Many Ways

ENDOCRINE DISRUPTORS: EXPLORING PRESENT CHALLENGES AND FUTURE DEVELOPMENTS (IN MEMORY OF ALFONSO LOSTIA)

Summary

Currently, at EU level, scientific criteria for the identification of Endocrine Disruptors (EDs) are implemented only for pesticides and biocides. As highlighted by the Fitness Check of legislation on EDs, there is a need for a more horizontal approach to identifying EDs across different sectorial legislation, supported by strengthened information requirements. For EDs, screening of chemicals and decision-making is dominated by use of vertebrate data in general and, mammalian data, in particular. The session aims at giving emphasis to advancements in the field of EDs.
It should serve as a platform for an open dialogue between regulatory and non-regulatory scientists to explore future possibilities to move to more integrated assessments. These would incorporate data generated by new technologies to reach better and faster decisions for more chemicals on a cross-sector basis, in line with the 'one substance-one assessment' ambitions within the Chemicals Strategy for Sustainability. Overall, the session outcome should help preparing for future challenges by putting shape on future directions and possible collaborations.

Vision

The session aims to explore advancements in the field of Endocrine Disruptors (EDs) with the scope of moving to a more integrated interdisciplinary approach for testing and assessment for the identification of EDs. Such approaches should enable a deeper understanding of the different mechanisms disrupting the endocrine system leading to an adverse effect at individual and population level. Improved mechanistic understanding supports (i) development of alternatives to vertebrate test methods, (ii) extrapolation across species, (iii) identification of key targets associated with Adverse Outcome Pathways (AOPs). In the context of the European Green Deal, these integrated approaches can be used to pioneer the way forward for simplifying and consolidating EU regulatory frameworks and the implementation of the 'one substance-one assessment' concept with the ultimate goal of a toxic free environment.

Background – Challenges and opportunities

Currently, at EU level, scientific criteria for the identification of Endocrine Disruptors (EDs) are implemented only for pesticides and biocides. As highlighted by the Fitness Check of legislation on EDs, a more horizontal approach is needed to identify EDs across different sectorial legislation, supported by strengthened information

Organiser: European Food Safety Authority
Co-organisers: ECDC European Centre for Disease Prevention and Control; ECHA European Chemicals Agency; European Environment Agency; European Medicines Agency Science Medicines Health; European Commission Joint Research Centre

requirements. Additionally, while at EU level, a hazard-based approach built on the World Health Organization definition for adversity is applied, a risk-assessment based approach is followed in other global regions. One of the challenges for the future of ED assessments is the harmonisation across jurisdictions.

For EDs, screening of chemicals and decision-making is dominated by the use of vertebrate data in general and, mammalian data, in particular. Methods for non-mammalian species are comparatively scarce and they include only a few endpoints that may be considered ED specific. In any case, reliance on animal testing is not a practical approach for effective screening, and new approaches are needed to fill the gap between the number of chemicals in use and the number of chemicals assessed to date. The development of new methodologies as valid alternatives to in vivo data is a key step. Improvements in our mechanistic understanding would also allow for a more reliable extrapolation between vertebrate species since it is well known that the vertebrate endocrine system is conserved across species.

Given the complexity of ED assessments at sectorial level and across legislation, constant engagement with stakeholders, Member State competent authorities, sister agencies and the public is essential for knowledge sharing and for consistency in assessments across legislation.

The session will provide an opportunity to engage with all stakeholders to explore future possibilities to move to more integrated assessments incorporating data generated by new technologies to reach better decisions, faster and for more chemicals on a cross-sector basis, in line with the 'one substance-one assessment' ambitions within the Chemicals Strategy for Sustainability.

Scope and objectives

The session aims at addressing identified gaps by soliciting contributions on:

- Current status (e.g. regulatory requirements, available scientific knowledge and testing methodologies) and challenges;
- New testing methodologies and strategies, including extended test protocols, application of New Approach Methodologies (NAMs), use of computational methods in predicting adverse outcomes, AOPs, AOP networks, Integrated Approaches to Testing and Assessment (IATA), extrapolation across species , approaches for prioritisation;
- Redefining ED identification on the basis of new approach methodologies;
- Approaches for grouping of similar substances and cumulative assessments.

