POLICY BRIEF
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ENKORE

Protecting people from endocrine disruptors: political will and strong regulatory focus are key

> **Remaining knowledge gaps and ongoing discussions should not negate the urgency to act through coordinated strategies and demonstrably effective measures, prevent exposure to EDs, and protect the reproductive health of women and future generations.**
>
> —Parent et al., 2025, MERLON

Endocrine disruptors (EDs) are chemical substances —either natural or synthetic— that can mimic, block, or interfere with the body's hormones. They occur in many sources and can enter the body through breathing, eating, drinking, or skin absorption. Some EDs act as hormone mimics, while others block natural hormones or alter the body's ability to produce, release, or eliminate them. Exposure to EDs can disrupt the delicate balance of the endocrine system[1].

The urgency of minimising exposure to endocrine disruptors is clear and backed by the scientific papers published by the ENKORE cluster since 2024. They highlight that epidemiological studies report rising trends in hormone-related cancers, cognitive changes, reproductive and metabolic disorders, while animal studies confirm the induction of similar effects after exposure to EDs[2-7]. Beyond the impact of EDs on our individual health and well-being, endocrine disorders impose a vast societal and financial burden[2-7]. In the EU alone, the estimated annual costs related to effects of exposure to EDs is 163 billion Euros[7].

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Continuous exposure of EDs at low doses is inevitable since they occur in the environment, food, and a wide range of products, such as food packaging, cosmetics, plastic household items, construction materials, paints, and medical devices[2,3,6,7]. Human biomonitoring studies continue to detect EDs in the general European population, and for some EDs, the observed levels infer an exposure that exceeds estimated tolerable intakes[8] (the maximum amount of a chemical substance that can be ingested daily over a lifetime without posing a significant risk to human health).

Despite this growing scientific understanding and increased efforts by EU regulators over the past 15 years to improve the identification of EDs[5], only 276 substances have been specifically evaluated for ED effects in the EU regulatory process[9,10], and fewer than 30 of these were regulatorily identified as EDs relevant for human health[11]. With over 26,000 substances registered under REACH and an estimated 40-60,000 substances in global commerce[12], there is an urgent need to increase the efficiency in the evaluation of EDs[7]. The recent inclusion of hazard classes for EDs in the Classification, Labelling and Packaging (CLP) Regulation[14] presents a valuable opportunity to accelerate the evaluation process and strengthen regulation of EDs in the EU and potentially beyond[5].

This policy brief is based on scientific evidence from the ENKORE cluster, which is studying the health impacts of EDs and exploring ways to reduce our exposure to these chemicals.

Increasing efficiency in the regulatory evaluation of EDs

New Approach Methodologies are essential

Traditional animal-based testing for endocrine disrupting properties is costly and takes years to complete[13]. With the thousands of chemicals in global commerce[12], even if prioritised, testing all industrial chemicals for endocrine disrupting properties through extensive animal studies is therefore not feasible. To increase the efficiency of ED regulation, ENKORE recommends exploring, and where possible applying, New Approach Methodologies (NAMs) that can predict the harmful effects faster[5].

Exploring and discussing the predictive capacity of (combinations of) NAMs

EU legal texts (including the CLP[14], REACH[15], Biocides[16,17] and Pesticides[18,19] regulations) permit the use of NAMs in ED identification as standalone methodologies, without a requirement to demonstrate adversity in an intact organism, i.e. an animal[5]. This requires that the NAMs exhibit predictive capacity similar to that of animal or human data[5]. However, current guidance lacks information on which NAMs, or combinations thereof, can be used to predict adverse effects, apart from the application of read-across[5] (a scientific method used to predict the properties or effects of one chemical based on data from similar chemicals). Therefore, there is a need to explore how (combination of) NAMs can be used to provide the same predictive capacity as animal and/or human data[5]. Such a discussion should include considerations of the inherent uncertainties, not only of NAMs data, but also of the animal and human data currently used in hazard and risk assessment.

Grouping and read-across to fill data gaps

The EU regulatory framework is in place to classify substances as EDs[5]. While for some substances there is enough evidence, for many others pieces of information are lacking. To make the best use of available data and reduce the need for animal testing, substances should be classified in groups using read-across to fill outstanding data gaps[5]. Therefore, the ENKORE cluster highly recommends CLP classification of groups of EDs.

