

TOWARDS SAFER CHEMICALS – RELIABLE TEST METHODS TO IDENTIFY ENDOCRINE DISRUPTORS

Reliable testing for endocrine disruptors is lacking

Endocrine disruptors (EDs) alter the functioning of the endocrine system in many different ways, and negatively affect human health and the environment. ED exposure, in particular during sensitive life stages, has been linked to increased risk for common diseases such as obesity, diabetes, hormone-related cancers, and reproductive and (neuro)developmental disorders¹.

Reliable testing is critical to identify EDs and to manage their risks appropriately. Currently, pesticide and biocide regulations require assessment of ED properties but soon thousands of industrial chemicals under REACH will have to fulfill the same requirements. There is a lack of validated, sensitive ED test methods for adverse effects especially on the thyroid hormone system, neurodevelopment, metabolic disorders and female reproductive health.

EURION – a European Cluster to Improve Identification of Endocrine Disruptors

EURION consists of eight European research projects developing new test methods for identification of EDs. The cluster was established in January 2019 in order to create synergies among the projects funded under the Horizon 2020 call SC1BHC-27-2018, 'New testing and screening methods to identify endocrine disrupting chemicals'.

By building on synergies among the eight projects, EURION is both establishing new, and optimising current, methodologies to increase the quality, efficiency and effectiveness of ED testing methods. These test methods are urgently needed for the evolving regulatory requirements in Europe and worldwide.

EURION projects contribute to better assays for testing of EDs to minimise exposure to humans and the environment:

- **Deliver** both novel and improved ED assay candidates and testing batteries that are necessary for implementation of regulatory requirements.
- **Pursue** a more mechanism-based hazard assessment, generating novel insights into endocrine modes of actions linked to health impacts, in line with a move towards animal-free chemical testing.
- **Support** the development of internationally harmonised strategies and guidelines for testing EDs and assessing associated hazards and risks.
- **Align** with the OECD work on testing and assessing chemicals for ED identification, particularly the OECD ED Screening and Testing Programme
- **Contribute** to achieving the aims of the EU Chemicals Strategy for Sustainability², especially in relation to development and uptake of methods to generate information on EDs.

¹ World Health Organization, United Nations Environment Programme, Inter-Organization Programme for the Sound Management of Chemicals, Bergman, Åke, Heindel, Jerrold J. et al. (2013). State of the science of endocrine disrupting chemicals 2012 / edited by Åke Bergman ... [et al]. World Health Organization. apps.who.int/iris/handle/10665/78101

² ec.europa.eu/environment/pdf/chemicals/2020/10/Strategy.pdf

ENDOCRINE RELATED SYSTEMS STUDIED WITHIN EURION

Thyroid hormone system

The thyroid hormones control various biological processes such as growth, development, reproduction and metabolism. The thyroid hormone system is highly complex, with several entry points where it is possible to disturb the system. **ATHENA**, **ERGO** and **SCREENED** are developing novel in vitro assays, including 3D models (**SCREENED**) to investigate points of perturbation of the thyroid hormone system that have the most critical effects on hormone disruption: for instance, inhibition of iodide uptake or inhibition of hormone synthesising enzyme. The novel testing strategies are based on Adverse Outcome Pathway (AOP) networks and can be adapted to work across different vertebrate species.

Metabolic disorders

The incidence of obesity and metabolic disorders has increased exponentially over the past few decades. Exposure to a class of EDs known as metabolism disrupting chemicals (MDCs), has been linked to disorders like obesity, diabetes, and non-alcoholic fatty liver disease. **EDCMET**, **GOLIATH** and **OBERON** are identifying the action of these chemicals, defining key events and pathways, and providing increased understanding for their role in adverse outcomes. The projects are creating a battery of in vitro and in silico assays, and improved animal studies for identification of MDCs and their health effects.

Developmental neurotoxicity

The brain is one of the organs that are most vulnerable to damage by toxins, particularly during development. Several EDs are known to target the brain. However, there remains a significant knowledge gap in understanding how EDs affect neurodevelopment. Furthermore, ED-induced developmental neurotoxicity (DNT) is insufficiently covered by the testing tools in current regulatory use. **ENDpoiNTs** is enhancing the human-relevance of current screening methods, and developing an integrated suite of assays to test and assess ED-induced DNT effectively.

