ayako Furuhami, NIHS (Japan)
8:50 – 9:10 am	Q&A (20 Min)
9:10 – 9:20 am	Break (10 Min)
9:20 – 9:50 am (LIVE session)	Debate (30 Min): Is Regulatory Science Ready for AI? Moderators: Maurice Whelan, JRC (EU) and Weida Tong, FDA/NCTR (US) Debaters: Ruth Roberts, Apconix (UK) is against the motion while Jurgen Borlak, Hannover Medical School (Germany) supports the motion.
9:50 – 10:00 am (LIVE session)	Closing Remarks Weida Tong, FDA/NCTR (US)

Day 3—Wednesday, October 6, 2021

Data Analytical Tools for Drug and Food Review by Global Regulatory Agencies

**All times are in U.S. Central Standard Time*

<p>7:00 – 10:00 am (LIVE session)</p>	<p>Chair: Shraddha Thakkar, FDA/CDER (US)</p> <ul style="list-style-type: none">• FDALabel™: A Tool to Manage Drug-Labeling Documents with Flexible Search Capabilities Used in Drug Reviews at FDA, Hong Fang, FDA/NCTR (US)• WILEE: The Warp Intelligent Learning Engine (WILEE) For Food Additive Safety, Ernest Kwegyir-Afful, FDA/CFSAN (US)• FoodTrak, Kasey Heintz, FDA/CFSAN (US)• CERES: Chemical Evaluation and Risk Estimation System, Kirk Arvidson, FDA/CFSAN (US)• ePI: Electronic Product Information for EU Medicines, Juan Garcia Burgos, EMA (EU)• LiSA: Swissmedic Literature Search Tool, Alexander Horst, Swissmedic (Switzerland)
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Opening Remarks

Janet Woodcock
Acting Commissioner
U.S. Food and Drug Administration
USA



Dr. Janet Woodcock began her long and distinguished FDA career in 1986 with the agency's Center for Biologics Evaluation and Research (CBER) as Director of the Division of Biological Investigational New Drugs, as well as serving for a period as CBER's Acting Deputy Director. She later became Director of the Office of Therapeutics Research and Review in CBER, a tenure which included the approval of the first biotechnology-based treatments for multiple sclerosis and cystic fibrosis.

In 1994, Dr. Woodcock was named Director of the FDA's Center for Drug Evaluation and Research (CDER), overseeing the center's work that is the world's gold standard for drug approval and safety. In that position, she has led many of the FDA's groundbreaking drug initiatives, including introducing the concept of risk management as a new approach to drug safety; modernizing drug manufacturing and regulation through the Pharmaceutical Quality for the 21st Century Initiative; advancing medical discoveries from the laboratory to consumers more efficiently under the Critical Path Initiative; and launching the Safety First and Safe Use initiatives designed to improve drug safety management within and outside the FDA, respectively.

From 2004 -2007, Dr. Woodcock served as Deputy Commissioner and Chief Medical Officer in the Office of the Commissioner. During that period she also served in other executive leadership positions, including Deputy Commissioner for Operations and Chief Operating Officer.

In 2007, Dr. Woodcock returned as Director of CDER, until last year, when she was asked to lend her expertise to "Operation Warp Speed" the initiative to develop therapeutics during the COVID-19 pandemic. From late 2020, she split her time advising "Operation Warp Speed" on advancing COVID-19 therapeutics while also serving as the Principal Medical Advisor to the Commissioner on key priorities on behalf of the Office of the Commissioner.

Dr. Woodcock was named Acting Commissioner of Food and Drugs on January 20, 2021.

Keynote Presenters

Frank Yiannas

Deputy Commissioner for Food Policy and Response
U.S. Food and Drug Administration
USA



Frank Yiannas is the Deputy Commissioner for Food Policy and Response at the U.S. Food and Drug Administration. He is the principal advisor to the FDA Commissioner on food safety policies, including implementation of the FDA Food Safety Modernization Act. His leadership role covers a broad spectrum, such as outbreak response, traceback investigations, product recall activities, and supply chain innovation. Mr. Yiannas came to the FDA from leadership roles with Walmart and the Walt Disney Company. He has long been recognized for his role in elevating food safety standards and building food safety management systems based on science and risk.

Stephen Quest

Director-General, Joint Research Centre
European Commission
Brussels, Belgium



Mr. Stephen Quest is the Director-General of the Joint Research Centre (JRC) of the European Commission as of May 1, 2020. Prior to this, he was the Director-General of the Directorate-General for Taxation and Customs Union (TAXUD) and the Director-General for Informatics (DIGIT), driving the digital transformation of the Commission. His career spans more than 25 years in the European civil service, and has included work on the EU budget, social and environmental policy and four years as Assistant to the Secretary-General. As Director-General, Stephen is particularly focused on modernizing organizational culture and promoting innovation within the Commission, both as regards the use of technology and empowering and involving staff in decision-making. He is particularly passionate about communication and the interface between policy and technology.

