

Many Ways

NEW APPROACH METHODOLOGIES: MOVING BEYOND ANIMAL TESTING

Summary

Chemical risk assessment has relied for over half a century almost exclusively on the data generated by animal testing. Yet, the approach of testing chemicals in rodents (and other animal species) for human safety purposes has been questioned repeatedly. In addition to ethical issues, the transferability of animal data across species is often problematic because of differences in physiology, metabolism and chemical susceptibilities. In this thematic session, we intend to explore the opportunities provided by new approach methodologies to shift the current paradigm from regulatory chemical risk assessment based on *in vivo* animal testing towards new generation risk assessment. This alternative will be supported by adverse outcome pathways and informed by mechanisms using integrated approaches based on *in vitro* testing in human-relevant cell models, alternative animal models (e.g., zebra fish, *Caenorhabditis elegans*) and *in silico* technologies.

Vision

The science of toxicology has advanced significantly as regards its ability to model complex toxicological processes in simpler systems, and in identifying modes of action that lead to adverse events. New Approach Methodology (NAM) performance-based models are therefore expected to replace animal tests, and alternative mechanistic assays can be used to integrate the *in vivo*, *in vitro* and modelling information into one organizational construct (Adverse Outcome Pathway).

During the ONE – Health, Environment, Society – Conference 2022, we will explore how the current paradigm based on *in vivo* testing can be shifted towards a mechanistic understanding using NAMs.

Background – Challenges and opportunities

Chemical risk assessment has relied for over half a century almost exclusively on the data generated by animal testing. Yet, the approach of testing chemicals in rodents (and other animal species) for human safety purposes has been questioned repeatedly. In addition to the ethical issues that arise from this, the transferability of animal data across species is often problematic because of differences in physiology, metabolism and chemical susceptibilities. Another issue is the sheer number of individual chemicals and mixture permutations on the European market.

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The result is that a full complement of in vivo toxicity data cannot be generated for many of the chemicals, to which humans or the environment are exposed.

Overall, the huge investment made in toxicity testing has provided us with a vast amount of publicly available data that can be used for broad in vitro and in silico profiling of bioactivities across large inventories of chemicals. Coupling this mechanistic data with an understanding of pathways of toxicity lays the groundwork for new approach methodologies (NAMs) to be used to evaluate chemical toxicity and change the regulatory toxicology paradigm. Mode of action-based High Throughput Screening (HTS) methods like ToxCast and toxicogenomics can already detect biological activity known to adversely affect human health endpoints, and these methods are already being applied in prioritizing the large number of chemicals to which humans may be exposed. These methods, put into an AOP framework, could be a valuable adjunct to, and potential replacement for, in vivo testing. However, to make this a reality, more work needs to improve how the mode-of-action or AOP landscape is catalogued, and to develop case studies where a hypothesis-driven selection of models is used to investigate the potential of agents to cause harm. The results can be compared, both qualitatively and quantitatively, to existing data that underpin regulatory decisions. Obstacles often exist at several levels blocking full engagement in the paradigm shift to NGRA.

While some success has been achieved in areas such as skin irritation and skin sensitisation, many of the NAM approaches dealing with other endpoints are often viewed critically as not being standardised or validated. Moreover, the available in vitro and in silico approaches are often considered only as complementary to the existing in vivo tests, with the assumption that in vitro and in silico tests are not able to fully address complex endpoints. The interpretation of NAMs and their integration and acceptance into the regulatory risk assessment process represents an additional hurdle.

The ONE conference provides a unique occasion to bring together the EU's scientific agencies that work in the remit of the Environment, Public Health and Food Safety (ENVI), the scientific community developing NAMs and EU risk managers to evaluate the current state of knowledge on NAMs and their use in regulatory risk assessment. The aim is to build the synergies necessary for a clear commitment and a holistic roadmap to enable a paradigm shift to NGRA.