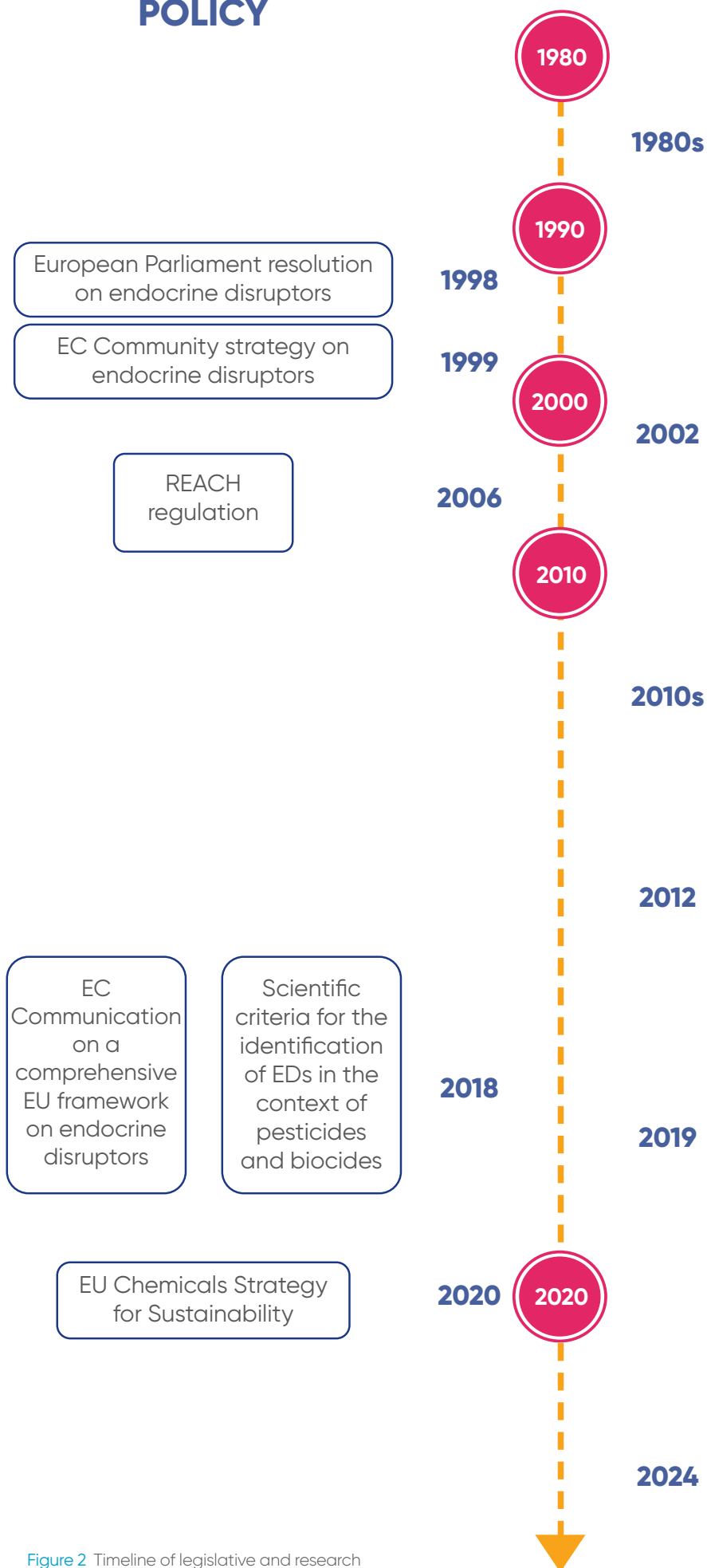
Reproductive health

One in six couples worldwide face fertility problems. Ovulation disorders, such as irregular menstrual cycles, polycystic ovary syndrome, and early menopause, account for infertility in one out of four infertile couples. Exposure to EDs in early life can affect ovarian development, however the mechanisms are mostly unclear. **FREIA** focuses on the ovary in different life-stages, increasing understanding of the mechanisms and processes underlying both normal ovarian development and adverse effects caused by EDs. The project aims to develop better test methods for identifying ED-impacts on the ovaries.



Figure 1 The EURION projects are working to bridge current gaps in testing and identification of EDs across four endocrine-related health domains: Thyroid hormone system, Metabolism, Neurodevelopment and Female reproduction.

POLICY



RESEARCH

First studies on impact of endocrine disruptors on reproduction



WHO report "Global assessment of state-of-the-science of endocrine disruptors"

More research focus studies on impact of endocrine disruptors on:

Metabolic systems



Foetal exposure



Brain and behaviour



WHO report "State of the science of endocrine disrupting chemicals"

EURION

Launched with €50M funding - largest of its kind in Europe.

New ED draft methods for validation:

Series of tests



Harmonised strategies



Novel scientific insights



Figure 2 Timeline of legislative and research developments for endocrine disruptors.

RECOMMENDATIONS TO POLICYMAKERS

EURION projects are filling a number of gaps to improve identification of chemicals with ED properties. The following actions are recommended to effectuate the EURION results:

- Support validation of EURION draft test methods
- Promote regulatory acceptance and uptake of EURION test methods under relevant regulations
- Increase the use and weight of academic data in regulatory assessments
- Support further research that enables the paradigm shift from animal to animal-free testing
- Implement animal-free methods for chemical safety assessment into the regulatory context

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