EndocRine Guideline Optimisation

Breaking down the wall between human health and environmental testing of endocrine disrupters: EndocRine Guideline Optimisation

Deliverable Report

D1.3 ERGO Report on international cooperation

Project acronym	**ERGO**
Project full title	**Breaking down the wall between human health and environmental testing of endocrine disrupters: EndocRine Guideline Optimisation**
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Contents

1 Abbreviations

- AOP: Adverse Outcome Pathways
- AOP-KB: OECD Adverse Outcome Pathway Knowledge Base
- AOP-WIKI: Collaborative Adverse Outcome Pathway Wiki
- ADHD: Attention-deficit/hyperactivity disorder
- B/E: Biomarkers and endpoints
- BIAC: Business at OECD
- CAS registrations: CAS registry numbers are unique numerical identifiers for chemical compounds, polymers, biological sequences, mixtures and alloys.
- ChemTrust: Collaboration between CHEM Trust, a UK-registered charity, and CHEM Trust Europe, a charity based in Germany
- DG Env: Directorate-General for Environment (in the European Commission)
- DRP: Detailed review paper
- DSS: Decision Support System
- ECHA: European Chemicals Agency
- ECHA EDEG: ECHA Endocrine Disruptor Expert Group
- ED: Endocrine disrupter
- EDC: Endocrine-disrupting chemical
- EDSP: Endocrine Disruptor Screening Program
- EDTA: Advisory Group on Endocrine Disrupters Testing and Assessment (OECD)
- EDTRA AG: Endocrine Disruptor Testing and Risk Assessment Advisory Group (SETAC)
- EHB4EU: European Human Biomonitoring Initiative
- EFSA: European Food Safety Authority
- EFSA ED WG: EFSA Working Group on Endocrine Disruptors
- ERGO: EndocRine Guideline Optimisation (acronym of the current H2020 project)
- EU EPA: European Union Environmental Protection Agency
- EURION: European Cluster to Improve Identification of Endocrine Disruptors
- GA: The Grant Agreement between the European Commission and the beneficiaries
- IATA: Integrated Approaches to Testing and Assessment
- JRC: Joint Research Centre (in the European Commission)
- JRC EURL-ECVAM: European Union Reference Laboratory for alternatives to animal testing (in JRC)
- KER: Key Exploitable Results
- KO: Knowledge output
- KT: Knowledge transfer
- KTP: Knowledge transfer plan
- MAD: Mutual Acceptance of Data
- NGO: Non-Governmental Organisation
- OECD: Organisation for Economic Co-operation and Development
- OECD EAGMST: Extended Advisory Group on Molecular Screening and Toxicogenomics
- OECD TG: OECD Test Guidelines
- OECD TGP: OECD Test Guideline Programme
- OECD VMG-Eco: OECD Validation Management Group for Ecotoxicity Testing
- OECD VMG-NA: OECD Validation Management Group for Non-Animal testing
- OECD WNT: OECD Working Party of National Co-ordinators
- OECD WPHA: OECD Working Party on Hazard Assessment
- Ostrava declaration: Declaration signed by WHO on 13-15 June 2017 in Ostrava, guiding the governments of European countries the following six years to take steps to improve the environment and the health of the European population.
- OTF: OECD Task Force (in ERGO)

- PARC: Partnership for the Assessment of Risks from Chemicals
- PBTK: Physiologically Based Toxicokinetic
- QSAR: Quantitative Structure-Activity Relationship
- REACH: Registration, Evaluation, Authorisation and Restriction of Chemical substances (EU)
- SAB: Scientific advisory board
- SAICM: Strategic Approach to International Chemicals Management
- SETAC: Society of Environmental Toxicology and Chemistry
- SETAC EDTRA AG: SETAC global advisory group on Endocrine Disrupter Testing and Risk Assessment
- THSD: Thyroid Hormone System disruption
- TG: Test Guideline (OECD)
- Toxcast: Toxicity Forecasting (US EPA)
- TGP: Test Guideline work programme (OECD)
- THSD: Thyroid hormone system disruptors
- UN: United Nations
- UNEP: United Nations Environment Programme
- URG: User reference Group
- US EPA: United States Environmental Protection Agency
- WHO: World Health Organisation
- WPHA: Working Party on Hazard Assessment
- WP: Work package (in the Horizon 2020 projects)

2 Introduction

The purpose of this document is to inform about the strategic cooperation which the EU-funded Horizon 2020 project ERGO (acronym for "EndocRine Guideline Optimisation") holds with international key players from related initiatives and regulatory bodies.
Furthermore, in the present report, we outline future perspectives for the optimal use of the results and data generated in ERGO as well as related exploitation of results by relevant stakeholders and research projects.

3 The ERGO project and the ERGO consortium

The project "ERGO - Breaking down the wall between human health and environmental testing of endocrine disrupters was funded by the European Union Horizon 2020 Research and Innovation programme (Grant Agreement NO 825753) with a granted budget of over €6 million, and to run from 2019 to the end of 2023 (Extended to June 2024).

3.1 The ERGO project

The overarching impact of ERGO's products is improved health of the citizens of Europe due to lower exposures to endocrine-disrupting chemicals (EDCs) at home and in the workplace. Citizens will remain confident that their environment is protected from EDCs and a sustainable circular economy based on EDC-free products is promoted (Fig. 1). ERGO provides practical solutions to support more effective EDC testing and screening in Europe over the next decades and economically, EU will benefit from reduced health care costs, and European industries will prosper due to faster and cheaper development of new products. This is a consequence of ERGO's fast, effective, and efficient EDC testing and screening approach, enabling better prediction of chemical risks for humans and the environment in line with regulatory requirements, with the long-term vision of an EDC-safe world.

The direct key end-users of ERGO's products are regulators and industry; all constrained by the scarcity of practical EDC test and screening tools for fast, cheap, and robust hazard and risk assessment of goods, feeding a growing sustainable European circular economy. With thyroid hormone system disruption (THSD) as object, the proof of concept is delivered with industry and regulators integrated up-front in the project (co-design). ERGO is a need- and application-driven project that combines excellent science with a full commitment to deliver novel testing strategies for EDCs and more efficient and effective hazard- and risk assessments.

The next generation of Europeans will be challenged by the global increase in the number of chemicals and the amount of chemical production, demanding faster testing of new products. Higher numbers of chemicals feeding the economy implies higher risk of adverse ED effects on human health. These include thyroid-related disorders suspected to be linked to learning disabilities, mental retardation (reduced IQ), attention-deficit/hyperactivity disorder ADHD, and even autism in children (cf https://academic.oup.com/endo/article/161/10/bqaa106/5866650).

Figure 1: *The three key societal impact areas of ERGO, which are affected by improved ED testing and screening methods*

With the present state of testing, Europe will be unable to meet the growing demand for fast and robust EDC hazard assessment with as less animal testing as possible to promote an EDC-free economy and (working) environment without compromising economic growth and ecological sustainability. European EDC hazard assessment therefore needs to become more efficient to adjust to this new reality and to be able to leverage that expansion and convert it into an opportunity for both an EDC-free and growing Europe. The proposed improvements of testing build on several elements delivered by ERGO. The ERGO communication, dissemination, and exploitation plan is supporting maximisation of the impact.

In ERGO, we position our research strategically to provide a realistic analysis of THSD hazard assessment, supported by a toolset which European policymakers, the Organisation for Economic Co-operation and Development (OECD), as well as industry can also apply effectively within a time-horizon of 10 years. ERGO has targeted the whole value chain with particular focus on support to OECD for the work to improve the Test Guideline (TG) battery for better identification of EDCs. ERGO has provided maximal impact through sound scientific support consistent with the Ostrava declaration and the United Nations (UN) Sustainable Development Goal 3 (good health and well-being), which "*aim to by 2030 substantially reduce the number of death and illnesses from hazardous chemicals…*".