Debater – Dr. Jürgen Borlak

Prof. Jürgen Borlak

Professor of pharmacology and toxicology
at Hannover Medical School
Hannover, Germany



Dr. Jürgen Borlak is a Professor of pharmacology and toxicology at Hannover Medical School. In 2002 he was appointed as director and founding chair of the Institute of Pharmaco- and Toxicogenomics at Hannover Medical School. This new field of genomic science applies a wide range of methods in genetics, molecular toxicology, and functional genomics for a better understanding of disease-causing mechanisms and drug-induced toxicities. An array of enabling technologies are applied for an identification of “drugable” targets and for a better understanding of inter-individual differences in drug response, therefore allowing individualized drug treatment regimens and disease prevention strategies. Under his leadership, the Institute has gained international reputation in clinical toxicology and in an evaluation of hepatobiliary adverse drug reaction. He is a member of the management committee of the Prospective European Drug-induced Liver Injury Network (<https://proeurodilinet.eu/about-us>). Additionally, he holds appointments as professor of molecular anatomy at the Medical Faculty of the University Leipzig and visiting professor of Experimental Medicine at Uppsala University, Sweden, and is a distinguished visiting professor at the University of Trento, Italy. Jürgen Borlak is author of >280 original publications and 25 book chapters and is editor of the Handbook of Toxicogenomics. He is reviewer and member of the editorial board for various scientific journals and served as an expert for the International Agency for Research on Cancer/World Health Organisation (WHO) and the European Medicines Agency EMA. He also serves as an international reviewer for many European, Asian, and U.S. research organizations.

Debater – Dr. Ruth Roberts

Prof. Ruth Roberts, Ph.D., ATS, FBTS, ERT, FRSB, FRCPath
Chair and Director of Drug Discovery, Birmingham University
Cofounder, ApconiX
UK



Ruth A. Roberts is Chair and Director of Drug Discovery at Birmingham University, UK and Cofounder of ApconiX, an integrated toxicology and ion channel company that brings together a team of world-renowned nonclinical safety experts with over 300 years of drug discovery and development experience. Before that, Ruth was Global Head of Regulatory Safety at AstraZeneca (2004-2014) and Director of Toxicology for Aventis in Paris, France (2002-2004).

Dr. Roberts is former secretary to SOT, former president of EUROTOX, former president of the British Toxicology Society (BTS), a fellow and past president of the Academy of Toxicological Sciences (ATS), and was elected fellow of the Royal College of Pathologists in 2012 and of the Royal Society of Biology in 2014. She is currently vice-chair of the Health and Environmental Science Institute (HESI) Board and has co-chaired the HESI Biomarkers of Neurotoxicity scientific committee since its inception in 2015.

Professor Roberts was the recipient of the SOT Achievement award in 2002, the EUROTOX Bo Holmstedt Award in 2009, and the SOT 2018 Founders award, given in recognition of outstanding leadership in fostering the role of toxicological sciences in safety decision making. With >150 publications in peer reviewed journals, she is interested in developing and implementing innovative models in drug discovery and development and particularly in ensuring academic research achieves its translational potential.

Debate Co-Moderators

Weida Tong, Ph.D.

Director, Division of Bioinformatics and Biostatistics
National Center for Toxicological Research (NCTR)
U.S. Food and Drug Administration (FDA)
Arkansas, USA



Dr. Tong is the Director of the Division of Bioinformatics and Biostatistics at the FDA's National Center for Toxicological Research. He has been a Senior Biomedical Research and Biomedical Product Assessment Service (SBRBPAS) Expert (formerly Senior Biomedical Research Service) since 2011. He has served on science advisory boards for several multi-institutional projects in Europe and the U.S. He also holds adjunct appointments at several universities. He is the founder and board chairperson of the international MAQC Society (2017-2020), President of the MCBIOS Society (2019-2020), and Chair of the SOT Board of Publication (2019-2020). He has published over 300 peer-reviewed papers in the areas of 1) assessing technical performance and practical utility of emerging genomic technologies with emphasis on regulatory application and precision medicine; gained from supervising and leading the FDA-led community-wide MicroArray and SEquencing Quality Control (MAQC/SEQC) consortium; 2) addressing the drug-safety concerns related to drug-induced liver injury (DILI); 3) developing machine learning and AI for digital health and drug repositioning; and 4) conducting molecular modeling and QSARs on various toxicological endpoints such as carcinogenicity.

Prof. Maurice Whelan

Head of the Chemical Safety and Alternative Methods Unit
Directorate for Health, Consumers and Reference Materials
European Commission, Joint Research Centre (JRC)
Ispra (VA), Italy



Prof. Maurice Whelan is head of the Chemical Safety and Alternative Methods Unit of the Directorate for Health, Consumers and Reference Materials of the European Commission's Joint Research Centre (JRC), based in Ispra, Italy. He also heads the JRC's EU Reference Laboratory for alternatives to animal testing (EURL ECVAM). Maurice is the EU co-chair of the OECD Advisory Group on Molecular Screening and Toxicogenomics that is responsible for the OECD programme on Adverse Outcome Pathways, and he is a member of the Steering Committee of the European Partnership for Alternative Approaches to Animal Testing (EPAA). His publications include over 200 scientific papers and a recent book on the validation of alternative methods for toxicity testing. He has held a number of external appointments including the 2017-2018 Francqui Chair for alternative methods at the Vrije Universiteit Brussel (VUB, Belgium) and is currently visiting professor of bioengineering at the University of Liverpool (UK).

Day 1: Digital Health and Safety

Burton Blais, Ph.D.

Head, Research and Development (Carling Laboratory)
Canadian Food Inspection Agency
Ottawa, Ontario, Canada



Burton Blais started his public service career in 1991 after completing a doctorate in biochemistry at Carleton University, first as a biologist in the National Laboratory for Enteric Pathogens, then as a research scientist in the Food Laboratory (Agriculture and Agri-Food Canada), and currently as Head of Research and Development (Carling Laboratory) and Senior Research Scientist at the Canadian Food Inspection Agency (CFIA) in Ottawa. His research interests include the development of analytical capacity supporting regulatory food safety programs, with a particular emphasis on the detection and characterization of food-borne bacterial pathogens using genomics tools.