New Approach Methodologies (NAMs): what are they?

In 2016, ECHA defined New Approach Methodologies as:

"NAMs include in silico approaches, in chemico and in vitro assays, as well as the inclusion of information from the exposure of chemicals in the context of hazard assessment. They also include a variety of new testing tools, such as high-throughput screening and high-content methods, e.g. genomics, proteomics, metabolomics; as well as some conventional methods that aim to improve understanding of toxic effects, either through improving toxicokinetic or toxicodynamic knowledge for substances"[20]. In 2022, it was further elaborated that "NAMs are not necessarily newly developed methods, rather, it is their application to regulatory decision making or replacement of a conventional testing requirement that is new" [21].

Scientific uncertainties and science-policy gaps that need to be addressed to improve the use of NAMs

Insufficient exploration of the predictive capacity of (combinations of) NAMs

Lack of clarity on the requirements for (combinations of) NAMs to predict ED adversity

Regulatory identification of EDs does not leverage grouping and read-across

Closing knowledge gaps

Despite growing evidence of the negative health effects of EDs, key knowledge gaps remain[2,4,7] (see Box 1). Closing these knowledge gaps and ultimately using the knowledge to build ED-relevant endpoints into internationally accepted test guidelines is key to effectively identifying, classifying, and regulating EDs[5]. Continued financial support for research in EDs is therefore highly needed.

Box 1. Major knowledge gaps identified by ENKORE

- Not all effects associated with exposure to EDs in humans can be captured by current regulatory test methods[7].
- We lack knowledge about the capacity of many alternative tests to predict effects in humans or animals[7]. One major challenge is how to incorporate Absorption, Distribution, Metabolism and Excretion (ADME) considerations[5,7].
- We do not fully understand the effect of exposure to EDs during foetal and early life stages on female reproductive health later in life and in future generations[2].
- We lack knowledge about sex differences and interspecies variations in effect patterns after exposure to EDs[7].
- Our quantitative understanding of causal pathways is limited[7], e.g. in extrapolations from in vitro to in vivo[7].
- We do not fully understand the underlying mechanisms or the sensitive windows of exposure for chemically induced metabolism disruption[4].
- We do not have methods (animal and non-animal) to reliably identify metabolism disruptors[4].
- We do not know enough about exposure patterns or understand mixture effects of metabolism disruptors[4].

Developing, validating and prioritising fit-for-purpose test methods

In recent years, regulators and researchers have made great efforts to develop and validate new methods and update OECD test guidelines for the detection of EDs. Despite this, methods that can adequately predict all human-relevant effects of EDs, including many not induced through the classical estrogenic, androgenic, thyroid, and steroidogenesis (EATS) modes of action, are still lacking[2,4,7]. In both the REACH[15], Biocides[16,17] and Plant Protection Products[18,19] regulations, identification of EDs relies heavily on data from animal studies[5]. Therefore, animal-based methodologies remain essential until alternatives are accepted and routinely applied[5]. Reducing and refining animal testing, along with the development of NAMs during the transition towards animal-free testing should be prioritised[5]. In the meantime, continued political and financial support for the development and validation of both animal and non-animal methods is needed[5].

The ENKORE cluster also encourages prioritising test methods of the highest regulatory relevance and readiness for validation. In the draft EU roadmap to phase out animal testing for chemical safety assessments — presented in Brussels in November 2025— policymakers outlined how they will set up the steering team to make this prioritisation[22]. ENKORE strongly supports the inclusion of representatives from academia in this steering team, since it is a valuable opportunity to incorporate stakeholders with extensive experience and great insight in the process.

Scientific uncertainties and science-policy gaps that need to be addressed to close gaps

Important knowledge gaps on EDs remain and require continued research within the field.

The validated animal models and non-animal methods are insufficient to identify all relevant effects of EDs.

For complex endpoints such as ED, it remains uncertain whether NAMs (other than read-across) currently are advanced enough to be accepted and routinely applied as full replacements of animal-based methodologies.

An EU system and organisation to prioritise validation of methods with highest regulatory relevance is missing.