The ambition of the ERGO project has been to improve human health and environmental hazard and risk assessment of EDCs. For this reason, ERGO has strategically built a multidisciplinary consortium that contains all the required expertise: (Eco-)toxicology, cell and developmental biology, analytical chemistry, multi-development, and validation of in vitro and in vivo EDC TG for OECD as well as regulatory knowledge. The purpose of the ERGO engagement with regulatory stakeholders and policy makers has been to facilitate uptake of the project outputs by regulators at both the European and International level and to contribute to the co-creation of new or updated regulations and agree to cluster resources to facilitate more rapid implementation of research outputs into regulation. ERGO has been engaging with a variety of stakeholders including OECD, the EU Joint Research Centre (JRC), European Union Environmental Protection Agencies (EU EPAs), the European Chemicals Agency (ECHA), the European Food Safety Authority (EFSA), the US EPA, Japan Ministry of Environment, and Business at OECD (BIAC). These stakeholders have participated in the ERGO Scientific Advisory Board (SAB) and the ERGO User Reference Group (URG) and, in this way, they have ensured direct interaction with partner contacts to key regulatory bodies.

From the start of the project, ERGO has been communicating the cross-vertebrate class testing approach to OECD and the national and international entities involved in the Test Guideline work programme (TGP). ERGO partners from SDU, MATT, UHEI and YCU are represented in the OECD Validation Management Group for Ecotoxicity Testing (VMG-Eco), the OECD Fish Drafting Group, and the OECD Validation Management Group for Non-Animal testing (OECD VMG-NA). To ensure full alignment between ERGO TG activities and the TGP, ERGO has also placed OECD National Coordinators represented in OECD EDTA and OECD WNT into the ERGO SAB and URG.

Major experimental work in ERGO has been related to optimization of existing OECD in vivo TGs, especially for fish, by inclusion of biomarkers and endpoints suitable for detecting THSD across vertebrate classes, and both new biomarkers and endpoints as well as updated TG protocols have been thoroughly discussed with the SAB before, during and after investigation, development, and pre-validation in ERGO. The development of a cross-class Adverse Outcome Pathway (AOP) network has been led by UA, benefitting from long experiences in development of AOPs in the AOP-Wiki as part of the OECD Adverse Outcome Pathway Knowledge Base (AOP-KB). Five AOPs describing THSD in fish were endorsed by the WNT/WPHA and published in the OECD Series on Adverse Outcome Pathways and one additional AOP was published as an AOP Report in Environmental Toxicology and Chemistry and is currently under OECD review.

3.2 The ERGO consortium (see Annex 1 for details on partners)

In accordance with the contract agreed between the European Commission and the beneficiaries in the ERGO consortium, the Grant Agreement (GA), the three impacts below were expected from the consortium in relation to international collaboration:

- **Support for the OECD work on testing and assessing chemicals for ED identification**
- **Enhanced international cooperation**
- **Contribution to the development of an international strategy and guidelines for testing of EDCs and assessing associated hazard and risk**

The ERGO consortium brings together 15 partners from eight countries (Denmark, Belgium, Germany, Ireland, Czech Republic, United Kingdom, France, and Japan) and is coordinated by SDU. The consortium consists of 10 research bodies, two industry companies, one small to medium enterprise, one environmental protection agency and one consultancy. With a strong focus on innovation, ERGO is working directly with internationally recognised industry experts and research bodies with proven track records. Bringing together these selected experts collectively provides the knowledge, competence, skills, and facilities needed for ensuring the achievement of project objectives as well as the successful delivery and application of project results.

4 International collaboration

The research in the ERGO project has been developed in different ways; as support for the OECD work on testing and assessing chemicals for ED identification, with enhanced international cooperation, as well as with the contribution to the development of an international strategy and guidelines for testing EDCs and assessing associated hazard and risk.

4.1 Support for the OECD work on testing and assessing chemicals for ED identification

At the beginning of ERGO, the OECD Task Force (OTF) led by SDU with representatives from partners UBA, UA, UFZ, UHEI, ENSL, ATT, BASF, YCU and MATT, all benefitting from professional experience with OECD work was established to facilitate interaction with OECD. ERGO partners had already been deeply involved in the development and validation of 9 adopted OECD TGs for the identification of endocrine disruptors (OECD TG 229, 230, 231, 234, 236, 240, 241, 242, and 243). As ERGO aims to have the greatest impact within the regulatory sector, to ensure real impact of ERGO results on the OECD TGP, the OTF, in collaboration with each WP and partner, continuously engaged with the OECD through the VMG-Eco to ensure alignment of ERGO and the OECD TGP and timely uptake of ERGO's outputs into OECD TGs. This expertise assured successful communication with OECD and effective TG optimisation during the project period.

One of the aims of ERGO was to recommend to further develop the interpretation of and to better interlink the structure of the OECD Conceptual Framework for Testing and Assessment of EDs by breaking down the existing wall between mammalian and non-mammalian vertebrate in vivo testing at the levels 3-5. Results obtained by ERGO provide the documentation for this novel approach and the ERGO OTF ensures alignment with the OECD TGP. The development of new thyroid hormone system sensitive endpoints and tests in ERGO has been performed in collaboration with the OECD TGP, especially under VMG-Eco. Validation of biomarkers and endpoints investigated and pre-validated in ERGO has been discussed in OECD VMG-Eco to ensure fast acceptance and uptake of TG optimization.

The figure below shows the communication in the ERGO project of the cross-vertebrate class testing approach to OECD and the national and international entities involved in the TGP.