Food Safety Genomics

The CFIA has an ongoing commitment towards the development of new or modified methods and techniques to improve the agency's ability to analyze foods in a shorter period of time, to detect even lower numbers of bacteria which may be present in a food sample, and/or to provide more informative assessments regarding the identity of the bacteria present in a sample. The increasing availability of faster methods employing DNA-based technologies has provided CFIA with the tools necessary to produce faster results. The Blais laboratory has led the way in the development and validation of DNA-based food microbiology methods meeting Canadian federal food inspection needs. A notable achievement was the early adoption of DNA-based methodology for the definitive identification of food-borne pathogenic bacteria in regulatory food safety in Canada. The methods developed by Dr. Blais quickly confirm the presence of *E. coli* O157 (as well as other non-O157 verotoxigenic Enterohaemorrhagic *E. coli*, or EHEC), *Salmonella* spp. and *Listeria monocytogenes*. Burton's present focus on the integration of next generation genomics technology in food inspection is leading to new approaches for food pathogen analysis currently being implemented at CFIA, and has placed Canadian regulatory food microbiology testing labs on the leading edge of providing rapid and highly informative test results supporting food safety investigations. Burton is currently leading a team of international partners in a Global Coalition for Regulatory Science Research initiative to establish international standards for the analysis and reporting of next generation sequencing data in food safety regulatory applications.

Kern Rei Chng, Ph.D.

Specialist Team Lead, Research & Exposure Science Department
National Center for Food Science (NCFS)
Singapore Food Agency (SFA)
Singapore, Singapore



Dr. Kern Rei Chng is a Specialist Team Lead in the Singapore Food Agency's National Center for Food Science (NCFS/SFA). He leads the Biological Research Team in the Research & Exposure Science Department. His team develops and evaluates biotechnologies and computational analytics to enhance SFA's capabilities in ensuring microbiological food safety and supporting foodborne outbreak investigations. Prior to him joining SFA, he has held research appointments in the National University of Singapore and Genome Institute of Singapore, working on cancer genomics, microbial genomics, microbiome genomics, genome informatics, and the development of genomics technologies. His current research interests focus on the development and application of genomics tools and analytics for foodborne outbreak infection prevention and control. His recent works seek to realize the potential in coupling state-of-the-art DNA sequencing methodologies to metagenomics analytics for microbial safety of food, water, and the environment.

To Unpack a Bag of Genomes: Metagenome Analytics for Rapid Detection and Genomic Characterization of Individual Pathogens in Mixed Microbial Communities

The development of microscopy has enabled the first observations of microorganisms that catalysed the beginnings of microbiology centuries ago. This has drawn a striking parallel with the recent advancements in high-throughput DNA sequencing technologies that have transformed the field of microbial genomics. Whole genome sequencing (WGS) enables the detailed genomic characterization of microbes at a high resolution, offering unparalleled sensitivity and specificity for phylogeny resolution. This has profound implications and extensive applications for microbiological testing in diagnostics, biosurveillance, and outbreak investigations. While compelling, WGS comes with its set of limitations. For instance, the laborious and time-consuming process of isolation for the different individual microbial isolates remains a requirement for the WGS workflow. My research interests and efforts endeavour to further develop and leverage on the potential of metagenomics to address this gap. In this presentation, I will provide a brief introduction on metagenomics, its utilities, and challenges. Specifically, I will also give an overview of my recent work on the application of metagenomics for surveying and characterising microbes, plasmids, and phages. Finally, I will share some of the ongoing work to develop and apply real-time nanopore sequencing analytics for rapid diagnostics of foodborne pathogens in complex food matrices. The main objective of the presentation is to highlight the potential of metagenomics as the next transformational technology for supporting biosurveillance and outbreak investigations.

Alok Adholeya, Ph.D.

Program Director, Sustainable Agriculture, IHC, TERI, New Delhi
Director, TERI- Deakin Nanobiotechnology Centre, TERI Gram, Gurugram
India



Dr. Adholeya has more than 35 years' significant experience and expertise in the area of translational research and reaching out to millions of common people worldwide through his developed technologies which includes a new biological organism for soil fertility and crop productivity enhancement known as "Mycorrhizal" bioremediation of industrial solid waste aeron chemical and fertilizer industries. He has developed more than 25 IPR's and commercialized most of them through technology transfer to industries. His current involvement in the area of nano intervention in agriculture, micro encapsulation technology developed for beneficial, yet fragile microorganisms, and seed coating technology are few which are making inroads to benefit mankind. Dr. Adholeya is also chairman of national task force of department of biotechnology, ministry of science and technology government of India on "Biological agents," He was conferred most prestigious award from Science and Technology Ministry — "Product, Process and Technology Award 2004" — for his exemplary and only technology in the world of commercial production of Mycorrhiza, a next generation bio fertilizer. Through this advancement, India being developing country-provided technology to developed countries such as the USA. His path-breaking work received Marrico foundation award for addressing global problem of industrial solid wastes remediation. Dr. Alok Adholeya currently leads the research and technology platforms on mycorrhizal research, Nanobiotechnology, micropropagation technology, community farming and livelihood with over 250 employees. Dr. Adholeya has chaired numerous advisory committees on agriculture and bioremediation, published over 170 research articles, guided 26 doctoral students and many masters' students and has been an Honorary Professor of Deakin University, Australia since March 2010. He also worked as Director, Product and Technology Development at Mycorrhizal Applications, Oregon, USA between 2014-2017, a subsidiary company of Sumitomo Chemicals. He currently heads National Centre of Excellence in Agri-nanotechnology of Govt. of India, Department of Biotechnology.