People behind the session

Session Coordinator: Maria Arena (EFSA)

Chairpersons: Manuela Tiramani, European Food Safety Authority (EFSA); Martin Wilks, University of Basel
Moderators: Sharon Munn, European Commission; Andreas Kortenkamp, Brunel University London
Rapporteurs: Maria Arena, European Food Safety Authority (EFSA); Aude Kienzler, European Food Safety Authority (EFSA); Francesca Pellizzato, European Chemicals Agency (ECHA); Andrea Terron, European Food Safety Authority (EFSA)

Many Ways – Session affiliate profiles

ENDOCRINE DISRUPTORS: EXPLORING PRESENT CHALLENGES AND FUTURE DEVELOPMENTS (IN MEMORY OF ALFONSO LOSTIA)

Martin Wilks, University of Basel
Chair/Co-chair

Martin Wilks obtained a doctorate in medicine in 1986 following his medical studies and internship at the Medical School Hannover (Germany). After completing a Ph.D. in toxicology at the University of Surrey (UK) in 1990 he worked as a medical toxicologist in the chemical industry and the national health service in the UK and Switzerland, including two years as a consultant at Guy's & St Thomas' poisons unit in London. He has been the director of the Swiss Centre for Applied Human Toxicology at the universities of Basel, Geneva and Lausanne since its establishment in 2009 and was appointed Adjunct Professor at the Medical Faculty of the University of Geneva in 2012 and at the Faculty of Sciences of the University of Basel in 2019. He is a Past President of the European Association of Poison Centres and Clinical Toxicologists (EAPCCT) and current Secretary-General of EUROTOX, the Federation of European Toxicologists and European Societies of Toxicology. He serves on a number of scientific expert and advisory committees including EFSA's Panel on Plant Protection Products and their Residues (PPR) and the German Federal Institute for Risk Assessment's Committee on Pesticides and Biocidal Products.

Andreas Kortenkamp, Brunel University London
Speaker and Panellist

Andreas Kortenkamp is professor of human toxicology at Brunel University London where he directs the Centre for Pollution Research and Policy. He researches the combined effects of chemicals on endocrine diseases. Professor Kortenkamp has served on the US National Research Council Panel on cumulative risk assessment for phthalates, and on the US National Research Council Panel for non-monotonic dose-response relations for endocrine disruptors. He was a member of the US Consumer Health Advisory Panel on the assessment of phthalates and produced the 2009 State of the Art Report on Mixture Toxicology for the European Commission and the 2012 State of the Art Assessment of Endocrine Disrupters. He joined the WHO/UNEP panel for evaluating the state of the science of endocrine disruption in 2012. He coordinates the EU-funded ATHENA project on developing new test methods for thyroid hormone system disrupting chemicals and is involved with the

EU-funded exposome project ATHLETE, the PANORAMIX project on mixtures and the HBM4EU initiative.

Title of talk: Endocrine disruption across taxa: support for a One Health perspective

Abstract of talk

More than 5 decades of research has shown that many chemicals with a wide variety of structural features can act as endocrine disruptors in humans and wildlife species. This includes legacy chemicals as well as current-use substances. Due to the multitude of effects involved, the identification of hazards requires novel and dedicated testing strategies, beyond traditional toxicity testing. Focusing on reproduction, one of the original concerns of endocrine disruptor research, this presentation will trace the similarity of endpoints in humans and wildlife and show that despite the differences in the endocrine organisation of reproduction, many chemicals produce similar effects across taxa. There is concern about deterioration in semen quality in Western countries, with recent indications that similar trends are now evident in East Asia. PCDDs, PCBs, PBDEs, bisphenols, certain pesticides and plasticisers have been linked to poor semen quality and disruption of other hallmarks of male sexual development. The same EDCs that contribute to reduced reproductive success in humans affect mammalian wildlife and other vertebrates. Recent evidence from studies among marine mammals, particularly cetaceans, ascribe reproductive failure to PCBs, perfluorinated chemicals and others. New studies among breeding dogs reveal similar trends, with associations with plasticisers and other EDCs. However, despite considerable advances in our understanding of contributing chemicals, the contours of the exposome relevant to disruptions of reproductive ability have not fully come into view. This requires approaches that embrace the reality of mixture exposures. The outcome of a recent mixture risk assessment for male reproductive health with a focus on deteriorating semen quality will be presented. The assessment revealed unacceptably large exceedances of combined tolerable exposures, with the largest contribution from bisphenols, PCDDs, painkillers and certain phthalates. In the spirit of the One Health philosophy, these insights could provide valuable orientation for further research in marine mammals and pets.