Scope and objectives

This session aims to showcase the added value NAMs bring to chemical risk assessment and to explore the synergies necessary to draw up a holistic roadmap to enable a shift in the current risk assessment paradigm to NGRA. The session will discuss the EFSA 2027 roadmap for NAMs, currently under development through the

SPIDO initiative, contributing to its finalisation. Moreover, it will also explore the current status quo of NAM approaches for regulatory use and identify challenges and opportunities as well as how EU agencies, the wider risk assessment community and the research community can make a clear commitment to and draw up a holistic roadmap for shifting the paradigm to NGRA.

People behind the session

Session Coordinator: Georges Kass (EFSA)

Chairpersons: Maurice Whelan, Joint Research Centre (JRC)

Moderators: Maurice Whelan, Joint Research Centre (JRC)

Rapporteurs: Edoardo Carnesecchi, European Food Safety Authority (EFSA); George Kass, European Food Safety Authority (EFSA); Anna Lanzoni, European Food Safety Authority (EFSA); Annamaria Rossi, European Food Safety Authority (EFSA)

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Many Ways – Session affiliate profiles

NEW APPROACH METHODOLOGIES: MOVING BEYOND ANIMAL TESTING

George Kass, European Food Safety Authority (EFSA)
Rapporteur

George Kass was trained as a biochemist. He received his PhD in biochemical toxicology from the Karolinska Institute in Stockholm in 1990. After a post-doc at the Swiss Federal Institute of Technology in Zurich he returned to the Karolinska Institute as Assistant Professor. In 1994 he moved to the University of Surrey in the UK where he became Professor of Toxicology.

He moved to the European Food Safety Authority in 2009. George Kass was awarded a DSc from the Karolinska Institute and the University of Turku in Finland and he holds or has held visiting posts with the University of Surrey, the National University of Ireland in Galway, Newcastle University, the University of Turku and the University of Rome.

He has published over 100 papers in the field of Toxicology. A substantial part of his research has focused on the molecular mechanisms of drug toxicity and on liver injury. He has been an invited speaker at many national and international conferences and is currently Associate Editor of the journal Toxicology and Applied Pharmacology and on the editorial board of Chemico-Biological Interactions. In 2020, he was elected to the Académie d'Agriculture de France.

Suzanne Fitzpatrick, U.S. Food and Drug Administration (US FDA)
Panellist

Carl Westmoreland, Unilever
Panellist

Dr Carl Westmoreland works for Unilever and is based in the Safety and Environmental Assurance Centre (SEAC) in the UK. He is the Director of Science & Technology where a large part of his role focuses on the strategic development and application of the science needed for non-animal, risk-based safety assessments. He received his first degree in biology from the University of York, UK and subsequently his PhD in 'The use of in vitro models for mechanistic studies in toxicology' from the University of Surrey in the UK. Following this, Carl worked for 10 years at GlaxoSmithKline in the UK in the areas of in vitro toxicology, genetic toxicology and pharmaceutical regulatory toxicology.

Carl represents Unilever on a number of groups including the European Partnership for Alternative Approaches to Animal Testing (EPAA), UK NC3Rs, ECETOC, Cefic and the Animal Free Safety Assessment (AFSA) collaboration. He has previously served on many scientific groups including the EURL-ECVAM Scientific Advisory Committee.

Katrin Schutte, European Commission

Speaker

Dr Katrin Schütte is a policy officer at the EU Commission's Directorate for the Environment, which she joined in 2014. Her responsibilities cover several aspects of REACH (mainly Registration and Evaluation) as well as the implementation of Directive 2010/63/EU on the protection of animals used for scientific purposes. Related to the Directive, she has been closely involved in the organisation of the 2016 and 2021 Commission scientific conferences about furthering the use of Non-Animal Approaches. She is also member of the steering committee of EPAA (European Partnership for Alternative Approaches to Animal testing) and in several EPAA project teams. Katrin has a degree in nutrition sciences from the University of Hohenheim, a PhD in neurobiology from the University of Heidelberg (DE) and is Diplomate of the American Board of Toxicology (DABT) and a European Registered Toxicologist (ERT). Before joining the Commission, she worked for 15 years as a toxicologist and regulatory affairs manager in the consumer products sector.