Communicating effectively about the risk of exposure to EDs

Due to the ubiquitous occurrence of EDs in the environment, food and everyday products, and the frequent human exposure, there is a growing need for effective communication about exposure reduction to the general population.

ENKORE has found that a scientific understanding of human behaviour is necessary to create effective communication campaigns and interventions that would bring about sustainable changes in daily habits and consumption choices[23]. Decades of behavioural science research show that awareness of a health threat often does not automatically translate to action—a range of psychological and social factors come into play. For instance, to build motivation to change, the person must not only know about the health risk, but also believe they are personally at risk, be aware of what they can do to avoid the threat and feel capable of taking action. After they eventually make the decision to change, the so-called intention-behaviour gap might still impede actual adoption of measures to reduce EDs exposure.

To bridge this gap, interventions could for example provide support for planning concrete actions to avoid procrastination and facilitate the implementation of new daily habits. The inclusion of the person's social circle, such as a partner, parents, or a wider environment, such as school in the case of children, is also crucial to support the change. Public authorities should integrate scientific knowledge from behavioural sciences when planning actions. In practical terms, this means understanding the barriers that stop the target behaviour from happening, using evidence-based models of human behaviour and collecting data from the target group if needed. Once the behaviour determinants are known, appropriate behaviour change techniques can be selected to build the preventive actions.

Scientific uncertainties and science-policy gaps that need to be addressed to increase effectiveness in communication

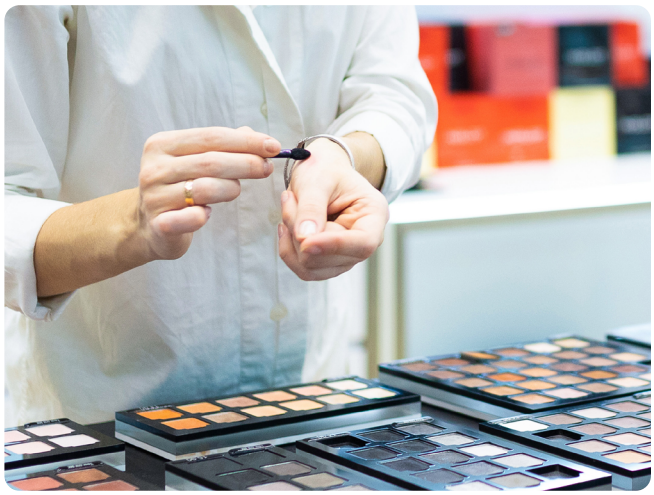
Theoretical models of decision-making and behaviour are not leveraged and the richness of evidence-based behaviour change techniques are not drawn on in interventions on ED exposure reduction.

Strengthening EU and global regulation of EDs: A sustained effort

Over the past 15 years there have been significant advancements in EU regulations aimed at better identifying EDs[5], and now both a scientific understanding of EDs and regulatory tools are available to act (see Box 2). It remains essential to seize emerging opportunities to reduce exposure to these harmful substances through targeted and effective regulatory measures.

More substances need testing for ED effects

Currently, over 26,000 substances are registered under REACH, while an estimated 40-60,000 are present in global commerce[12]. Most of these substances have not been tested for ED effects[12]. With the new ED hazard classes in the CLP Regulation, EDs are expected to be identified mainly through this classification system[5]. However, the CLP regulation does not generate new data; it relies on existing information, including what is generated under the REACH, biocides, and pesticides regulations[5]. Updating the REACH information requirements to include ED-relevant testing for all tonnage levels and uses is therefore critical to ensure accurate CLP ED classifications[5].



Revisions of relevant EU regulation need to consider a restriction of EDs

The EU Chemical Strategy for Sustainability envisioned that consumers, workers, and other vulnerable groups be protected against exposure to the most harmful substances, including EDs[24]. A significant milestone in this direction has been the introduction of hazard classes for the identification of EDs in the CLP Regulation[5].

To further advance the Strategy's objective of avoiding the use of EDs in consumer products, a crucial next step is to extend the generic risk management approach under REACH to include EDs[5]. Another opportunity is to consider restrictions of EDs in revisions of relevant product-specific EU regulations, such as the regulations for cosmetics, detergents, electronics, food contact materials, and medical devices.