Donna Macmillan, Humane Society International
Speaker

Donna Macmillan is a Senior Strategist for Regulatory Science in the Research and Toxicology Department at Humane Society International. She co-leads the Chemicals workstream within the Animal-Free Safety Assessment (AFSA) Collaboration where she focuses on advancing a paradigm shift from traditional toxicology to New Approach Methodologies (NAMs) in chemical safety assessment,

in collaboration with AFSA industrial partners. She is experienced in computational toxicologydrug development. She received her BSc (Hons) in Biomolecular and Medicinal Chemistry and her PhD in Medicinal Chemistry from the University of Strathclyde in Glasgow, Scotland.

Title of talk: Poster pitch 1 - Identifying endocrine disruptors – thoughts and recommendations for implementation in the EU)

Abstract of talk

The endocrine system is responsible for the regulation of growth, reproduction, metabolism and weight in humans and other animals. Endocrine disruptors (EDs) are substances that are thought to disrupt these processes and can lead to cancer and reprotoxic effects. Endocrine disruptors can also impact the environment, potentially harming wildlife by causing reproductive abnormalities and population decline. Due to increasing concern over EDs, the European Commission's (EC) 'Chemicals Strategy for Sustainability' has proposed to identify and restrict the use of EDs. The EC proposes to amend the European Union's Classification, Labelling and Packaging (CLP) Regulation and the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Annexes to include ED-specific information requirements identified using in vivo tests which are fundamentally not fit-for-purpose – they demonstrate poor reproducibility and have a lack of relevance to human health.

Lucia Vergauwen, University of Antwerp
Speaker

Lucia Vergauwen has a Master in Biomedical Sciences and a PhD in Biology. At present, she is postdoctoral researcher and project coordinator in the Zebrafish lab of the Department of Veterinary Sciences at the University of Antwerp. Her research is funded by the Horizon 2020 and Horizon Europe programmes and involves understanding the mechanisms underlying aquatic toxicity, the development of Adverse Outcome Pathways (AOPs), and the development of alternative testing strategies for ecological and human risk assessment using in vitro and zebrafish embryo assays. Her work is currently focused on the development of AOPs outlining mechanisms of thyroid hormone system disruption in fish to facilitate the development of new test methods for endocrine disruptor evaluation. Furthermore, she is working on the evaluation of the taxonomic applicability of a broader network of all thyroid related AOPs in order to facilitate cross-species extrapolations and support the use of non-mammalian models for human health and vice versa. Additionally, she has teaching assignments in the Department of Veterinary Sciences and the Department of Biology and as a part-time assistant professor in the Department of Biomedical Sciences in the study program Environmental Health

Sciences. She has published over 40 peer-reviewed articles (WoS H-index 23) and is Editorial Board member of Environmental Toxicology & Chemistry.

Title of talk: Poster pitch 2 - Evaluation of an adverse outcome pathway network for thyroid hormone system disruption across taxonomic groups

Abstract of talk
Thyroid hormone system disrupting chemicals (THSDCs) are widely regarded as potential threats to human and environmental health. Thus, efforts are under way within the human health and ecotoxicology communities to develop screening assays capable of identifying THSDCs and to describe adverse outcome pathways (AOPs) that link thyroid hormone system disruption (THSD) to adverse outcomes. The Horizon 2020 project EndocRine Guideline Optimisation (ERGO) aims to break down the wall between the human and environmental health assessment of chemicals using an AOP network (AOPN) approach and promoting the use of non-mammalian assays for predicting effects in mammals, including humans, and vice versa.