Title of talk: NAMs in regulatory risk assessment – the REACH experience

Abstract of talk

NAMs in regulatory risk assessment – the REACH experience The Chemical Strategy for Sustainability encourages the exploration of NAMs in risk assessment across all EU chemicals legislation, including REACH standard information requirements but also pesticides and biocides, life cycle assessment of chemicals, development and for generation of information on endocrine disruptors, risk assessment of mixtures and combined exposure, supporting the development and uptake of innovative risk assessment tools internationally. This talk will share experiences from the exercise of developing options for revising the REACH information requirements at Annex VII - X, where the options should at the same time lead to identification of more critical hazards and also rely on NAMs as much as possible. The key challenges that still exist with using NAMs under REACH will be highlighted. Hazard information for use under REACH must be suitable for both risk assessment and classification, and there is no suggested system for classification based on NAMs data yet for most endpoints. The talk will aim to raise some proposals on how to address the slow validation of NAMs for regulatory purposes as well as how the acceptance of NAM-related applications in regulatory toxicology could be accelerated.

Maurice Whelan, Joint Research Centre (JRC)

Chair/Co-chair

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; a member of the Steering Committee of the European Partnership for Alternative Approaches to Animal Testing (EPAA); and chair of the Regulatory Advisory Board of the European Organ-on-Chip Society (EUROoCS). His publications include over 200 scientific papers and a 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).

Michael Empl, European Medicines Agency (EMA)

Panellist

Michael graduated as a veterinarian from the University of Veterinary Medicine Hannover in 2010 and is a certified specialist for veterinary pharmacology and toxicology as well as a European Registered Toxicologist. Between 2010 and 2018, he worked as researcher at the Institute for Food Toxicology of the University of Veterinary Medicine Hannover, where his work mostly revolved around toxicological (cancer) research and cancer chemoprevention, the absorption and metabolism of xenobiotics as well as the application and development of in vitro 3Rs methods. Before joining EMA's Veterinary Pharmaceuticals Service in mid-2019, he worked as study director and researcher at the Fraunhofer Institute for Toxicology and Experimental Medicine in Hannover, with a focus on inhalation toxicology. At EMA, his role mainly consists in managing MRL and initial/post marketing authorisation procedures for veterinary pharmaceuticals and in acting as subject matter expert for questions pertaining to toxicology, user and consumer safety, environmental risk assessment and 3Rs. He provides scientific and procedural support to the Agency's Joint CVMP/CHMP 3Rs Working Group (J3RsWG) and to the Committee for Veterinary Medicinal Products (CVMP) Environmental Risk Assessment Working Party (ERAWP).

Anna Lennquist, ChemSec

Panellist

Anna Lennquist has been working for ChemSec since 2011. ChemSec is an EU based non-profit environmental organisation and a leading advocate of chemicals policy. It works to speed up legislative processes, engage business and act as a catalyst for progressive dialogue and action. As senior toxicologist at ChemSec, Anna has worked on a number of different projects to support substitution of hazardous chemicals with safer alternatives. When she started at ChemSec she first worked with the EU funded project SUBSTPORT. Since 2013 she has been the project manager for the SIN (Substitute It Now) List, which has proven to be an important driver for innovation. She is also participating in a number of different expert groups and stakeholder committees as an expert on chemicals management, policy and the underlying science. Anna holds a PhD in ecotoxicology as well as a journalist degree from the University of Gothenburg, Sweden. She has a strong interest in communicating scientific findings to a wider audience.