Dr. Adholeya has been leading TERI-Deakin Nano Biotechnology Centre since 2010 and developed many technologies on nano products, some having already been commercialized through licensing. He has also worked to develop [national policy guidelines](#) on agri-nano food product technologies released by Government of India recently.

National Policy Guidelines on NanoAgri and Food Products Technologies: India's Step Towards Encouraging Translational Research and Industry Engagements

Nanotechnology strategies offer to improve agriculture performance at lesser treatment cost while increasing the yield potential of food crops and reducing carbon footprints. New consideration of application of nanotechnology in agriculture necessitates defining regulatory aspects of the nano-

based products for agriculture and food. Therefore, guidelines for evaluation and regulation of NanoAgri inputs and food products in India and across the world are highly desired. In India, there are different government agencies and different provisions that regulate different agri-inputs and food products; however, no specific provisions for nano-variants are available.

India is forging ahead at the global level and has developed comprehensive and inclusive guidelines with the intent to support appropriate regulation landscape for nano-agri products in India. These guidelines will empower the researchers, innovators and regulators in agriculture and food industry to achieve a greater social and economic impact. The present guidelines are developed to support the existing national regulatory provisions with specific requirements and adaptations for Nano-agri-inputs and nano-agri food products of Central insecticide Board and Registration Committee (CIB&RC), Food Control Order (FCO), Food Safety and Standards Authority of India (FSSAI), Bureau of Indian Standards (BIS), Ministry of Food Processing Industries (MoFPI), Department of Animal Husbandry & Dairying (DAHD). These guidelines are also harmonized with the applicable provisions for NAIPs and NAPs as per the international guidelines of REACH, OECD, U.S. EPA, TSCA, APVMA, FAO/ WHO, U.S. FDA, EFSA, FSANZ and Codex, as well as the principles of ICH.

Francesco Pappalardo, Ph.D.

Deputy Director, Department of Drug and Health Sciences
University of Catania
Catania, Italy



Prof. Francesco Pappalardo is Deputy Director of Department of Drug and Health Sciences at the University of Catania, Italy. He is involved in several multi-institutional funded projects in Europe and USA. He holds computer science professorship appointment at University of Catania and he is visiting professor at the Boston University and Health Informatics Research Lab, Computer Science Department, USA. In addition, he is the founder of the COMBINE research group (www.combine-group.org). Research activity of Francesco Pappalardo is focused on the application of computational models in the field of systems biomedicine. He is one of the pioneers of in silico trials, where he currently also deals with regulatory aspects with the European authorities. The most visible projects from his group are 1) scientific coordination of the “In Silico World” funded project with the aim of lowering barriers to ubiquitous adoption of in silico Trials; 2) development of in silico trials framework for immunotoxicity risk assessment of chemicals evaluating the potential for unintended effects of chemical exposure on the immune system; 3) scientific coordination of the “STriTuVaD” project where an in silico trial computer model is being developed to drastically reduce the cost of innovation in tuberculosis care; 4) in silico vaccine developing for prompt actions against SARS-CoV-2; and 5) development of immune system in silico trial modeling and simulation suite to support specific research on immunotherapies. In addition, his group also specializes in molecular modeling and biological pathway analysis with specific interest in precision medicine. Professor Pappalardo has published more than 150 articles in international journals and conferences. He serves the scientific community as president and member of the program commissions for prestigious international conferences and is a member of editorial boards for major bioinformatics journals.

From in silico Medicine to in silico Toxicology: Applying the Universal Immune System Simulator

The Universal Immune System Simulator (UISS) is a simulation framework to model the immune system. It integrates simulation engines, optimization techniques and other prediction models. UISS is then capable to reproduce general immune system behavior connected to several immune system responses (to viruses, bacteria, tumors, and autoimmune disease) and drug-induced immune system responses. The UISS model is used in several funded projects to model knowledge on immunological aspects of different pathologies and support in silico trials, with a special attention on those regulatory aspects that are still not addressed. Immunotoxicity risk assessment of chemicals is an evaluation of the potential for unintended effects of chemical exposure on the immune system. These effects manifest as following principal types of immunotoxicity: immunosuppression involving infection and carcinogenesis, immunoaccentuation involving sensitization, and autoimmunity, or immunostimulation. This immune dysregulation may lead to a variety of illnesses. Included among

them are illnesses that are associated with a dysfunctional immune system, such as infections, inflammatory diseases, allergic diseases, and autoimmune diseases. For example, exposure to chemicals is associated with immunosuppression manifesting the reduction of resistance to infections, development of autoimmune disease and hypersensitivity responding directly as an allergen or enhancing the induction of allergic sensitization. In this context, it is interesting to understand the conditions under which a mathematical model developed for one purpose and application (e.g., in the pharmaceutical domain) can be successfully translated and transferred to another (e.g., in the chemicals domain) without undergoing significant adaptation.

Mônica da Luz Carvalho Soares, Ph.D.