As in the recent revision of the Toys Regulation[25], all EDs identified under the CLP Regulation as falling under category 1 or 2 should be considered in such revisions. Both categories can cause severe health effects. However, CLP classification reflects the strength of evidence, not the severity of effects. Currently, REACH standard information requirements provide limited data on ED-related effects that can be used to strengthen the evidence. As a result, only a relatively small proportion of substances registered under REACH are expected to have information available needed to support a category 1 classification.

Holistic approaches and global action are needed

Real-world scenarios of exposure to EDs always involve exposure to mixtures rather than individual substances in isolation[6]. ENKORE echoes the call of researchers to acknowledge and tackle the risk of combined effects[26]. ENKORE urges policymakers to use the REACH revision to move beyond the current chemical-by-chemical assessment approach and implement a pragmatic Mixture Assessment Factor (MAF) to better safeguard people and their health against the combined effects of chemicals.

In addition, exposure to EDs is a global challenge with a global need for action. Introducing ED hazard classes in the Globally Harmonized System (GHS), similar to the EU CLP hazard classes will aid with the protection of environment and health in the EU and beyond. We urge EU policymakers to continue the work of introducing ED hazard classes in the GHS, including both category 1 and category 2 for human health and the environment.

Scientific uncertainties and science-policy gaps that need to be addressed to strengthen ED regulation

It is uncertain whether the upcoming REACH revision will include measures that increase protection against exposure to EDs, including:

- If the generic approach to risk management will be extended to include all regulatorily identified EDs
- If the standard information requirements will be updated to include testing for ED effects at all tonnage levels
- If a mixture assessment factor (MAF) to protect against combined effects of chemicals will be proposed

To read ENKORE's recommendations for the REACH revision in full, please access our position paper[27].

It remains unclear whether all regulatorily identified EDs will be restricted in revisions of relevant product specific EU regulation.

It is unsure whether ED hazard classes will be introduced in the global GHS system

Box 2. We have the scientific understanding of EDs and available tools —it is time to act

We have the understanding: ENKORE publications highlight that epidemiological studies report rising trends in endocrine-related disorders, while animal studies confirm similar effects after exposure to EDs.

Highlighted effects include:

- Reproductive cancers[7]
- Cognitive changes[7]

Reproductive disorders including:

- Impaired fertility[2,7]
- Genital malformations[7]
- Changes in puberty onset[2,7]
- Early menopause[2,7]
- Polycystic ovary syndrome[2]

Metabolic disorders such as:

- Obesity[3,6]
- Type 2 diabetes[3]
- Metabolic dysfunction-associated steatotic liver disease (MASLD)[3,4,6]

We have the tools: In the EU regulatory system, EDs can be identified and classified. Specific criteria are implemented in various pieces of legislation and guidance is available on how to do[5].

It is time to act to reduce exposure.

Overview of the ENKORE cluster

The ENKORE is a cluster of five research projects studying the health impacts of EDs and exploring ways to reduce our exposure to these chemicals. Through collaboration, the ENKORE cluster aims to increase the knowledge on health impacts of EDs, ultimately delivering benefits to society and vulnerable populations. In policy briefs and other communications, the cluster seeks to compile and integrate research findings of the cluster projects to highlight scientific uncertainties and science-policy gaps that need to be addressed and point out clear, actionable policy recommendations.

Projects in the ENKORE cluster:

EDC-MASLD

EDC-MASLD explores the role of EDs in the progression of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

edc-masld.eu

HYPIEND

HYPIEND studies the effects of EDs on the hypothalamus-pituitary axis during development stages, focusing on pregnant and breastfeeding women and children

hypiend.eu

NEMESIS

NEMESIS investigates how EDCs disrupt normal metabolic processes and lead to metabolic diseases.

nemesis-project.eu

ENDOMIX

ENDOMIX investigates how EDs target the immune system to cause disease, aiming to deliver new knowledge and recommendations

endomix.eu

Merlon

MERLON Improves knowledge on how ED exposure impacts reproductive health during critical life stages, and develops tools to better identify and regulate EDs

merlon.dtu.dk

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