Russell Thomas, U.S. Environmental Protection Agency (US EPA)

Speaker

Russell Thomas is the director of the Center for Computational Toxicology and Exposure at the U.S. Environmental Protection Agency (EPA). The Center is performing solutions-driven research to rapidly evaluate the potential human health and environmental risks due to exposures to environmental stressors and ensure the integrity of the freshwater environment and its capacity to support human well-being. Dr. Thomas has a broad, multidisciplinary background and experience. Dr. Thomas' formal academic training includes a B.A. in chemistry from Tabor College, an M.S. in radiation ecology and health physics from Colorado State University, and a Ph.D. in toxicology also at Colorado State. Following his doctoral studies, Dr. Thomas performed postdoctoral research in molecular biology and genomics at the McArdle Cancer Research Laboratory at the University of Wisconsin. Following his academic training, Dr. Thomas performed bioinformatics and genomics research in the biotechnology sector, developed high-throughput in vitro screening assays in the biopharma sector, and worked as an investigator and senior manager at a non-profit research institute.

Title of talk: Developing NAMs for regulatory risk assessment at US EPA – experience, state-of-the-art, lessons learnt

Abstract of talk

Thousands of chemicals are used in commerce and are present in the environment, while hundreds more chemicals are introduced each year. In many cases, the chemicals have limited data that can inform potential human health and ecological risks. Developing and applying emerging scientific and technological approaches are important to address these challenges and enable regulatory agencies to continue

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protecting human health and the environment. New Approach Methods (NAMs) are included among these emerging approaches and have the potential to transform the way the U.S. Environmental Protection Agency (US EPA) evaluates chemicals in a diverse array of human health and environmental decision contexts. The NAMs include a broad range of in vitro and in silico approaches for evaluating potential chemical hazards, identifying modes or mechanisms of action, extrapolating between internal and external doses, and estimating exposure. In many cases, the endpoints and uncertainties associated with these new methods are qualitatively and quantitatively different from the traditional approaches. The inherent differences have required new efforts to characterise the uncertainties in both the NAMs and traditional methods while developing new frameworks to build confidence in the approaches for application to a range of decision contexts. The US EPA continues to invest in NAM research and has released an updated Agency Work Plan outlining broad objectives for developing and applying NAMs as well as long-term and short-term strategies to achieve those goals. This presentation will provide an overview of the ongoing efforts at US EPA to develop and improve NAMs related to toxicology, toxicokinetics, and exposure; evaluate NAMs for fit-for-purpose regulatory application through case studies and scientific confidence frameworks; and outline a path forward for increasing integration into regulatory decisions. *The contents of the abstract and associated presentation do not necessarily reflect U.S. EPA policy.

Tomasz Sobanski, European Chemicals Agency (ECHA)

Speaker

Tomasz is Team Leader for Alternative Methods Team in the Computational Assessment Unit at the European Chemicals Agency. He is a physicist specialised in metrology and a computer scientist (applications of AI in the measurement systems). He has worked at ECHA for over 13 years focusing on the development and application of alternative methods in the regulatory processes. For many years, he was a ECHA project manager of the OECD QSAR Toolbox, while in recent years he focused on NAMs and their applications in regulatory science. Before ECHA, he was first a post doc and later a scientific officer in the Institute of Health and Consumer Protection at the Joint Research Centre, where he contributed to the development of the novel in vitro systems for mutagenicity, cardio toxicity and developmental neuro toxicity. Tomasz has co-authored over 30 publications and book chapters.

Title of talk: Experience of ECHA in developing and applying NAMs for regulatory applications

Abstract of talk

The objective of the REACH chemicals regulation is to provide a high level of protection for human health and the environment. The safe use of chemicals is

ensured through chemical safety assessments, and the data requirements laid down in the legislation are the basis for establishing that safe use. Recent developments in New Approach Methodologies (NAMs) are promising because of their potential to bring new toxicological information that could be useful in managing risks relating to chemicals. The growing library of mechanistic assays, the wider utilisation and standardisation of genomics techniques and the introduction of robust IVIVE modelling tools all create an opportunity to address not only local but also more complex effects related to systemic toxicity after repeated exposure. The wider application of NAMs in a regulatory context will increase throughput, provide insights on toxicological modes of action, limit reliance on animal tests and lower the costs of hazard assessments. However, the remaining challenge is how to interpret and calibrate the NAM results to fit the current regulatory system of risk assessment and classification. This presentation will give an overview of ECHA activities related to developing NAMs and applying them in regulatory applications. Examples will include input on the development of the metabolomic biomarker list M700+, ECHA standardised workflows to cover specific areas of concern, APCRA (Accelerating the Pace of Chemical Risk Assessment) case studies and ECHA's efforts to support OECD harmonisation activities.