General Manager of Knowledge,
Innovation and Research,
Brazilian Health Regulatory Agency
ANVISA, Brazil



Dr. Monica Da Luz Carvalho-Soares is a pharmacist with a Ph.D. in Biological Science from the Carlos Chagas Filho Biophysics Institute at the Federal University of Rio de Janeiro (IBCCF/UFRJ) and a master's degree in Biophysics from IBCCF/UFRJ; she is also an expert in International Health with a degree from São Paulo University (USP) and an expert in Health Surveillance with a degree from Oswaldo Cruz Institute (FIOCRUZ).

Dr. Carvalho-Soares has worked as a Health Regulatory Expert at the Brazilian Health Regulatory Agency (Anvisa), where she has held various leadership positions, since 2005. From 2009 to 2011, she was Head Manager of Pharmaceutical Technology Management, where she coordinated technical and regulatory activities regarding the registration and post-approval changes of generic and herbal drugs. During this period, she was also a member of the Multidisciplinary Commission for Updating the List of Essential Medicines in Brazil. In 2011, she was the Coordinator of Generic Drug Registration and published a study about “Regulatory Efficiency: Generic Drug Registration Time in Brazil.” In 2009, Dr. Carvalho-Soares coordinated the work “Review of Post-Approval Procedures for Drugs in Anvisa” that was selected among the most important initiatives for Public Administration in Brazil and received an award in Federal Public Management Innovation.

Dr. Carvalho-Soares was a member of the Deliberative Council and Coordinator of the Brazilian Pharmacopoeia from 2011 to 2015. She was also the Anvisa coordinator at the Mercosur Pharmacopoeia. At the time, Dr. Carvalho-Soares was an advisor to the World Health Organization (WHO) on matters relating to interchangeability of multi-source products (generics), pre-qualification of medicine guides and specifications for pharmaceutical preparations. In 2016, Dr. Carvalho-Soares was at the University of Maryland Baltimore County (UMBC) as a Postdoctoral Fellow, where she worked with new data analysis to predict critical post-market risks for biological products. From 2017 to 2018, she was a member of the drug-induced liver injury (DILI) work group of the Council for International Organizations of Medical Sciences (CIOMS).

Since 2019, Dr Carvalho-Soares has been General Manager of Knowledge, Innovation and Research at Anvisa and a member of the Real-World Data and Real-World Evidence work group of CIOMS.

ANVISA Open Data: The Way to Build Evidence for Health Decision Making

Open data can be used freely, reused and redistributed by anyone, without copyright or patent restrictions. They are qualified and standardized data from reliable sources. The Brazilian Health

Regulatory Agency - Anvisa - will make available to society 29 databases on Health Surveillance products and services by the end of 2021. This availability moves towards promoting transparency and knowledge on health in Brazil, through access to data of various types. It will contribute to studies on data sources for drug utilization research in Brazil, pharmacovigilance, price regulation, and health registration, among others.

The purpose of this presentation is to show the methodology and tools used to make the Anvisa Data Plan. We will present how databases were prepared, the information provided in each database, and the user participation process. We will, in addition, present the results obtained so far and the perspectives for including new bases for the coming years. The availability of open data fosters new ideas and actions to promote health decision-making, transparency, public health, scientific knowledge, and innovation.

Patrick E. Beeler, M.D.

Swissmedic (“Swissmedic 4.0” Initiative)
Senior Researcher, Occupational and Environmental Medicine,
Epidemiology, Biostatistics and Prevention Institute,
University Hospital Zurich & University of Zurich, Switzerland



Dr. Patrick Beeler studied medicine and has long been interested in the advantage of processing and analyzing “big clinical data” for research purposes. He programs SQL and R to transform large, routinely collected data into clinically meaningful results. He applies a variety of techniques, for example, multivariable regression modeling, electronic phenotyping, and cluster analyses – and furthermore, he often develops novel approaches to tackle problems related to the inherently complex nature of real-world clinical raw data. The goal of his research is to better understand clinical problems and ultimately to improve patient safety, diagnostics, and quality of care.

The Potential of Nationwide Administrative Hospital Data for Post-Marketing Surveillance

Drug-related hospital admissions are considered serious adverse drug events (ADE). The Swiss Federal Statistical Office comprehensively collects administrative hospital data of all inpatient stays at any hospital in Switzerland. This national dataset includes information on patient demographics, up to 50 ICD-10 coded diagnoses, clinical outcomes such as in-hospital mortality, and more. We analyzed all ADE-triggered inpatient stays from 2012 to 2019 to characterize serious and potentially deadly ADEs in Switzerland, while focusing on the utilization of timely administrative hospital data for pharmacovigilance purposes. This “Swissmedic 4.0” supported study and report will: 1) present a nationwide overview of ADE-triggered hospital admissions and related mortality; 2) further explain the sophisticated use of real-time, real-world data to enhance current pharmacovigilance practices; and 3) envision the potential future of automated pharmacovigilance signal detection based on comprehensive national data in Switzerland.

Day 2: Artificial Intelligence and Machine Learning

Matthew Diamond, MD and Ph.D.