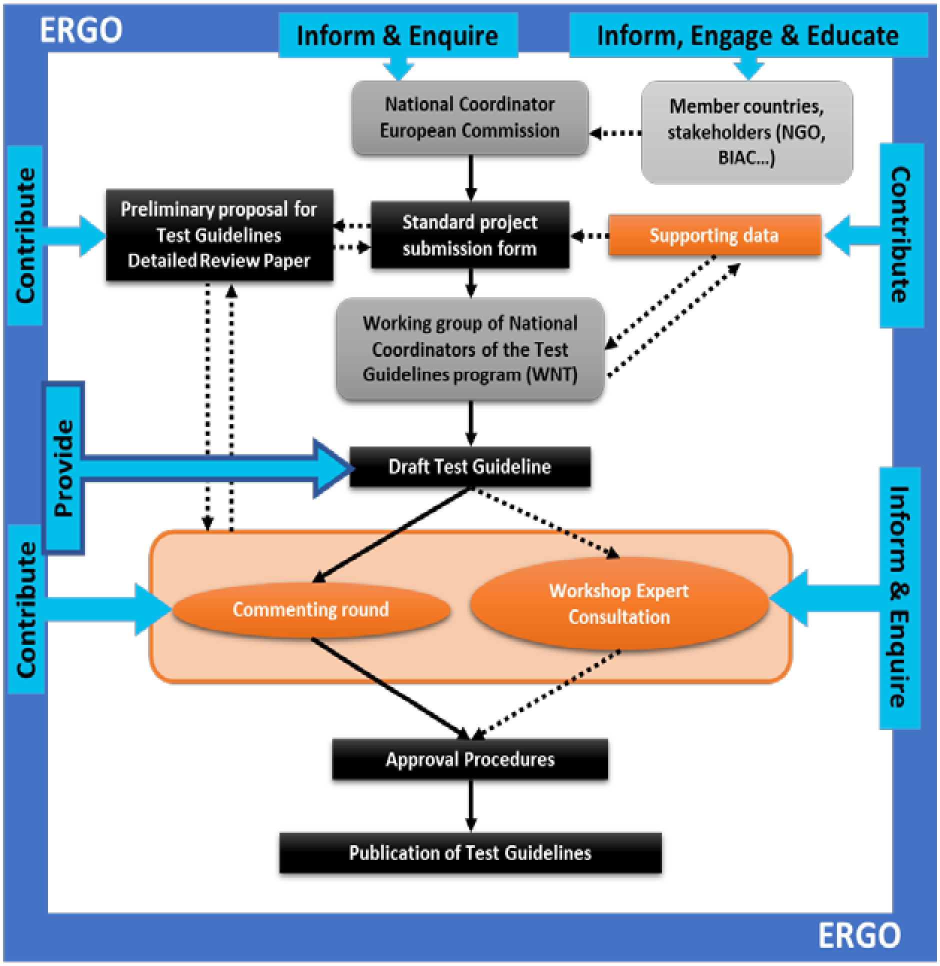

__Figure 2__ From the start of the project, ERGO has communicated the cross-vertebrate class testing approach to OECD and the national and international entities involved in the TGP. ERGO partners from SDU, MATT, UHEI, and YCU have been represented at VMG-Eco, and the OECD VMG-NA. ERGO include OECD and National Coordinators represented in EDTA and WNT in the SAB to ensure full alignment between ERGO TG activitiesand the OECD TGP. Major experimental work in ERGO is related to optimisation of existing OECD in vivo TGs by inclusion of biomarkers and endpoints (B/Es) suitable for detecting TD across vertebrate classes, and both new B/Es as well as updated TG protocols are thoroughly discussed with the OTF before, during, and after investigation, development, and validation in ERGO. The AOP cross-class network development has been led by UA, benefitting from long experiences in development of AOPs in the AOP-KB, and the outcome is published in collaboration with OECD.

4.2 Enhanced international cooperation

The intention of the ERGO project to improve human and environmental health on a global scale by ensuring the fastest possible international exchange of results and concepts developed in ERGO is supporting international cooperation on improvement of hazard/risk assessment of ED's. Experienced partners/collaborators from non-EU countries Japan (YCU), Brazil (SAB), Canada (SAB) and USA (SAB) have been involved in the consortium, and several ERGO partners (SDU, UA, UHEI, BASF, UBA, LOR, MATT and YCU) are involved in identification, hazard and risk assessment of EDs at a global level (OECD, the United Nations Environment Programme (UNEP), the World Health Organisation (WHO), the Strategic Approach to International Chemicals Management (SAICM), and the Society of Environmental Toxicology and Chemistry (SETAC)). The ERGO partners consider cooperation at the European as well as at the global level as essential for attaining the project goals. The consortium does not only use its already broad existing network, but has also set up a pro-active strategy to enhance international collaboration:

The ERGO URG as well as the EURION cluster consist of international partners, and the multi-actor approach in the project ensures engagement and co-production at the international level throughout the project.

The URG consists of 10 expert stakeholders from regulators (national EPAs, ECHA, EFSA, OECD) and policy makers from various European countries, representatives of industry, and Non-Governmental Organisations (NGOs) (UN/WHO, BASF, and ChemTrust, a collaboration between CHEM Trust, a UK-registered charity, and CHEM Trust Europe, a charity based in Germany). The URG serves as an expert panel representing the recipients of the tools and tests that are being developed within ERGO. The URG facilitates understanding in the project, providing background information on legislation, regulations and policies currently being applied in Europe and internationally as well as constraints and regulatory needs. The URG ensures that ERGO outputs and outcomes are relevant for end-users.

Worldwide partnerships involve alignment and close collaboration with OECD, the US EPA (an advisor to the project) as well as scientific advisors from University of São Paulo, Brazil and University of Saskatchewan, Canada. Links to OECD and the US EPA (including EDSP and ToxCast project) are established through the OTF and the SAB, including JRC. JRC is collaborating with ERGO and OECD, and they have a seat in the SAB to ensure co-design and co-production.

ERGO Stakeholder Engagement

Exploitation of ERGO's results by key stakeholders is ensured through a range of strategic engagement and exchange activities to translate research results and approaches. ERGO and the EURION Cluster ensure robust communication with each stakeholder group throughout the full project duration of 5.5 years. The consortium has extensive experience in multinational, multi-lingual, multi-disciplinary and multi-partner collaborative innovation activities within the field of ED research. ERGO additionally has expertise in the effective communication of progress and results through a professional communication and knowledge management partner AquaTT, who is responsible for implementing the Dissemination and Exploitation Plan (D8.1 DEP) in collaboration with all partners. The Stakeholder Engagement Strategy draws on the expertise of the whole partnership, particularly ERGO's industrial partners and those that work with regulatory bodies, to provide valuable insights into the perception and communication channels of key target users.

Stakeholder engagement has been managed across the full project work plan, at different times, for different purposes and for various target audiences. The Table 1 below summarises the stakeholder engagement strategy and identifies the overall key stakeholders, the main tools of engagement and the key expected impact of this interaction.

Stakeholders	Tools of Engagement	Impact of Engagement
Regulators OECD, JRC, EU EPAs, ECHA, EFSA, US EPA, Japan	• Participation in ERGO Steering Group, URG, Advisory Board, OTF. • Workshops/Brokerage events to foster coordination among regulators, ERGO, concurrent projects and other stakeholders. • Regular direct interaction with partner contacts within key regulatory bodies.	• Uptake of the project outputs by regulators at both the European and international level contribute to the co-creation of new or updated regulations and agree to cluster resources to facilitate more rapid implementation of research.
Private Sector	• Outreach and interaction with industry and other private sector stakeholders through hosted or attended events. • Targeted knowledge transfer (KT) activities, based on outcomes of the	• Make private sector aware of project objectives and progress. • Inform relevant stakeholders from the private sector on the outputs of the project and potential reactionary

	Knowledge Management process, e.g. workshops, individual meetings and final event.	changes to their business / industry policies, materials, etc.
Scientific Community	• Interactive presentations at scientific conferences, particularly those attended by concurrent projects. • Peer reviews by appropriate scientific communities will ensure quality standards.	• Build upon the existing Scientific Knowledge Base. • Uptake of innovative scientific methodologies. • Access to data that could be used by other scientific groups.
Policy Makers DG Env.	• Participation in ERGO Scientific SAB and URG. • Regular direct interaction with key policy makers at the national, supra-national, and international levels. • Open invitations for policy makers to attend the regulator workshops and training.	• Scientific Evidence to support the adoption of suitable regulatory framework and tools to enable the streamlining of regulatory approval.
General Public Society, Citizen Interest Groups	• Active use of social media/mainstream media and other suitable portals, to ensure that key project outcomes and benefits are communicated to and understood by the public in general.	• Increased public awareness of ED and related health risks and improve the visibility and appreciation of EU funded research, as well as raise awareness of ERGO and its impact on society.

Table 1: *Stakeholder Engagement Strategy*

The ERGO stakeholder database aims to facilitate dialogue, relationship-building and process generation that takes place between the ERGO consortium and other organisations involved or interested in the project. The ERGO and EURION stakeholder databases consists of those who have subscribed using the 'Subscribe to News' button on both the project and the cluster websites, ensuring compliance to GDPR.