Bob Diderich, Organisation for Economic Co-operation and Development (OECD)
Speaker

Bob Diderich is the Head of Environment, Health and Safety Division at the Environment Directorate, Organisation for Economic Cooperation and Development. Bob Diderich has been involved in environmental hazard and risk assessment of chemical substances since 1992, when he joined the German Federal Environmental Agency. He was working in France between 1995 and 2002, first for the French Ministry of the Environment and then the French National Institute for Industrial Environment and Risks, where he was assessing the environmental risks of industrial chemicals and biocides. In 2002 he joined the Organisation for Economic Co-operation and Development where he was in charge of the OECD Cooperative Chemicals Assessment Programme and the OECD Project on (Quantitative) Structure Activity Relationships. Since 2012 he is the head of the Environment, Health and Safety Division.

Title of talk: Development and Implementation of NAMs at the OECD

Abstract of talk

The Organisation for Economic Cooperation and Development (OECD) is committed to finding alternatives to animal testing when the suitability of the alternative can be demonstrated. Molecular and cell-based methods are increasingly included in OECD Test Guidelines to provide mechanistic information and to predict in vivo effects. In

addition to the uptake of these new approach methods (NAMs) through the 'traditional' path of creating new test guidelines, the 'Integrated Approaches to Testing and Assessment (IATA) Case Studies' project provides experts with a platform to share experiences using new approach methods in a regulatory context. Case studies illustrate how new biotechnology and modelling approaches can be used to evaluate chemical safety and are a starting point for developing best practices and common understanding, as well as for developing tools and guidance on using alternative approaches to address a variety of regulatory decision scenarios. While many of the exploratory projects are not (initially) harmonised or covered by the agreement on Mutual Acceptance of Data (MAD), OECD projects undergo review cycles by regulatory scientists to help define the strengths and limitations of such approaches, to consider applications to regulatory decisions and to help to build confidence in using twenty-first century approaches for evaluating the safety of chemicals. In addition, these experiences have helped to provide a roadmap for the first OECD Defined Approach Test Guideline, which uses alternative methods in combination as a substitute for animal data predicting human dermal sensitisation, the results of which are covered by the Mutual Acceptance of Data.

Bob Van De Water, Leiden University
Speaker

Bob van de Water (M) is head of the Division of Drug Discovery and Safety within LACDR. He has ample experience in molecular mechanisms of toxicity, applying in particular in vitro 2D and 3D approaches in combination with toxicogenomics and functional genomics strategies. One focal point for his group has been the deployment of high-throughput methodologies in AOP-based toxicity testing strategies. His group established a large panel of BAC-GFP reporter cell lines that can be routinely used to monitor cellular stress pathway activation with high-content confocal imaging allowing time-resolved single cell information following chemical exposure. In addition, his group has developed integrated high-throughput targeted transcriptomics analysis to derive MoA information and assess variability in cellular stress response activation, enhanced by web-based methods for weighted gene co-expression network analysis based on large toxicogenomics datasets. He is coordinator of the Horizon2020 EU-ToxRisk and RISK-HUNT3R projects.