Chief Medical Officer, Digital Health Center of Excellence
FDA/CDRH
Maryland, USA



Dr. Diamond is the Chief Medical Officer for Digital Health at FDA's Center for Devices and Radiological Health (CDRH). At the CDRH Digital Health Center of Excellence, Dr. Diamond serves as the senior clinical expert for digital health medical devices and provides leadership for digital health policy development for emerging technologies including artificial intelligence. Dr. Diamond has also served as a leader on CDRH's COVID-19 response team. Prior to joining the Agency, Dr. Diamond served on leadership teams of large and small technology companies, including as Chief Medical Officer at Nokia, and as Medical Director at Fossil Group and the startup Misfit Wearables. He was Vice Chair of the Consumer Technology Association (CTA) Health & Fitness Technology Board of Directors, where he promoted public health applications of mobile technology and established an ANSI-accredited standardization committee to develop standards in digital health for wellness-related hardware and mobile applications. Dr. Diamond served on numerous advisory boards including at the Center for Personalized Health Monitoring at UMass Amherst and for the venture firm NGP Capital. He earned his MD and PhD (biophysics) from the Mount Sinai School of Medicine, and he is board certified in rehabilitation medicine and sports medicine and certified in medical acupuncture. A faculty member at NYU, Dr. Diamond is passionate about helping people improve their mobility and performance through a holistic approach to rehabilitation and technology that promotes wellness

Tailoring FDA's Regulatory Framework to Encourage Responsible Innovation in AI/ML

Artificial intelligence (AI) and machine learning (ML) technologies have the potential to transform health care by deriving new and important insights from the vast amount of data generated during the delivery of health care every day. Medical device manufacturers are using these technologies to innovate their products to better assist health care providers and improve patient care. One of the greatest benefits of AI/ML in software resides in its ability to learn from real-world use and experience, and its capability to improve its performance. Dr. Diamond will discuss FDA's vision, that with appropriately tailored total product lifecycle-based regulatory oversight, AI/ML-based software will deliver safe and effective functionality that improves the quality of care that patients receive.

Didier Verloo

Head of Assessment and Methodological Support
European Food Safety Authority (EFSA)
Parma, Italy



Didier Verloo has worked for the European Food Safety Authority (EFSA) since 2005 where he has headed the Assessment and Methodological Support Unit since 2008. This multidisciplinary unit leads and supports the development, implementation and review of evidence-based risk assessment and decision-support approaches in all fields within EFSA's remit (food safety, feed safety, animal health, plant health and nutrition) and was responsible for the development and implementation for the EFSA guidance on Systematic Review in food and feed safety risk assessment, the EFSA guidance on Expert Knowledge Elicitation and the EFSA framework for Promoting Methods for Evidence Use in Scientific Assessments underpinning the science quality system. Building on this sound basis, several feasibility studies were executed around artificial intelligence/machine learning and crowdsourcing in risk assessment and in the two years since the unit initiated, created, and manages the continuously growing knowledge community on the implementation of AI with other EU agencies such as EMA, ECDC, EUIOPO, EUROFOND, and CdT.

Didier started his professional career at the Institute of Tropical Medicine in Belgium, being confronted with the reality of decision making under uncertainty by working on evidence-based medical decision making in human and animal trypanosomiasis (sleeping sickness) and worked before joining EFSA for the Belgian government as an epidemiologist and risk assessor mainly in the area of antimicrobial resistance and infectious diseases. Over the years, he built up academic and hands-on experience in biostatistics, epidemiology, risk analysis, statistical process control, and test validation and provided risk analysis consultancy in public health, construction, finance, and engineering.

Human Centric AI in Regulatory Science: Who is Needed Where?

Risk assessment, as executed by EFSA (and used here as a more general model for regulatory science), is a structured decision-support process where selected scientists are asked to provide scientific recommendations to inform managerial decisions. Upon receipt of the mandate it starts with a problem-formulation phase that includes: 1) the clarification and acceptance of the mandate that takes place in dialogue with the requestor; 2) the translation of the general question into a scientifically answerable assessment question; and 3) the definition of the related conceptual model and selection of the overall approach for the assessment. The conceptual model illustrates all the sub-questions derived from breaking down the assessment question, along with a description being purely descriptive to mathematical with all the sub-questions expressed as parameters/variables. EFSA recognized the value of complementing problem formulation (i.e. description of the what) with an upfront definition of methods for conducting the assessment (i.e. description of how the assessment will be conducted), which include the methods for answering each sub-question and for integrating

evidence across sub-questions, including uncertainty analysis which can arise from limitations in the evidence (i.e. heterogeneity, degree of relevance, degree of internal validity, and/or precision) and in the methods used throughout the assessment. This plan phase is followed by the “do phase” which is the actual assessment, where the pre-defined and documented plan is implemented, and conclusions are drawn in light of the identified uncertainties. The different approaches to answer sub-questions are: 1) collecting, appraising, synthesizing, and integrating evidence coming from the scientific literature collected or directly submitted; 2) extracting, assessing, and analyzing data from databases and sources other than literature; 3) eliciting expert judgement, when evidence is scarce and/or of limited validity; or 4) carrying out primary research studies. Combinations of different approaches can be adopted for the same sub-question or, for broad assessments containing many sub-questions, for the various sub-questions.

The above-described process has reached its limits both in the ability to execute timely as in the physical ability of the available human brains to read, appraise and integrate the exponentially growing amount of evidence in a structured way.

Automation of the process in which AI models play a role, hence practically moving the workload from the human experts to the machine, is the only way forward. However, AI-powered models are still far from demonstrating human-like causal reasoning, imagination, top-down reasoning, or artificial general intelligence that could be applied broadly and effectively on fundamentally different problems such as what is described above for the plan and “do phase” of the risk assessment process. Nevertheless, a human-centric approach — where the core accountability of the risk assessment planning is human while the execution (do) is more a human-augmented approach — becomes more realistic, allowing human and artificial intelligence to work in tandem. These models could be applied to narrow, well-defined areas of the risk assessment where AI guardrails could be manifested in terms of human intervention or by incorporating rule-based algorithms that hard-code human judgment. Examples will be given on areas of the risk assessment process where this approach is currently implemented or under full development such as on the use of those human-centric AI approaches such as for the answering of the sub-questions and specific parts of the plan phase.