As of April 2024, the ERGO and EURION stakeholder databases have 174 and 275 stakeholders respectively. Collectively 449 stakeholders coming from 21 international countries; Denmark, Ireland, France, Portugal, Italy, Canada, the Netherlands, United States, Spain, New Zealand, United Kingdom, Sweden, Finland, India, Belgium, Norway, Saudi Arabia, Germany, Japan, Czech Republic, and Argentina.

Several ERGO partners have attended high profile international conferences and events representing the ERGO project and promoting its results; from the start of the project to the most recent reporting period:

From January 2019 - June 2023, a total of 338 dissemination and communication activities have been recorded by ERGO partners, with an estimated reach of over 3.4 million stakeholders.

Organisation of a conference	1
Organisation of a workshop	2
Press release	3
Non-scientific and non-peer reviewed publications (popularised publications)	7
Exhibition	2
Flyers	2
Training	0
Social media	90

Website	99
Communication campaign (e.g. radio, TV)	2
Participation to a conference	51
Participation to a workshop	16
Participation to an event other than a conference or workshop	10
Video/film	9
Brokerage event	0
Pitch event	0
Trade fair	0
Participation in activities organised jointly with other H2020 project(s)	25
Other	16
TOTAL	**338**

Table 1: *Dissemination and communication activities by ERGO partners (from January 2019-June 2023)*

Scientific Community (Higher Education, Research)	36,270
Industry	6,212
Civil Society	135
General Public	3,387,062
Policy Makers	2,975
Media	200
Investors	0
Customers	0
Other	209
TOTAL	**3,433,063**

Table 2: *Reach per stakeholder type (from January 2019-June 2023)*

A summary of some international dissemination and communication activities by ERGO partners:

- In October 2020, (1 - SDU and 2 - UA) presented OECD Project 2.64 (inclusion of thyroid endpoints in OECD fish Test Guidelines) at the 15th Meeting of the Validation Management Group on Ecotoxicity (OECD VMG-Eco).
- In November 2021, (1 - SDU) presented EURION for the PARC (EU Partnership for the Risk Assessment of Chemicals) steering committee meeting.
- In November 2021, (1 - SDU) presented ERGO and other related initiatives at the ECHA Endocrine Disruptor Expert Group Meeting.
- (2 - UA) presentation at SETAC North America in November 2021.
- (1 - SDU) presented the EURION Cluster at a public seminar 'Endocrine Disrupting Effects of Chemical Substances' by the Ministry of The Environment, Japan - March 2022.
- (6 - AU) presented 'Molecular Fingerprint of Thyroid Hormone System Disruption in zebrafish (Danio rerio) and its Reversibility' and 'Are Hormone Measurements the Best Way to Look for Endocrine Disruption?' at SETAC Europe in Copenhagen - May 2022.
- (1 - SDU) presented 'What works well and what needs improvement in ED assessments: a stakeholder view (Academia)' in a pitch talk and panel discussion at the endocrine session of the EFSA ONE Conference in Brussels - June 2022.
- Poster presentation by (9 - MU): Cross-species-relevance of in vitro bioassay battery for the assessment of thyroid hormone disruption at EUSAAT 2022 in Linz, Austria from 26-28 September 2022.

- Poster presentations by (4 - UHEI): Potential endpoints to identify thyroid hormone system disruption in zebrafish (Danio rerio) embryos; Thyroid-disrupting effects of carbamazepine in zebrafish; Performance of OECD TG 210 (FELS) with implementation of thyroid-related endpoints at SETAC Europe in Dublin, Ireland - May 2023.
- Oral presentation by (10 - CNRS): Identification of molecular markers on zebrafish embryo for thyroid signalling disruption by transcriptomic analysis at Congress of North American Society of Comparative Endocrinology in Queretaro, Mexico from May 28 May - 1 June 2023.

The ERGO project website has supported the general dissemination of the project's results (public deliverables and publications), news, events, media and outreach (ERGO Researcher Profiles, Endocrine Disrupting Chemicals, EDCs under the Spotlight and How to make your own EDC-free…. The site also has a dedicated page to EURION; https://ergo-project.eu/eurion. The website raises awareness and facilitates engagement with society in general as it provides easy to read information about EDCs and what the public can do to reduce exposure.

	Country	Users	% Users
1.	United States	1,051	20.00%
2.	Netherlands	459	8.73%
3.	France	406	7.72%
4.	Germany	354	6.74%
5.	Finland	338	6.43%
6.	United Kingdom	215	4.09%
7.	India	185	3.52%
8.	Austria	166	3.16%
9.	Belgium	146	2.78%
10.	Italy	124	2.36%

Figure 3: *Top 10 international visitors to the ERGO website (from January 2022-June 2023)*

ERGO's social media has also supported the project's dissemination through a dedicated ERGO X account and through LinkedIn, promoting ERGO's activities and results as well as connecting with fellow EURION cluster projects, relevant academic, industry, policy and regulatory bodies. All ERGO partners have been encouraged to regularly disseminate through these channels. As of April 2024, the ERGO X account has 600 followers and 2,058 posts. Compared to its fellow EURION cluster projects, ERGO has the highest number of followers and engagement, showing its commitment to frequent and quality communication to the general public, reflecting the EC's ambition to make the general public aware of EDC issues:

- ATHENA: 113 followers, 57 tweets
- EDCMET: 188 followers, 201 tweets
- ENDpoiNTS: 151 followers, 110 tweets
- FREIA: 324 followers, 120 tweets
- GOLIATH: 183 followers, 250 tweets
- OBERON: 214 followers, 444 tweets
- SCREENED: 133 followers, 76 tweets

Figure 4: *ERGO X account (April 2024)*

4.3 Contribution to the development of an international strategy and guidelines for testing EDCs and assessing associated hazard and risk

ERGO planned to increase human and environmental safety on the global scale by contributing to an international combination and coordination of the joint resources invested in assessing chemicals for endocrine effects. ERGO evaluated experimental data to select those being of relevance for TG development (by the steering group and the OTF) to the OECD level where it contributes to the development of an internationally accepted strategy for safer testing of EDC.

ERGO has strongly supported an internationally agreed testing strategy formed and controlled under the auspices of OECD, because OECD set the international standards on the safety of chemicals. In this context, ERGO has promoted safer testing of EDC via multiple OECD relationships like project 2.64 and 1.35 in the OECD TGP.

The ERGO multi-actor approach implemented through the SAB, the URG, and the EURION cluster consisting of international partners (regulators, academia, internet groups, NGOs, legislation, and industry) from 5 continents has ensured that ERGO’s results will be rapidly available to relevant decision-makers and multipliers.

ERGO share the obtained knowledge and developed tools, including open-access OECD TGs, open access publications and a Quantitative Structure–Activity Relationship (QSAR)/Physiologically Based Toxicokinetic

(PBTK)-based in silico Decision Support System (DSS) available for regulators, the industry, as well as for the public.

The ERGO strategy for identifying chemicals relevant for human exposure- and epidemiological studies has been developed within ERGO in synergy with the European Human Biomonitoring Initiative (EHB4EU), a joint European platform for the research on links between chemical exposure and human health and a science-to-policy interface supporting European countries in protecting citizens from environmental hazards (supported by the Joint Programming under the Horizon 2020 programme), where MU plays an active role as national hub coordinator and a member of the EHB4EU project Management Board. This close link further supports wide international collaboration and provides ERGO an opportunity to contribute to the research priorities identified in this initiative.

ERGO partners have continuously supported an international strategy for testing of EDCs at a global level via involvement in powerful global institutions on EDC Hazard and Risk assessment including OECD, UNEP, WHO, and SETAC.