Title of talk: Developing NAMs for regulatory risk assessment – academia's experience

Abstract of talk

There is a need for a paradigm shift in toxicology towards an animal-free, mechanism-based integrated approach to human chemical safety assessment. The aim of the Horizon2020 EU-ToxRisk project was to unite all relevant disciplines and

stakeholders to establish: i) pragmatic, solid read-across procedures incorporating mechanistic and toxicokinetic knowledge; and ii) ab initio hazard and risk assessment strategies of chemicals with little background information. The project focused on repeated dose systemic toxicity (liver, kidney, lung and nervous system) as well as developmental/reproduction toxicity. Different human tiered test systems were integrated to balance speed, cost and biological complexity. Advanced technologies, including high throughput transcriptomics and high throughput microscopy, provided quantitative and mechanistic underpinning of AOPs and key events (KE). The project combined in silico tools and in vitro assays, using computational modelling approaches to provide quantitative data on the activation of KE of AOP. This information, together with detailed toxicokinetics data and in vitro-in vivo extrapolation algorithms, forms the basis for improved hazard and risk assessment. The presentation will outline the EU-ToxRisk project and its achievements. At the end of the presentation there will be an introduction to the new RISK-HUNT3R project supported by the European Commission. The critical challenges that RISK-HUNT3R will address include the (ab initio) safety evaluation of chemicals without prior knowledge of their properties and taking the step from a hazard identification to a full risk assessment. The project will develop, validate and implement integrated approaches to next generation risk assessment (NGRA) using innovative, mechanism-based, human-relevant in silico and in vitro new approach methodologies (NAM). Through a systematic and iterative evaluation of the NAM toolbox, we will optimise the strategy to assess exposure and toxicokinetics, as well as toxicodynamics. Adverse outcome pathway (AOP) network activation and in vitro to in vivo extrapolation will form the basis of human adversity prediction.

Julia Baines, PETA Science Consortium International Panellist

Dr. Julia Baines serves as a science policy advisor for the PETA Science Consortium International e.V., a European Chemicals Agency-accredited stakeholder organisation, advising on strategies to minimise the use of animals under the Registration, Evaluation and Authorisation of Chemicals (REACH) regulatory framework, communicating with the European Commission and European Parliament. Dr Baines has advocated, in both the regulatory and public arenas, for the cosmetics animal testing ban to be fully upheld as intended by EU legislators, with reliance only on non-animal methods for safety assessment purposes. She also works to advance animal-free approaches with a focus on regulatory tests that protect human health and the environment, collaborating with other scientists and policy advisors to create a world in which robust toxicological assessments are conducted without using animals. Dr Baines has also applied her expertise by representing the Science Consortium at many ECHA Board of Appeal cases, advising on non-animal approaches that meet regulatory needs.

Sylvia Escher, Fraunhofer ITEM

Panellist

Dr. Sylvia E. Escher received her doctorate in chemistry from the University of Hannover in 1999 and has been working at the Fraunhofer Institute for Toxicology and Experimental Medicine in Hannover since September 2006, where she is currently head of the In-silico Toxicology department in the field of human risk assessment. Her research interests include the development and maintenance of toxicological databases such as RepDose®/ToxTool®, and their use to develop and improve human risk assessment methods. Examples include the development of NAM supported read-across approaches and the TTC concept. Her team is currently contributing to i) the development of structure activity relationships of Nitrosamines, ii) the development of adverse outcome pathways (AOPs) for pulmonary fibrosis and to a PBK model addressing in particular the integration of in vitro ADME properties of airborne compounds for example in the RiskHunt3R project. She recently coordinated the EFSA project on the “Development of a Roadmap for Action on New Approach Methodologies in Risk Assessment”.

Marcel Leist, University of Konstanz

Panellist

Marcel Leist obtained an MSc in toxicology (Guildford 1989), and a PhD in pharmacology (Konstanz 1993). Since 2006, he has been Head of the department of in vitro toxicology and biomedicine at the University of Konstanz (inaugurated by the Doerenkamp-Zbinden foundation), and director of the Center for Alternatives to Animal Testing in Europe (CAAT-Europe), a joint venture with Johns-Hopkins University. From 2000-2006, he worked as ‘Head of Department of Disease Biology’ on the discovery of neurology and psychiatry drugs in the Danish pharmaceutical company Lundbeck A/S. The current research addresses stem cell differentiation to neuronal lineages as well as the pharmacological and toxicological characterization of test methods and in vitro disease models. The novel test methods are used both to reduce the use of animals in scientific research and to shift research applications towards the use of human cells. The lab is particularly well-known for its test methods for developmental toxicity and neurotoxicity. It is also broadly involved in work on standardizing and quality controlling new approach methods, for instance in large-scale European research programs or in projects with EFSA.