Binay Panda, D.Phil.

Professor
School of Biotechnology
Jawaharlal Nehru University
New Delhi, India



Binay Panda is a professor of biotechnology in Jawaharlal Nehru University, New Delhi, India. He studied, lived, and worked in the UK, USA, and Japan before moving back to India in 2010. Binay received his doctorate degree from the University of Oxford, UK, post-doctoral training at the Scripps Research Institute, La Jolla, California, USA with a Fellowship from the American Cancer Society, and was a visiting researcher of genome science at the University of Tokyo, Japan. His group's main interests are data integration and genomic medicine and building and optimizing computational tools for high-throughput and imaging data. In disease genomics, the main thrust of research in his lab has been understanding head and neck squamous cell carcinoma using integrated analysis of heterogeneous data.

The Future of Machine Learning in Identifying Actionable Biomarkers in Cancer: An Example from Head and Neck Oncology

Genomic data deluge has defined biology and medicine in the last decade. The field of cancer is one of the largest beneficiaries of this change, leading to the generation of millions of variants in multiple cancer types. However, finding clinical relevance from this large amount of data will require building tools based on robust algorithms that can integrate molecular data with clinical and epidemiological information in a multi-dimensional context.

We are interested in understanding head and neck cancer with a long-term aim to discover signatures for robust diagnosis, prognosis, choice-of-therapy, and patient follow-up. In that context, we have catalogued variants in head and neck tumors using high-throughput assays and have identified signatures for various clinical attributes along identifying human papilloma virus (HPV) types in those tumors 1-4. From an example in head and neck cancer, I shall describe the process of data generation and making of a platform that can integrate data to derive clinically relevant signature(s). The platform is a computational and statistical framework that is cancer type- and clinical attribute-type agnostic. The platform integrates mutations and indels, gene expression, DNA methylation, and copy number variations to discover a classifier first and predict an incoming tumor for the same by pulling defined class variables into a single framework that incorporates a coordinate geometry-based algorithm, called Complete Specificity Margin Based Clustering (CSMBC) with 100% specificity. We built a tool, called CAFE MOCHA (Clinical Association of Functionally Established MOlecular CHANGES), as an integrated GUI-driven computational and statistical framework that is cancer type- and clinical attribute-agnostic. We tested CAFE MOCHA in head and neck squamous cell carcinoma (HNSCC) for discovering a signature linked to distant metastasis and recurrence (MR) in 517 tumors

from TCGA and validated the signature in tumors from an independent cohort. The signature MR44 in HNSCC yielded 80% sensitivity and 100% specificity in the discovery stage and 100% sensitivity and 100% specificity in the validation stage⁵.

1. Campbell et al., Cancer. DOI: <https://doi.org/10.1002/cncr.33309> (2020).
2. Krishnan et al., Mol Can Research. DOI: <https://doi.org/10.1158/1541-7786.MCR-15-0395> (2018).
3. Palve et al., Journal of Global Oncology. DOI: <https://doi.org/10.1200/JGO.18.00058> (2018).
4. Krishnan et al., F100Res. DOI: <https://doi.org/10.12688/f1000research.7302.1> (2015).
5. Krishnan, Mohanraj, and Panda. JCO Clinical Cancer Informatics (2018). DOI: 10.1200/CCI.17.00045.

Miquella “Kelly” Rose, Ph.D.
Program Officer
Interfaces in Science and Regulatory Science
Burroughs Wellcome Fund
North Carolina, USA



Dr. Miquella “Kelly” Rose joined the Burroughs Wellcome Fund in January 2019 and oversees the Interfaces in Science and Regulatory Science programs that invest a combined \$10 million a year in biomedical research. Dr. Rose serves on the Committee of Inclusive Excellence for the National Organization of Research Development Professionals and is co-chair of the Diversity, Equity and Inclusion Working Group for the Health Research Alliance. Prior to BWF, Dr. Rose was Executive Director for the Research Triangle Material Research Science and Engineering Center (RT-MRSEC), and coordinated research, education, and outreach activities between four partner universities in the Research Triangle area (Duke, UNC-CH, NC State and NC Central). Before moving to North Carolina, Dr. Rose was the program coordinator for the California Institute of Regenerative Medicine Bridges to the Baccalaureate Program for Berkeley City College. She completed a postdoctoral fellowship at the University of California-San Francisco (UCSF) that was funded through a National Institute of Health (NIH) Institutional Research and Academic Career Development Award (IRACDA). At UCSF, she worked on a joint project in the Departments of Bioengineering and Craniofacial Biology, and her work focused on bioengineering a stem cell niche for tooth regeneration with Drs. Tejal Desai and Ophir Klein. She earned her Ph.D. in Biomedical Sciences from the University of New Mexico in the laboratory of Dr. Laurie Hudson in the College of Pharmacy. Her Ph.D. project focused on the dynamics of cell-cell junctions during epidermal wound healing.