Regulatory & Scientific fora of relevance	ERGO partner involvement	ERGO partners	Status
OECD WNT	Experts and project developers	UHEI, UA, SDU and ERGO SAB	WNT has approved validation at the OECD level. In April 2023, the validation of 4 thyroid hormone system sensitive endpoints in the fish TG 236 and TG 210 was approved. The endpoints were developed and pre-validated in ERGO and project 2.64 on the OECD work programme (https://www.oecd.org/chemicalsafety/testing/work-plan-test-guidelines.pdf). A detailed review paper (DRP) on thyroid hormone system sensitive endpoints in fish, partly developed by ERGO partners has also been approved and published in the OECD series on testing and assessment as publication number 381 (No. 381 DRP on the thyroid hormone system in fish and identification of potential thyroid hormone system related endpoints for inclusion in existing OECD fish Test Guidelines (https://one.oecd.org/document/ENV/CBC/MONO(2023)17/en/pdf)
OECD VMG-Eco	Experts and chairs	YCU, MATT, SDU, UA, LOR	Project 2.64 on the OECD work program. Led by ERGO partners from BE, NL, DE, and DK. Bringing ERGO results on thyroid hormone system sensitive endpoints in fish test guidelines onto validation in OECD. Validation has started in spring 2024 and will continue in 2025, after ERGO is finalized, with support from the lead countries. This ensures maximum continued impact of ERGO derived data on fish embryo and in
OECD VMG-NA	Experts	MU, LOR, BASF	In vitro based assays from ERGO are supporting test guideline development, and ERGO partners are involved in the development and validation of thyroid hormone system sensitive in vitro tests.
OECD Advisory Group on Emerging Science in Chemicals Assessment (ESCA)(EAGMST)	Expert	UA	AOP work from ERGO used to support project 1.35: Thyroid hormone system disruption AOPs in fish (co-led by BE, DE, US, and DK) under ESCA to support the endpoint selection and validation with AOPs and AOP networks in project 2.64 (co-lead by DK, DE, BE, and NL) under OECD VMG-Eco and the development and endorsement of specific AOPs. As of April 2024, within ERGO, 5 AOPs have been reviewed, endorsed by WNT/ Working Party on Hazard Assessment (WPHA) and declassified by the OECD Chemicals and Biotechnology Committee.

JRC European Union Reference Laboratory for alternatives to animal testing (EURL-ECVAM)	Experts	BASF, MU	Interaction with the JRC led validation of in vitro assays to identify thyroid hormone system active chemicals.
EFSA ED WG	Experts	UHEI, SDU	Participation in the EFSA Endocrine Disruptor Working Group. Using knowledge gained in the ERGO project to support the Working Group tasks on thyroid hormone system disruption in fish and amphibian test guidelines for the investigation of endocrine disrupting properties of plant protection products.
ECHA Endocrine Disruptor Expert Group (EDEG)	Nationally appointed Experts	SDU, UBA	Continuous participation in the Endocrine Disruptor Expert Group in ECHA, giving advice on data interpretation and potential data gaps for identification of chemicals as endocrine disruptors under REACH and the Biocide regulation
SETAC Endocrine Disruptor Testing and Risk Assessment Advisory Group (EDTRA) AG	Experts	UHEI, UA, SDU	Supporting the work in the SETAC EDTRA AG on disseminating research outcomes on topics related to identification of endocrine disrupting chemicals.

***Table 4**: Role of ERGO participants in EDC associated regulatory and scientific bodies, impacting scientific development of EDC test guidelines and the regulatory strategies to optimize TGs for safer ED assessment.*

5 EURION

In order to optimize synergies and avoid overlaps between the projects selected for funding from the call SC1-BHC-27-2018 'New testing and screening methods to identify endocrine disrupting chemicals (EDCs)', it was decided the granted projects would form a cluster.

The EURION cluster was launched on 1 January 2019. It is made up of eight research projects funded by the EU Horizon 2020 Research and Innovation Programme, and it is the largest public funding of this type of research in Europe, as it has been funded €50 million by the European Commission's Horizon 2020 Research and Innovation Programme.

The cluster projects collectively contribute to the requirements of the new EU endocrine disruptor strategy, entitled 'Towards a comprehensive European Union framework on endocrine disruptors. It calls for advancement in the development and validation of test methods. The projects specifically meet the needs of the OECD, which is the leading recognised body for developing internationally agreed test guidelines, which are transposed into relevant EU legislation as appropriate.

Each project in the cluster has been focusing on a different aspect of new testing and screening methods identifying EDCs. Forming this cluster group optimise synergies and avoid overlaps between the projects to maximise impact.

The eight projects are listed below (acronyms and full titles):

- ATHENA - Assays for the identification of thyroid hormone axis disrupting chemicals: elaborating novel assessment strategies
- EDCMET - Metabolic effects of endocrine disrupting chemicals: novel testing methods and adverse outcome pathways
- ENDPOINTS - Novel testing strategies for endocrine disruptors in the context of developmental neurotoxicity
- ERGO - Breaking down the wall between human health and environmental testing of endocrine disrupters: EndocRine Guideline Optimisation
- FREIA - Female reproductive toxicity of EDCs: a human evidence-based screening and identification approach
- GOLIATH - Beating Goliath: Generation of novel, integrated and internationally harmonised approaches for testing metabolism disrupting compounds
- OBERON - An integrative strategy of testing systems for identification of EDs related to metabolic disorders
- SCREENED - A multistage model of thyroid gland function for screening endocrine-disrupting chemicals in a biologically sex-specific manner

For partner details, see EURION website https://eurion-cluster.eu/

The overall purpose of the creation of the cluster has also been to ensure a number of outputs, among others the following:

- Improved hazard and risk assessment of EDs, including in the workplace;
- Novel ED assay candidates for regulatory use;
- Support for the OECD work on testing and assessing chemicals for ED identification;
- Enhanced international cooperation;
- Contribution to the development of an international strategy and guidelines for testing EDs and assessing associated hazard and risk.

The EURION cluster was chaired by the projects: GOLIATH and OBERON chaired the cluster for the first 15 months. From April 2020 to June 2021, the projects ENDpoiNTS and ERGO held the chairmanship. From July 2021 to September 2022, the projects ATHENA and SCREENED chaired and currrently, FREIA and EDCMET hold the chairmanship until the projects close in June/December 2024.

Moreover, 15 thematic working groups (WGs) in the EURION cluster have been established, each with a special thematic focus in accordance with the cluster mandate to optimize synergies and avoid overlaps and facilitate cross-project collaboration on the following topics:

- Animal studies rodents
- Animal studies aquatic organisms
- AOPs
- Chemicals
- Data management
- Dissemination & communication
- Epidemiology
- Evidence-Based Tools
- IATA
- In silico

- In vitro models
- Omics
- Validation
- Regulatory affairs and policy
- Thyroid Hormone Analytics

The WGs have leaders from all the eight sister projects in EURION as well as from the JRC. The WGs have collaborated on common activities such as the selection of chemicals being tested, training, data sharing and annual meetings.

Important parts of the work carried out in EURION have been a large number of activities, among others are the following:

- Common events (e.g., kick-off, annual and final meetings, workshops/trainings; e.g.; AOP workshops – OECD: On the 27 January 2021, the first AOP development workshop was organised and aligned with the EURION Annual Cluster Meeting, facilitating collaborative AOP development and entering of project data into the AOP-WIKI.
- Common dissemination activities (e.g., website, logo, brand guidelines, templates (e.g., PowerPoint, poster, and pull-up banner), factsheet, and Introductory video
- Collaboration with all projects and especially sister projects ENDpoiNTs and Athena on method developments, data evaluation and future projects planning has improved projects impact and prevented projects overlapping
- Policy briefs:
  - Policy brief January 2022: Towards safer chemicals – reliable test methods to identify endocrine disruptors
  - Second policy brief to be finalised and published in 2024
- Reports
- Publications
- Presentations
- Newsletters
- Stakeholder Consultation for Development of Endocrine Disruptor Test Methods (2020)
- Stakeholder workshop (EURION Stakeholder Workshop 2020 Summary Report)
- Interactive presentations at scientific conferences, particularly those attended by concurrent projects. Specific collaboration with EURION sister projects.
- EURION session at the European Commission's Annual Forum on Endocrine Disruptors from 2020-2023: Progress update from the cluster, including its visions on knowledge gaps and future research needs on endocrine disruptors.