The research output is documented by 300 publications (cited over 30,000 times), and was awarded with many research prizes. The experience in the field is used for a teaching program incorporating 3R information into courses in biochemistry, disease biology, toxicology & pharmacology.

Anna Lanzoni, European Food Safety Authority (EFSA)

Rapporteur

Anna Lanzoni joined EFSA in 2013 as senior scientific officer. She worked in the GMO (Genetically Modified Organisms) Unit till 2021, focusing on the risk assessment of GMOs and the development of guidance documents. She is currently working as toxicologist in the pesticide peer review area and is involved in toxicology development projects in the context of the Adverse Outcome Pathway (AOP) frame. Her area of interest is the risk assessment of (novel) proteins, in particular the prediction of protein toxicity by new and tailored in silico tools. Previously, she worked for 20 years in the pharmaceutical industry as toxicologist and toxicological pathologist, participating to research and development projects on potential new medicines in various therapeutic areas (such as central nervous system, antimicrobials, gene therapy) and in the development of animal models of disease (atherosclerosis, pulmonary infection, stroke). Anna graduated as veterinary medicine doctor in 1990 and has a PhD in veterinary hygiene and pathology from the University of Milan.

Annamaria Rossi, European Food Safety Authority (EFSA)

Rapporteur

Annamaria Rossi has more than 25 years of experience in the field of molecular and regulatory toxicology. She was trained as cellular biologist and received her PhD in molecular toxicology from the Karolinska Institute in Stockholm (Sweden). After a post-doc at the RITOX (Utrecht University), she started her career in the pharmaceutical industry first as Head of Cellular Toxicology (Pharmacia, Italy), continuing as Head of the Toxicology Laboratories (Organon, NL), and later as Head of Investigative Toxicology and Point of Contact for Regenerative Medicine (Pfizer UK). Since 2013, she serves as Senior Scientific Officer in EFSA where she worked, previously in the field of flavouring and enzymes and presently in the Novel Food/Nutrition and Food Innovation (NIF) Unit. In NIF she is the reference point for assessment of genotoxicity and toxicity of Novel Food applications. In her role, she is contributing to assuring the safety of the Novel Food that will be placed on the market after authorization by the European Commission.

Edoardo Carnesecchi, European Food Safety Authority (EFSA)

Rapporteur

Edoardo Carnesecchi was trained as a food scientist. He received his PhD in toxicology from Utrecht University, Institute for Risk Assessment Sciences (IRAS) in 2021. He joined the European Food Safety Authority (EFSA) in 2015, firstly as a trainee and one year later as Junior Scientific Officer in EFSA's Animal and Plant

Health unit. In 2018, he moved to the Institute for Pharmacological Research Mario Negri, where we worked as a researcher within the Laboratory of Chemistry and Environmental Toxicology. In this context, Edoardo carried out his PhD thesis in joint collaboration between the Mario Negri Institute, IRAS and EFSA. The PhD project was part of an EFSA funded project entitled "Openfoodtox integrated with non-testing methods for toxicity evaluation". During his PhD, Edoardo has been awarded international prizes such as the best oral presentation at the European Commission Joint Research Centre' Summer School on "Non-animal approaches in sciences" (Ispra, 2019) and the Lush Prize for young researchers (London, 2020). In 2020, Edoardo joined the Organisation for Economic Co-operation and Development (OECD, Paris) as a Junior Policy Analyst - Chemicals working within the Environment, Health and Safety (EHS) division. Edoardo moved back to EFSA in 2021 where is now a Data Officer working on the development of new approach methodologies (NAMs) applicable to the risk assessment of chemicals.

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