Technology Innovations in Regulatory Science for Equitable Clinical Outcomes

In this talk, Dr. Rose will highlight two programs offered by Burroughs Wellcome Fund. The first is Innovations in Regulatory Science Award (IRSA). IRSA provides investigators up to \$500,000 over five years to develop innovative and implementable solutions to regulatory questions. Applications are open to faculty at U.S. and Canadian degree-granting institutions. Research proposals must indicate the direct implications for regulatory policy—including the strategy and timeline for an agency to receive and consider the findings in their regulatory decision-making, as well as any potential pitfalls and the major validation steps required. Beyond this, the possibilities are as limitless as the frontier of medical therapies. In addition, BWF is launching a one-time initiative called Technology Innovation for Equitable Clinical Outcomes (TIECO). TIECO addresses the prevalence of bias in healthcare tools, both physical (medical devices) and computational (diagnostic algorithms) that leads to serious detrimental health outcomes for individuals of which the system is not designed. Some examples include pulse oximeters for dark-skinned patients, hip implants for female patients (physical bias), and kidney function estimation and lung spirometers, which use race correction algorithms (computational bias).

Joaquim Berenguer Jornet

Digital Strategy Solution in the Digital Business Transformation Task Force &
Lead Data Scientist of the Analytics Centre of Excellence
European Medicine Agency (EMA)
Amsterdam, The Netherlands



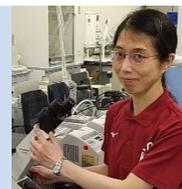
As Lead Data Scientist in the Analytics Centre of Excellence (ACE), Joaquim develops and delivers new applications and services where analytics has a big impact on the Agency's operations. He leads the development and execution of ACE's Strategy and Roadmap in support of an overall EMA digitalization strategy, advising and driving innovation through delivering new processes and digital solutions in collaboration with EMA's ecosystem of users and stakeholders.

ACE is a cross-agency initiative led by the Digital Business Transformation Taskforce. ACE explores how data analytics - including Artificial Intelligence, Machine Learning, and Robotics – can be used to build pragmatic solutions to existing EMA business needs with the main objective of gaining efficiency. ACE team works in parallel on a variety of digitalization projects. These projects have in common that they contribute to achieving EMA's digital ambition through the use of analytics or machine learning and/or AI.

AI and Machine Learning in European Medicine Agencies

Ayako Furuhama, Ph.D.

Division of Genetics and Mutagenesis, Center for Biological Safety and Research
National Institute of Health Sciences
Kawasaki-city, Kanagawa, Japan



Dr. Ayako Furuhama is a senior staff scientist at the Division of Genetics and Mutagenesis, National Institute of Health Sciences (DGM/NIHS), Japan. Her background is in theoretical chemistry, including quantum chemistry and in silico toxicity modeling. At the Department of Chemistry, Faculty of Science, Ochanomizu University, Tokyo, Japan, her bachelor and master research involved quantum chemistry: the molecular orbital studies of tetra-aza macrocycles and their lithium complexes. She received her doctorate from Nagoya University, Nagoya, Japan, where she studied theoretical chemistry, focusing on the development of distributed partial wave integral equation theory and its application to molecular liquids. After graduation, Dr. Furuhama became a Japan Society for the Promotion of Science (JSPS) research fellow at the University of Tokyo, Japan, and a long-term visitor at the Pacific Northwest National Laboratory, USA, where she did a direct *ab initio* dynamics study of ionization in a (H₂O)₁₇ cluster. Also, as a JSPS postdoctoral fellow at Imperial College London, UK, she worked on Quantum Mechanics/Molecular Mechanics calculation for photoactive yellow protein.

In 2008, she started (eco)-toxicity QSAR studies at National Institute for Environmental Studies as well as NIHS; she has more than 10 years of experience developing in silico models, including models for predicting both fish and *Daphnia magna* chronic toxicities of chemicals from *D. magna* acute toxicities. When combined with structural and physicochemical descriptors, activity data were efficient for estimating chronic toxicities. Estimation of such chronic toxicities will play an important role in the screening assessment of chemicals under the Japanese Chemical Substances Control Law. Presently, Dr. Furuhama is a member of the 2nd AMES/QSAR International Challenge Project at DGM/NIHS.

Bigdata Analysis: Outcome of the 2nd AMES/QSAR International Challenge Project

The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) M7 guideline allows in silico methods for predicting AMES mutagenicity for the assessment and control of mutagenic impurities in pharmaceuticals. However, to be used under the regulation, the power of QSAR models for predicting AMES mutagenicity (AMES/QSAR) must be increased. In the first AMES/QSAR International Challenge Project, DGM/NIHS established an AMES mutagenicity database containing 12,140 chemicals that were collected under the Japanese Industrial Safety and Health Act (ANEI-HOU); the AMES assays were conducted in accordance with OECD Test Guideline 471 and ANEI-HOU under Good Laboratory Practice (GLP)-compliant conditions. This database contains high-quality bigdata. DGM/NIHS provided this AMES database to 12 QSAR builders/vendors for the purpose of the improvement of their QSAR models for predicting AMES mutagenicity; the details of the first project are available at

<https://www.nihs.go.jp/dgm/amesqsar.html>. This presentation explains the outcome of the second AMES/QSAR International Challenge Project (https://www.nihs.go.jp/dgm/2nd_amesqsar.html), which focused on further validating and improving current QSAR models. By the end of 2020, 19 teams—both QSAR vendors and from academia—had participated in the second challenge project. Using the AMES data of the 12,140 chemicals from the first project, participants in the second project further improved QSAR tools and predicted the AMES mutagenicity of >1500 new chemicals. Due to the bias of the positive:negative data (approximately 15:85), the sensitivity of the models decreased and the specificity increased. Subsequent challenge projects will further improve AMES/QSAR models so that they will be increased availability for regulatory use.

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