6 Next steps

ERGO is highly engaged in ensuring the optimal use of the results of the work done in ERGO as well as related exploitation of results by relevant stakeholders and research projects.

ERGO consortium:

As part of ERGO's WP8, knowledge management systems have been integrated into the project design from the start to ensure that all Knowledge Outputs (KOs) arising from the project, including scientific outputs, new methodologies, protocols, and experimental approaches as well as de novo knowledge and new strategies, are captured and transferred to relevant user groups in a measurably impactful way. The principles and guidelines around knowledge transfer (KT) and exploitation as outlined in D8.1 DEP. Now in the final year of the project, ATT are developing Knowledge Transfer Plans (KTPs) for the KOs collected that are deemed to be Key Exploitable Results (KERs). The aim of these KTPs is to reach all the relevant stakeholders and end users of the KOs in a targeted way so that they can exploit and take up the outputs for maximum impact. First the knowledge landscapes i.e., value chains, key actors, relevant legislation, milestones and events are mapped for the KERs and verified with the relevant partners. Using these landscapes, specific target users from within the five audience types i.e., regulators, private sector, scientific community, policymakers and general public that are deemed relevant are profiled. WP8's final deliverable is D8.6 KT Key Achievements Booklet. Within this report, the KOs and KERs generated and their associated KTPs and activities will be outlined. The success of these activities will be described both quantitatively and qualitatively and a roadmap for post-project exploitation activities to maximise the impacts of the project will also be included.

Research projects/scientific communities:

PARC: ERGO partners (MU, UA, AU, UFZ, SDU, UBA, CNRS) are involved in several tasks in the Horizon Europe Partnership for the Assessment of Risks from Chemicals (PARC) where the partners ensure to bring results and data generated in ERGO into the next generation hazard and risk assessment of chemicals in Europe to support a safer hazard and risk assessment of chemicals including endocrine disrupting chemicals. ERGO partners are bridging results from WP3 (AOP development) into PARC WP5.3 task 5.3.2 AOP development. Results from ERGO WP5 are bridged with PARC WP5.2 task 5.2.2 on development of New Approach Methodologies (NAMs) and ERGO results, in general, are bridging with PARC WP 6.1 task 6.1.1 on the development of Integrated Approaches for Testing and Assessment (IATA).

NeXED: ERGO partners are coordinators of (UA) and partners in (MU, CNRS and SDU) a new Doctoral Network (DN) funded under MSCA Doctoral Networks 2023 (HORIZON-MSCA-2023-DN-01). This DN, starting in 2025, will build on, and further develop, several of the results and concepts from ERGO including the One Health approach combining toxicology and ecotoxicology, the use of data across species and classes and the continued development of new test methods for ED assessment covering less well-characterised mechanisms and effects. NeXED aims to facilitate a paradigm shift in EDC assessment by training a new generation of cross-disciplinary toxicologists specialised in using harmonised approaches in a One Health framework. NeXED will train its 15 doctoral candidates through research, secondments, and training events using an interdisciplinary and intersectoral training programme.

Industry:

ERGO has a strong interaction with industry who will be end users of several of ERGOs test guideline related outputs. ERGO include industry partners (BASF and L'Oréal) and also engage Bayer in ERGO User Reference Group. The interaction will continue after ERGO via the OECD validation of fish THSD sensitive endpoints under project 2.64 on the OECD TGP.

Regulatory activities:

ERGO partners are actively involved in setting-up and amending regulatory frameworks with respect to Eds. Among them are the implementation of specific ED relevant tests under the REACH standard information requirements and the development of a specific guidance document led by ECHA for the newly introduced ED criteria under the EU CLH regulation. Furthermore, ERGO partners are involved in the OECD Thyroid Disruptor Methods Expert Group. These activities ensure that the ERGO results are directly fed into actual and highly relevant regulatory developments.

7 Conclusion

The ERGO concept of breaking down the wall between environmental and human health assessment of endocrine disrupting chemicals has gained more international acceptance during the project period and data generated for human health assessment are to a larger extent used in environmental assessments and vice versa. One example is the AOP network and IATA development in ERGO for thyroid hormone system disruption in different vertebrate taxa that is now implemented and further developed in PARC project tasks.

OECD validation of thyroid hormone system disruption sensitive endpoints in fish tests is an example of strong ERGO support to international improvement of in vivo tests ensuring safer assessments of EDs and better use of animal data.

Due to the intense international collaboration in the ERGO consortium, the research being carried out has impact at the global scale when considering the Mutual Acceptance of Data (MAD concept) in OECD test guidelines.

Upon finalisation of the ERGO project, as well as the EURION cluster, the enhanced international cooperation which has taken place throughout the project should facilitate for a better use of data among researchers and regulators working on hazard and risk assessment of ED’s.

Appendix 1

ERGO partners (confer ERGO website https://ergo-project.eu/about/consortium/):

- Syddansk Universitet (SDU)
  SDU was founded in 1966 as a research and educational institution with strong contacts with regional industries and the international scientific community. The SDU Ecotoxicology Group is the leading research group in environmental endocrine disruption in Denmark with more than 20 years of experience in the development and validation of Organisation for Economic Co-operation and Development (OECD) Test Guidelines for detection and evaluation of endocrine disrupting chemicals (EDCs). The group is experienced in the development of highly sensitive biomarkers and endpoints for endocrine disruption (ED) in both vertebrates and invertebrates, and collaborates with research groups, contract laboratories and business organizations worldwide. The group has received more than €6 million for ED-related projects and coordinated both national projects for the Danish Environmental Protection Agency (EPA) and international project for OECD and the Nordic Council of Ministers related to OECD test guideline development.

  ERGO is coordinated by SDU. SDU leads WP1, WP7 and WP9 of the project.

- Universiteit Antwerpen (UA)
  UA is one of the leading universities in Belgium with modern and up-to-date educational and research facilities. UA is ranked 13th in top young universities in the QS world university. Zebrafishlab was founded in 2010 as a joint academic laboratory of UA with members from the Veterinary Sciences and Biology departments. The research of Zebrafishlab focuses on the use of zebrafish (embryos) in ecotoxicology and food safety. Zebrafishlab uses an AOP-based strategy to develop alternative testing approaches using zebrafish embryos and in vitro/in chemico methods. Endocrine disruption has always been one of the main research lines and during recent years thyroid disruption has become a particular focus area. Together with collaborators from the US Environmental Protection Agency (EPA), Zebrafishlab recently built an AOP network for thyroid disruption in fish (OECD AOP project 1.35) and integrated this network with existing information in mammals and amphibians resulting in a cross-class AOP network which will provide the starting point for the ERGO project.