Aldert Piersma, National Institute for Public Health and the Environment (RIVM)
Panellist

Aldert H. Piersma Ph.D. has served as professor of reproductive toxicology at the Institute for Risk Assessment Sciences (IRAS) of Utrecht University in the Netherlands since 2007; and has been employed as a senior scientist at the National Institute for Public Health and the Environment (RIVM) in the Netherlands since 1988. His work combines fundamental research in reproductive toxicology with advisory work in national and international advisory committees, such as of the Dutch Health Council, EU, OECD and WHO. The main theme is the innovation of hazard and risk assessment methodology in reproductive and developmental toxicology, including the design and implementation of animal-free alternative methods and molecular and computational approaches towards mechanism of action-based understanding of toxicity. He is known for his work on alternatives to animal testing in developmental toxicology, using animal-free assays with embryonic stem cell lines, as well as zebrafish and rat embryos. He applies molecular approaches to understand mechanisms of action and to identify adverse outcome pathways, facilitating the understanding and implementation of alternative methods. He also invests in the design of alternative testing strategies, combining assays and applying computational systems toxicology approaches to enhance the prediction of developmental toxicity and to reduce and replace animal use in chemical and pharmaceutical risk assessment. He has published over 250 original scientific papers, over 350 abstracts and around 10 book chapters.

Title of talk: Poster pitch 3 - Developing a quantitative AOP for liver-mediated thyroid modulation after prenatal exposure to a xenobiotic compound in rats

Kevin Schlüppmann, Leibniz Research Institute for Environmental Medicine (IUF)
Panellist

Kevin Schlüppmann successfully obtained his Bachelor of Science in Biology at the Hamburg University. He then proceeded to obtain a Master of Science in Toxicology at the Heinrich-Heine-University Düsseldorf. Since July 2021, he has been working as a PhD student in the team of Prof. Ellen Fritsche that develops new approach methodologies to reduce animal testing and increase regulatory acceptance of alternative, in vitro, test methods. In his PhD studies he investigates the effects of endocrine signaling pathways, and their disruption, on neurodevelopmental key events and develops assays to identify substances with endocrine disrupting properties in the framework of the Horizon 2020's ENDpoiNTs project. He co-authored an important scientific study on the validation of the human Neurosphere Assay for application in developmental neurotoxicity evaluation for regulatory purposes. Recently, he joined the Research Training Group 2578 as an associated PhD student. Moreover, he is actively striving to help maintain and increase the quality of PhD studies at the Leibniz institute by being part of the PhD committee.

Title of talk: Poster pitch 4 - Refining EDC hazard assessment by integrating an in vitro testing battery for endocrine disruptor (ED)-induced developmental neurotoxicity (DNT)

Henrik Holbech, University of Southern Denmark
Speaker and Panellist

Henrik Holbech did his Master and PhD in Ecotoxicology at University of Southern Denmark (SDU) and is now Associate Professor and research group leader at Department of Biology, SDU. For 20 years, Henrik's main research focus has been on endocrine disrupting chemicals in the aquatic environment and the development of biomarkers and endpoints to be included in OECD test guidelines to improve protection of environmental species. Henrik was leading the OECD validation phase 1 and 2 of The Fish Sexual development Test, TG 234 (2006-2011) and has been a member of OECD VMG-Eco since 2007. Currently, he is coordinating the Horizon 2020 project, ERGO with focus on new endpoints to assess thyroid hormone system disruption in vertebrates and better use of data between human health and environmental assessment of endocrine disrupters. Based on his long experience with testing for EDs, Henrik is appointed by the DK EPA to represent DK in the ECHA ED expert group, the OECD VMG-Eco and in the OECD endocrine disruptor testing and assessment advisory group (EDTA AG).

Title of talk: Flash report | What works well and what needs improvement in ED assessments: a stakeholder view