- AquaTT UETP CLG (AquaTT)
  AquaTT is a small to medium enterprise (SME), with a not-for-profit mandate. It was founded in 1992 under the EU COMETT programme as the University Enterprise Training Partnership (UETP) for the European aquaculture industry, to coordinate the training requirements of the industry through a single body. Over the past 26 years AquaTT has grown beyond its original remit to become a leader in scientific knowledge transfer and dissemination. We partner with research consortia to design projects that make a difference. We devise best practice work packages related to dissemination, communication and knowledge transfer. Traditionally we have worked with the marine and aquaculture research sectors, but recently we have become involved in projects in the areas of environment, health, food and sustainable development.

- Ruprecht-Karls-Universität Heidelberg (UHEI)
  Within UHEI, the Aquatic Ecology and Toxicology Group is affiliated with the Centre for Organismal Studies (COS). The COS Heidelberg studies organismic biology beyond the borders of organizational level. Research and teaching at COS is dedicated to study organismic biology from basic molecular principles from cell biology, developmental biology, plant and animal physiology to evolution, ecology, biodiversity, systems biology and biotechnology. The Aquatic Ecology and Toxicology Group has twenty-five years of experience in aquatic toxicology, especially fish ecotoxicology. Over

the years, the group has made contributions to the effects of pesticides, dioxin-like substances, endocrine disruptors, genotoxicants, teratogenic compounds and neurotoxicants in fish. Most recent projects, however, have focused on the development of alternative protocols designed to replace conventional testing schemes with intact fish, be it at the level of basal (acute) and prolonged toxicity (including teratogenicity) or at the level of more specific modes of actions such as dioxin-like action, endocrine disruption, genotoxicity or neurotoxicity.

- École Normale Supérieure de Lyon (ENSL)
  The Institute of Functional Genomics of Lyon (IGFL) is a research unit of ENSL, a prestigious elite French public institution that trains professors, researchers, senior civil servants as well as business and political leaders. IGFL is supported by CNRS, the Université Claude Bernard Lyon 1 and the National Institute for Agronomical Research (INRA). It gathers more than 100 members organised into 15 independent groups from different backgrounds. The IGFL's originality comes from bringing together embryologists, endocrinologists, specialists in bioinformatics, evolutionary scientists, palaeontologists, physiologists and genome specialists. It is the Functional Genomics of Thyroid Hormone Receptors Group that will be most involved in ERGO. The group have six permanent members and their research is dedicated to the understanding of thyroid hormone signalling in vivo, with a specific interest in the mammalian brain. The group received international recognition for its genetic investigation of the neurodevelopmental function of the nuclear receptors of thyroid hormone, which heavily relies on expertise in transgenic mice technology, developed on an in-house platform. It continues to address basic questions on the mechanisms underlying the neurodevelopmental function of thyroid hormone. The group has also been a pioneer in toxicogenomics, applying advanced genomic technology to the field of thyroid hormone disruptors. It has been repeatedly funded by the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) to develop innovative tools to study endocrine disruptors.

- Aarhus Universitet (AU)
  AU was founded in 1928. Internationalisation is a key part of AU's mission and it continuously works to strengthen the international profile of the University through a series of initiatives. AU has participated in 295 FP7 and 173 H2020 projects and is currently hosting 39 ERC projects. The Department of Environmental Science at AU executes basic and problem-oriented research within organic, chemical and physical connections in the environment and within economic, political and social conditions in the interaction between environment and society. The Environmental Endocrine Disruptors Laboratory conducts lab and field experiments at the molecular level, to understand the environmental occurrence, fate and effects of endocrine disrupting pollutants, such as natural substances, pesticides and medicine residues. Effect-oriented in-vitro and in-vivo testing in combination with wildlife investigations and state-of-the-art mass spectrometry-based technologies provide means to identify emerging environmental endocrine disruptors.

- BASF SE (BASF)
  BASF create chemistry for a sustainable future. They combine economic success with environmental protection and social responsibility. BASF aims to strengthen its position as the world's leading chemical company. Innovations based on chemistry will play a key role in three areas in particular: resources, environment and climate; food and nutrition; quality of life. In 2017 BASF spent around €1.9 billion on research and development worldwide. In the experimental Toxicology and Ecology department of BASF SE, Ludwigshafen, Germany, about 30 scientists and 170 technicians are employed. All types of regulatory in vivo toxicity studies are performed. Additionally, screening and mechanistic studies for agrochemicals are developed. The BASF Toxicology is GLP certified since 1983. Additionally, the ecology department is DIN EN ISO/IEC 17025 accredited and the toxicology

department is DIN EN 150/IEC 17020 accredited with regular audits by the national accreditation body. Apart from this, the animal facility of the BASF toxicology is AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care) accredited since 2007. The experimental toxicology department cooperates intensively with about 40 regulatory toxicologists of the BASF Environmental Health and Safety department.

The toxicology department of BASF SE has established a MetaMap Tox database containing the plasma metabolome (about 250 metabolites) of rat repeated dose studies with pharmaceutical, agrochemical and chemical reference compounds. These data will be used by BASF SE to evaluate metabolite pattern for characterizing AOPs of the project.

- Umweltbundesamt (UBA)
  UBA is Germany's main environmental protection agency. UBAs task is to ensure a healthy environment with clean air and water, free of pollutants to the greatest extent possible. UBA gathers data on the state of the environment, detects environmental problems, assess them and proposes solutions. They are concerned with a broad spectrum of issues e.g. waste avoidance, climate protection, pesticide approvals and chemical regulation under the REACH framework. UBA provides scientific assistance to the German Federal Ministry for the Environment and provides the general public with information on all environmental issues. UBA is one of three German federal authorities responsible for the REACH implementation and in this respect deals with all issues concerning the environment. UBA is engaged in evaluating information submitted by registrants to the ECHA (European Chemicals Agency), identifying substances that require regulation, supporting REACH stakeholders, further developing chemical safety evaluation methods, making proposals on the further development of the REACH Regulation and introducing them to the discussion process at EU level. One major task of UBA under the REACH framework is the identification and regulation of endocrine disrupting substances in the environment for the biocide directive and the plant protection directive. UBA initiates regulatory risk management measures to minimize the environmental exposure of endocrine disruptors. To further develop the science based identification and evaluation of endocrine disrupting chemicals UBA launches research projects, is involved in discussion processes with ECHA, the EC and other EU member states and is involved as national coordinator in the OECD test guideline program. The aim of UBA´s activities with ERGO is to address the existing knowledge and testing gaps from a regulatory point of view.

- Masarykova Univerzita (MU)
  MU is the second largest university in the Czech Republic. The Research Centre for Toxic Compounds in the Environment (RECETOX) is the largest department at the Faculty of Science of MU recognised internationally for their research on chemical exposures and their impact on ecosystems and human health. RECETOX has an expertise in the assessment of sources of legacy and emerging pollutants, their environmental fate, levels and impacts, human exposure pathways, tissue levels, toxicological effects and associated risks. It is a leading institution in endocrine disruption related research in the Czech Republic. RECETOX research infrastructure consists of environmental monitoring networks, human cohorts, accredited trace analytical laboratories and environmental databases and information systems. The experts from Division of Environmental Chemistry and Modelling, Division of Ecotoxicology and RECETOX research infrastructure focused on human cohorts will collaborate within ERGO. The former one offers advanced instrumentation to study the environmental fate of chemicals and exposure patterns in various environmental media as well as in human samples. The Division of Ecotoxicology covers research in the field of toxicity and ecotoxicity assessment of environmental pollutants and complex matrices, including development of advanced biodetection systems for practical use such as in evaluation of endocrine disruptive

potency of compounds and their mixtures. The birth cohort CELSPAC, initiated as a collaborative project of Masaryk University and University Hospital Brno, Czech Republic, aims to assess multiple factors potentially affecting children´s health. In the last decade, MU-RECETOX scientists coordinated two FP5 projects and participated in three FP6 projects. They have been participating in eight FP7 projects (isoSoil, ArcRisk, AquaRehab, EuroEcotox, TaToo, REFORM, SOLUTIONs and DENAMIC).