Abstract of talk
Identification, assessment and regulation of endocrine disrupting chemicals (EDCs) for the protection of humans and wildlife species rely on three aspects: first, a strong toolbox of validated tests being able to identify EDCs exerting their ED effects through different modes of action on different parts of the endocrine system at sensitive life-stages in relevant species; second, implementation of information requirements and guidance on testing strategies in chemical regulations; and third, regulatory actions based on ED identification. This flash report will focus on the first aspect while touching upon the second and the third. The toolbox of validated test guidelines is compiled in the OECD conceptual framework (CF) for Testing and Assessment of Endocrine Disrupters. It is a dynamic framework of test guidelines that is regularly replaced, renewed, and updated. In 2018, OECD Revised Guidance Document 150 on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption presented the – at that time – validated test guidelines and comprehensive guidance on the use of them. The CF toolbox as of 2022, as well as toolbox gaps identified at OECD and EU workshops, will be presented and discussed. Emphasis will be put on the latest improvements in the toolbox but also on the unused potential of cross-species and cross-class extrapolation of effects of EDs in vertebrate species. The lack of test methods covering non-EATS mediated effects and the lack of methods for specific species and classes, particularly belonging to the invertebrate phyla, will be presented. The need for updated information requirements in several regulations, including REACH, in relation to the vision of horizontal criteria for identification of EDs will be discussed. New tools aiming at improved testing and assessment of EDs, such as new approach methodologies (NAMs), integrated approaches to testing and assessment (IATA), adverse outcome pathways (AOPs) and AOP networks will be included in the discussion, including considerations related to replacing, reducing and refining in vivo experiments.

Daniel Pickford, Syngenta
Speaker and Panellist

Dan is an ecotoxicologist and Principal Technical Expert in Syngenta Product Safety, who has been working in the field of endocrine disruption in non-target organisms for over twenty years, with experience in academia, industry and on the EFSA PPR panel. Dan has worked extensively in amphibian models for assessing endocrine disruption, investigating effects on female reproduction in graduate studies, and subsequently developing an interest in thyroid, being closely involved with development and validation of the Amphibian Metamorphosis Assay, OECD TG 231.

Dan moved to Syngenta over 7 years ago, and is based at Jealott's Hill Research Centre, UK, where he splits his time between ecological risk assessment, specialising in aquatic organisms, and leading endocrine disrupter evaluation and data generation in non-target organisms across the Syngenta portfolio. He is a member of Crop Life Europe Aquatic and Endocrine disrupter groups, participated in the ECETOC task force on developing ED guidance, and represented ECPA at the Commissions stakeholder workshop on the new ED Guidance document (2017). He has finally got used to working at home, but much prefers riding his motorcycle to the office to interact with colleagues.

Title of talk: Flash report | What works well and what needs improvement in ED assessments: a stakeholder view

Abstract of talk
The ECHA-EFSA ED Guidance Document (GD) offers a relatively clear definition of data required to conclude on EAS-mediated activity and adversity for (eco)toxicology. For human health, the weight of evidence (WoE) assessment for EAS adversity is generally robust and produces reasonable outputs, and reasonable differentiations between secondary systemic toxicity vs specific endocrine-related adversity have been achieved in ED assessments. In ecotoxicology, negative in vivo mechanistic studies are generally considered sufficient to conclude that the ED criteria are not met for non-target organisms. Nevertheless, full use is not made of all available data in PPP dossiers. Potentially valuable evidence is being disregarded and a true WoE of available data is thus not achieved. Moreover, triggering of level 5 studies based on positives from single (often in vitro) mechanistic studies is unjustified in many cases. A hypothesis-based testing approach using all levels of the conceptual framework would likely reduce animal testing and improve decision making. In human health, the definition of maximum tolerated dose is restrictive, some elements being unavailable in studies conducted for ED evaluation, and should be revisited. For non-target organisms, the definition of maximum tolerated concentration varies among Test Guidelines (TGs) and focuses on lethality as the measure of systemic toxicity, while sublethal effects are likely to affect endocrine responses and should be considered. Guidance on interpretation of in vitro assays is not fit for purpose. Such assays are known to be over-sensitive (e.g. H295R steroidogenesis assay) or there are no agreed/validated TGs (e.g. for thyroid activity). The GD should include more substantive consideration of in vitro assay relevance as well as an assessment of PBPK approaches (alongside other IVIVE methods) to assess the physiological relevance of in vitro responses. Appendix A of the GD presents an inconsistent view on human relevance of thyroid effects in lab species and should be revised to include a tiered testing and assessment scheme, using robust, validated methods in lieu of animal intensive studies. Finally, guidance on how to evaluate population-relevance in non-target organisms, and the

acceptance of population modelling approaches is urgently needed to bring the ED GD into compliance with the legal text of the ED criteria.

Sander Van der Linden, European Chemicals Agency (ECHA)
Speaker and Panellist

Sander van der Linden has worked as a researcher on the development and application of in vitro assays with a focus on assays that address endocrine and genotoxic molecular initiating events. These assays have been used to assess biological activity of pure substances as well as to assess activity in drinking water and other (environmental) matrices. In 2013, Sander joined the European Commission at the Joint Research Centre in Ispra (Italy), where he worked at the Systems Toxicology unit, initially as a post-doc and later as a contract agent. At the JRC, Sander worked mainly on the topics of the toxicological assessment of mixtures, endocrine disruption and the regulatory acceptance of alternative tests. While at the JRC, he also helped drafting the current EFSA/ECHA guidance on the assessment of endocrine disrupting properties of plant protection products and biocidal products. In 2018, Sander joined ECHA, where he works in the Biocides Active Substances unit as an environmental expert, process coordinator on the assessment of technical equivalence and as an expert on and coordinator of endocrine disruption related activities for biocides.

Title of talk: Flash report | What works well and what needs improvement in ED assessments: a stakeholder view

Abstract of talk

In 2018, the new scientific criteria for the determination of endocrine disrupting (ED) properties became applicable to the Biocidal Products Regulation (BPR) (EU) No 528/2012 and the Plant Protection Products Regulation (PPPR) (EC) No 1107/2009. In the same year, ECHA and EFSA jointly published a guidance document on how to identify endocrine disruptors in accordance with these new criteria. After the publication of the ED guidance and the ED criteria, it became clear that for many dossiers, there is insufficient data available to complete the ED assessment. This is particularly true for the assessment of non-target organisms. As a result, the generation of additional data is needed, which is time consuming, expensive and requires the use of experimental animals. While some delays due to absence of data were inevitable after the publication of the guidance, in many cases this has caused a significant delay in the assessment. Several ways forward have been proposed to tackle the delays due to the (incomplete) ED assessment, all with their own advantages and disadvantages. In addition to the guidance document from 2018, additional guidance was needed to address specific issues, e.g. how to incorporate new tests into the testing strategy or how to address the assessment of non-active

substances in a biocidal product. Several documents have been published to address these specific issues. Discussion on a (partial) update of the ED guidance is currently ongoing. From a regulatory perspective, several issues have been addressed, including a change in the data requirements for biocides to avoid data gaps when performing the ED assessment. Now, in 2022, experts from industry, Member States and the two agencies involved (ECHA and EFSA) have gained several years of experience in performing the ED assessment. Therefore, it is time to reflect on the experience so far on ED assessment. This presentation will focus on the agency's view on the progress made and lessons learned. It will also provide an update on the status of the guidance and will reflect on the lessons learned along the way and provides an outlook on the ED assessment in the future.

Emily Mcvey, Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)
Speaker

Synthesizing seemingly disparate information, identifying key data, always curious and eager to communicate, Dr. McVey is an eternal student. She is a senior ecotoxicologist at the Pesticides and Biocides authority of the Netherlands (Ctgb), writing and reviewing numerous draft and review assessment reports (DAR/RARs) for pesticide active substances and participating in ecotoxicology and endocrine disruption expert meetings. Dr. McVey is a member of the EFSA Working Group for the update of the Birds and Mammals Guidance and a SETAC Europe Certified Environmental Risk Assessor (CRA), as well as an acknowledged expert in the assessment of endocrine disruption. Upon completing her doctorate in molecular medicine at the Johns Hopkins Medical School, she joined the Office of Pharmaceutical Science (OPS) at the Center for Drug Evaluation and Research (CDER) of the USFDA as a toxicologist. While there, she led the reproductive and developmental toxicology section of the Bisphenol A (BPA) Joint Emerging Science Working Group until her departure from the Agency and was an active participant in the collaboration-award-winning Pharmaceuticals in Water Working Group. Since moving to the Netherlands from Washington, D.C., she has learned to speak Dutch and bike with aplomb under virtually any circumstances, but still refuses to eat herring in the traditional manner (being a life-long vegetarian).