- Centre National de la Recherche Scientifique (CNRS)
  CNRS was founded in 1939 and is a state-funded science and technology establishment placed under the authority of the French Minister for Research and Higher Education. Laboratory Evolution des régulations endocriniennes (UMR 7221) is a joint research unit under the umbrella of several establishments, including CNRS and the Muséum National d'Histoire Naturelle (MNHN). Several MNHN employees are involved in the ERGO project. MNHN is a museum and research centre created in 1635, with the mission to make knowledge about the natural world accessible to everyone and to make as many people as possible aware of the importance of protecting our planet. The main objective of the research unit is now to understand the physiological regulations that control development, tissue homeostasis, regeneration and aging in normal and altered conditions. The unit focuses on how the modulation of gene regulatory networks mainly through thyroid hormone signalling contributed to the evolution and generation of biodiversity and how these regulatory processes might be affected by disruption. The group's objective is to determine the physiological consequences of exposure to endocrine disruptors and environmental changes related to stress and life cycle transitions. The team develops four axes of research: 1) the evolution of molecular control of life cycle transitions with a special emphasis on amphibian metamorphosis, a post-embryonic developmental process that is linked to change of environment, controlled by environmental challenges and initiated by thyroid hormones, 2) the control of cell fate plasticity by thyroid hormones, 3) the impact of endocrine disruptors on thyroid signalling, and 4) the interaction between thyroid hormone signalling and glucocorticoid signalling, one of the mediator of stress and environmental changes.

- Helmholtz-Zentrum für Umweltforschung GMBH (UFZ)
  UFZ was founded in 1991 under the name UFZ- Environmental Research Centre Leipzig-Halle GmbH and has more than 1,100 employees on its premises in Leipzig, Halle/S. and Magdeburg. They conduct research to support a sustainable use of our natural resources to benefit both mankind and the environment. UFZ belongs to the Helmholtz Association of National Research Centres. In FP7 and Horizon 2020, UFZ participated in 91 projects with 33 as coordinator, it hosted two ERC Starting Grants and one ERC Advanced Grant and has coordinated 3 ITNs. Since 2014 the UFZ is leading the European Topic Centre on inland, coastal and marine waters funded by the EEA.

- Peter Matthiessen (MATT)
  Peter Matthiessen is the sole, self-employed staff member of the Peter Matthiessen ecotoxicology consultancy. This consultancy has been in continuous operation since 2006, and has a wide range of clients in government, NGOs and industry. The consultancy has tended to specialise in the provision of advice in the field of endocrine disruption, but has also been directly involved in research on the effects of various endocrine disrupters (EDs) on fish and amphibians. A particular speciality of the consultancy has been the development and validation of new ecotoxicity test methods for endocrine disruptors.

- l'Oréal (LOR)
  LOR is among the world's largest cosmetics companies and has developed activities in the field of

cosmetics, concentrating on hair colour, skin care, sun protection, make-up, perfume and hair care. LOR has a long-standing commitment in researching and developing alternatives to animal testing for human and environmental safety assessment of chemicals and mixtures. L'OREAL launched its "Sharing Beauty with All' global sustainability program in 2013, setting out its 2020 objectives to reduce its environmental footprint, strengthen its positive social impacts and transform its operations and manufacturing activities. Since its creation in 1995, LOR's Environmental Research Department has been working on method developments to assess the impact of cosmetic products on wildlife and ecosystems. This department is organized around two main sectors:

– The predictive environmental assessment pole, which evaluates the environmental impact of the products developed by the LOR Group, in particular by analysing their life cycle and their water footprint (combining products aquatic toxicity and biodegradability).

– The Eco-models pole, which develops and carries out ecotoxicity tests on different aquatic species representative of soft and marine water food chains: bacteria, microalgae, invertebrates and fish embryos. Some of these organisms (fish embryos in particular) are also studied as a predictive models of human toxicity and/or pharmacology or biological modelling.

- Forschungsverbund Berlin (IGB)
  IGB is one of the eight institutes legally represented by Forschungsverbund Berlin e.V. (FVB) and thus a part of FVB. IGB is a creative, lively and diverse place for conducting research and teaching. Scientists from a whole range of disciplines work under one roof. Hydrologists, chemists, physicists, microbiologists, limnologists, fish ecologists, ecotoxicologists and fisheries biologists from all over the world investigate the fundamental processes governing rivers, lakes and wetlands, and join forces to develop measures conductive to sustainable water management by taking an integrative research approach. We pool our discipline-based research in six research departments. Added to this are three cross-cutting research domains in which we address topics of high scientific and/or societal relevance. IGB is Germany's largest research centre for freshwaters. IGB – Department of Ecophysiology and Inland Fisheries – Ecotoxicology group; The Department of Ecophysiology and Aquaculture focuses to investigate the ecophysiological impacts of multiple environmental factors on aquatic vertebrates, in particular fishes and amphibians. The goal is to create the scientific foundations for sustainable aquaculture and to shed light on how biotic and abiotic factors including endocrine disruptors influence on the various physiological functions of individual vertebrates with regard to reproduction, stress, development, growth and behaviour. The ecotoxicology group is an internationally recognized research group in endocrine disruption of amphibians with more than 20 years of experience in assessment of modes of action of endocrine disruptors using amphibians as model but also markedly involved in the development and validation of the OECD TG 231. The group is experienced in development of highly sensitive biomarkers and endpoints for endocrine disruption in both, amphibians and fishes, by using in vivo and in vitro approaches and collaborates with research groups, contract laboratories and business organizations worldwide. The group is equipped with state-of-the-art flow-through exposure system, chemical, biochemical and molecular biological labs to assess endocrine effects in vivo and in vitro.

- Yokohama City University
  Professor Taisen Iguchi comes from Department of Life and Environmental System Science, Graduate School of Nanobioscience, at Yokohama City University. He is an endocrinologist with over 40 years of experience in comparative endocrinology including over 20 years of experience in endocrine disruptor research in fish, amphibian, reptilian and invertebrates including Daphnids.

Taisen is a chair of UK-Japan research collaboration and US-Japan bilateral meeting funded by the Ministry of the Environment, Japan (MOE), concerning endocrine disrupting chemicals research. Taisen has been serving OECD Validation Management of Ecotoxicity (VMGeco), EAGMST, EDTA etc., since 1997, and currently co-chair of the VMGeco. He is a committee member of the Food Safety in the Cabinet of Japan. Taisen established reporter gene assay systems of medaka fish oestrogen receptor and androgen receptor, Xenopus tropicalis thyroid hormone receptor beta, and ecdysone receptor and juvenile hormone receptor of Daphnids for screening of chemicals for the MOE. Taisen is a member of the OECD Fish Drafting Group, the Endocrine Disruptors Working Group and the Amphibian Expert Group. Taisen has made major contributions to the drafting and validation of OECD endocrine disruption-related OECD TG 229, 230, 231, 234, 240, 241 and 211.

Taisen has supported the ERGO development of biomarkers and endpoints for detection of thyroid disrupting chemicals in fish and amphibians. He has coordinated collaboration between work in Japan on transgenic strains of Japanese medaka (Oryzias latipes) and Xenopus laevis for detection of thyroid disruption and work performed by ERGO partners. As a member of several OECD expert groups including VMG-Eco and OECD Fish Drafting Group, Taisen will ensure communication between Japan endocrine disruption entities, OECD and ERGO.