Title of talk: Flash report | What works well and what needs improvement in ED assessments: a stakeholder view

Abstract of talk
EU Member State competent authorities for pesticides and EFSA have been evaluating the potential for endocrine disruption of pesticide active substances according to the ECHA/EFSA Guidance since June 2018. In the interim, experience

has shown areas which are more clear and progress efficiently and other areas which could benefit from improvement. These can additionally be split into two areas of consideration: process-related and science-related. Many areas of the assessment process for pesticide active substances function well, in part due to updates in the way of working, including communication between the toxicology and ecotoxicology sections and designating specific MS experts to participate in the ED assessments. However, improvement is nevertheless possible, as the process is relatively slow and animal intensive. On the scientific side, many advances have been made both in the general scientific knowledge on endocrine disruption and in the experience gained from frequent evaluation of the same types of test data. The remaining 'sticking points' pertain to areas where the available tests or the state of scientific knowledge on a particular subject are less crystallised, meaning that the level of uncertainty may be higher when drawing conclusions. For example, during the development of many ED screening assays, highly positive substances were used for validation, however, in real-world testing with 'unknown substances', unexpected patterns can occur and require discussion and expert judgement to come to a decision as to whether or not these may represent direct endocrine activity. There are areas where the available tests are not able to discern the level of molecular activity which is required for an appropriate MoA analysis, or where no tests are available to discern a particular MoA. During the presentation, some problem areas, as well as some potential strategies for addressing those, will be discussed.

Ninja Reineke, CHEM Trust
Speaker

Ninja Reineke, Head of Science at CHEM Trust, holds a degree in chemistry and a PhD on the analysis of marine pollutants. She studied at the universities of Hamburg, Bremen and Durham (UK). She previously worked for WWF (World Wide Fund for Nature) on EU chemicals policy including REACH for almost 10 years before joining CHEM Trust in 2013. Her main work areas are EU regulations on endocrine disrupters and persistent chemicals, particularly REACH and CLP. She has been a member of the ECHA ED expert group since 2018 and also follows the CARACAL group on EDs (CASG ED). She also works at the science-policy interface to ensure the most up to date science is reflected in regulation, e.g. on combination effects and human biomonitoring studies. Since December 2018 she is the Chair of the Management Board of CHEM Trust Europe, based in Hamburg, Germany. More information about CHEM Trust publications and submissions to ongoing policy discussions can be found on the CHEM Trust website: www.chemtrust.org

Title of talk: Flash report | What works well and what needs improvement in ED assessments: a stakeholder view

Abstract of talk
On the positive side, the EU Chemical Strategy for Sustainability has identified the need for increased human health and environment protection from endocrine disrupters (EDs) as a priority. CHEM Trust has called for regulatory action on EDs to be strengthened urgently for many years. Together with our campaign partners from the EDCFree-Europe coalition we advocate for a better identification of EDs, followed by necessary protective measures to minimise exposure. Endocrine disruption is especially harmful to the developing foetus, leading to deleterious effects after birth or later in life or even in the next generation. Given widespread ongoing exposure and growing scientific evidence of health impacts from mixtures of Eds, it is important to step up efforts towards a minimisation of ED exposure. Among the issues needing improvement is the lack of speed of assessments, the recent re-evaluation of BPA being a case in point. Moreover, currently only around 20 substances have been officially identified as EDs in the EU since 2007. In contrast, several analyses have led to over 1000 substances being listed as potential EDs. Current assessments for identification are hampered by a lack of data on ED properties, a lack of test methods on specific endpoints (such as on thyroid and other important predictors of health impacts) as well as the burden of proof required to meet the current level of evidence. Identification should be based on all available data, including peer-reviewed academic studies, in a weight-of-evidence approach and be conducted by experts in the respective scientific areas and assessments. The new criteria via a new CLPs hazard class for identification of EDs and Suspected EDs will represent an important step for a more horizontal approach. Given the EU`s ambition to reduce reliance on animal tests, there is an urgent need to develop regulatory identification approaches based on in vitro and other methods, like grouping and read-across. This will be an important step forward to improve assessments and increase the protection level and live up to the EU Commission's Green Deal ambition of zero-pollution leading to a toxic-free environment.

Karin Nienstedt, European Commission
Panellist

Dr. Karin M. Nienstedt leads the Sector Pesticides - Placing on the Market in the Unit Pesticides and Biocides, European Commission (Directorate General for Health and Food Safety, Unit Pesticides and Biocides). Before joining the European Commission, she worked for the European Food Safety Authority and as a researcher in the areas crop protection, ecotoxicology, and biological control.

Jordane Wodli, European Commission
Panellist

Jordane Wodli is working since 2019 as a Seconded National Expert at the European Commission's Directorate General for Environment, within the Unit responsible for "Safe and Sustainable Chemicals". His main task is related to endocrine disruptors, in particular follow-up on the CLP Regulation's development of the draft proposal of criteria for endocrine disruptors. Jordane is also responsible for organising the annual "Forum" meetings on endocrine disruptors. Furthermore, he is also following the negotiation and implementation of the Stockholm and Rotterdam Conventions and in the same time involved in the on-going discussion on SAICM, the Strategic Approach to International Chemicals Management. Previous to this, he worked for five years in the French Ministry of Environment, also in charge of endocrine disrupting chemicals and the REACH Regulation. He supported the development of the first French National Strategy on Endocrine Disruptors. Moreover, he hold a position as parliamentary assistant for a Member of the French National Assembly.

Manuela Tiramani, European Food Safety Authority (EFSA)
Chair/Co-chair

Manuela graduated from the university of Milan as medical doctor. She continued her education with 4 years of specialised course in occupational health, industrial hygiene and toxicology, and a PhD in occupational health (with a focus on risk from non dietary exposure to pesticides). In 2000 she joined as regulatory toxicologist the International Centre for Pesticides and Health Risk Prevention in Milan, one of the EU national competent authorities dealing with the risk assessment of plant protection products at national and EU level. In 2005 Manuela was hired by EFSA as scientific officer for mammalian toxicology in the Pesticide Unit, where a couple of years later she took the position of team leader responsible for mammalian toxicology risk assessment and non dietary exposure assessment. In 2014 she was offered the position of Head of the EFSA FEED Unit, where she worked from 2015 to 2018 for a total of 4 years. In January 2019 Manuela went back to the pesticide area, being appointed as Head of the Pesticide Peer Review Unit (PREV) of the European Food Safety Authority.

Andrea Terron, European Food Safety Authority (EFSA)
Rapporteur
Andrea Terron is a senior scientific officer working in EFSA's PREV unit as a toxicologist in the mammalian toxicology team. He graduated with a degree in Veterinary Medicine and is a Fellow of the Royal College of Pathologists, with experience in Toxicological Pathology and Toxicology. He also has experience of the risk assessment of medicines and plant protection products. Andrea has authored

several pathology reports on drugs acting on the central nervous system, cardiovascular system, and on oncology. His interests also extend to target organ pathology, toxicological pathology, mechanistic studies, neurotoxicity, developmental neurotoxicity, and endocrine disruptors. He also participates in EFSA's activities regarding developmental neurotoxicity and the assessment of endocrine disrupting properties for pesticide active substances. Another of his interests is the development and application of new alternative methodologies and their integration in regulatory risk assessment throughout an integrated approach of testing and assessment.

Francesca Pellizzato, European Chemicals Agency (ECHA)

Rapporteur

Francesca Pellizzato is a scientific officer in the Hazard Assessment Directorate in the European Chemicals Agency (ECHA). Currently, she is a scientific area leader on the topic of Endocrine Disruption (ED) for the Environment. As a result, she is involved in several activities under REACH related to endocrine disruption, such as substance evaluation and identification of substances of very high concern (SVHC). In addition, she supports ECHA's ED expert group and attends OECD meetings on the development of new ED test guidelines. She also supports the European Commission in some tasks relating to the Chemical Strategy for Sustainability such as in the on-going work to develop new CLP criteria for ED and changes in the standard information requirements of REACH for endocrine disruption. She is a co-author of the ECHA/EFSA ED guidance for pesticides and biocides. She has been employed by ECHA since 2009, and previously worked at the Institute for Reference material and measurements of the Joint Research Centre of the European Commission (EC-JRC), and at the Aberdeen Marine Laboratory (Fisheries Research Services) in the UK. She holds a degree and a PhD in Environmental Sciences from the University of Venice.