CHEM Trust, European Environmental Bureau (EEB) and Health and Environment Alliance (HEAL) comments on REACH information requirements (CASG-IR-ED/04/2025)

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CHEM Trust, European Environmental Bureau (EEB) and Health and Environment Alliance (HEAL), thank the Commission for their proposals presented at the Joint Meeting of REACH and CLP Competent Authorities, Subgroups on Information Requirements and Endocrine Disruptors, on 18th of February 2025.

We have not yet received the full legal proposal, and this makes it difficult to give detailed suggestions without knowing the other foreseen changes to the annexes. Therefore, our comments are based on the documents sent out, the presentation given by the Commission at the meeting, and the summary received of the meeting (24.02.25).

For adequately answering the specific questions raised by the Commission in the briefing documents, it would be necessary to have a more detailed text proposal, including all other changes planned for the REACH annexes, including Annex XI. Therefore, we ask the Commission to accommodate an additional exchange or further round of written comments on the complete proposal for update of the information requirements.

Current REACH information requirements do not allow a sufficiently thorough hazard assessment, including for carcinogenicity, neurotoxicity, immunotoxicity and endocrine disruption. The lack of information occurs at all tonnage bands and is in particular significant for substances produced between 1-10 tpa. **In principle the information requirements should allow for hazard identification under CLP and a CSA at all tonnage levels.** The update of the REACH information requirements should ensure sufficient and appropriate information for self-classification by industry and for the authorities to allow the identification of endocrine disruptors as committed to in the CSS.

General comments

We strongly support the aim of updating the REACH information requirements, including for EDs, and also to allow REACH to better integrate the possibilities offered by New Approach Methodologies (NAMs) in the future.[1]

Closing information gaps should be one of the most important priorities for the REACH revision, as the information provides the basis for identification and subsequent control measures for an improved protection for human health and the environment. For a future integration of NAMs to be able to guarantee protection of human health and the environment, it will be necessary to reach agreement on taking regulatory conclusions for chemical hazard assessment based on different kinds of evidence compared to current requirements.[2]

[1] https://eeb.org/library/open-letter-need-to-update-reach-information-requirements/

[2] Chemical safety testing as part of a stronger REACH, protecting health and environment, promoting alternative methods, https://chemtrust.org/stronger-reach-alternative-methods/

- **Updating REACH information requirements has the purpose of closing data gaps which are currently preventing identification of harmful properties, as was found in the REACH REFIT review in 2018. Companies are currently still allowed to market chemicals without knowing whether they are EDs or not.**
- **To fully implement and gain the advantages of the new CLP hazard classes, it is absolutely necessary to obtain/generate more information on ED properties, so all actors are able to do adequate ED identification.**
- **We share the efforts to minimize animal testing without compromising the protection of human health and the environment, and we have also contributed to the Commission's roadmap process 'Towards Phasing Out Animal Testing for Chemical Safety Assessments'.[3] This is a long-term goal. But it is already possible to significantly reduce animal testing by doing more integrated assessments for human health and the environment, including the use of QSARs, read-across, grouping, and other NAMs.**

The new REACH information requirements for EDs will remain a combination of *in vitro*, *in vivo* and other methods for the identification of the inherent hazard properties of chemicals. In the future, more methods/tools will become available to partly complement, refine or replace the use of animal test methods. **Therefore, there is an urgent need to develop regulatory identification approaches based on *in-vitro* tests and other methods, such as systematic grouping and read-across. A transition to non-animal methods should, however, not lead to a decrease in the current protection level, and still, it would not be acceptable to leave dangerous substance properties unidentified. Regulatory acceptance of NAMs for the identification of EDs by authorities and industry will be key for a successful transition in the long run.**

Specific comments on the Commission proposal (documents and presentation)

We have **three main concerns** and some **additional comments** (under point 4)

1. Introducing Weight of Evidence as a first condition for further data generation creates uncertainty both for companies and the authorities. Instead, there needs to be a clear legal obligation to generate data in case no/little information is available and guidance on how to follow-up on ED concerns.
2. Some proposed waivers cannot be justified scientifically and create significant loopholes to avoid ED identification and therefore should be deleted.
3. It is problematic to deprioritize the identification of EDs for the environment, solely based on the availability of data that allow classification as Category 1 for human health – and without ensuring minimization of emissions to the environment and adequate protection of sensitive species in the environment.
4. Additional comments, including regarding effects on the thyroid hormonal system and non-EAS modalities.

[3] https://chemtrust.org/wp-content/uploads/Final-CHEM-Trust-on-Commission-roadmap-non-AT-Oct-2024.pdf

1) **Introduction of weight of evidence as a first condition for further data generation (Annex VII, slides 1-3)**

Introduction of a Weight of Evidence (WoE) approach as the first step to obtain information on adverse effects and as a condition for further data generation is a new approach for REACH standard information requirements. This proposal on EDs is puzzling, considering that the Commission has acknowledged in the REACH Review and the CSS that there is a gap of information on EDs that needs to be closed as these chemicals can lead to serious and irreversible effects. The need for information requirements for EDs reflects the current lack of data and therefore, a WoE approach as the determining parameter for further information requirements will not deliver meaningful results. The data from the compulsory battery of four *in vitro* assays will only provide information on the endocrine activity (i.e. interaction with the targeted receptor). However, adversity and activity are supposed to be assessed separately in the subsequent WoE. In reality, for most substances there will be hardly any data on adversity available. Therefore, we cannot support this approach as presented.

- A weight of evidence approach can only work if there is evidence. The proposed approach will lead to uncertainty and unpredictability instead of clarification and simplification. It will also overlook EDs, in case of false negative results of the *in vitro* tests or non-EAS modalities.
- How will the decision about a ´positive weight of evidence´ be taken? How is ECHA supposed to check if the WoE conclusion was justified? How can companies plan for delivering on the legal requirements when the work is dependent on an assessment with unclear outcome?
- The text needs to include clear legal obligations so that registrants know what they have to do, and that any indication of endocrine disrupting activity/effects needs to be followed up with either classification or further data generation. The lessons learnt from court cases in the past and BoA disputes between ECHA and registrants should inform and guide the drafting of the annex updates.
- The current REACH obligation for companies to compile all available information should be reinforced and we propose to introduce an obligation to conduct QSAR-modelling by using the OECD QSAR toolbox or the Danish QSAR database for different specified endpoints and endocrine modes of action, as well as read-across analysis which need to be considered in the conclusion.
- It would be important for the weight of evidence assessment to include information on thyroid and non-EAS activity.

2) **Column 2 adaptations (slides 4-5)**

- The adaptation proposed on slide 4 as regards the environment is commented under 3).
- The adaptation proposed on slide 5 is based on scientifically unjustified assumptions and cannot be supported. The long- biological half-life considerations introduce inappropriate exposure-based considerations; therefore, this fundamental issue will not be resolved in a guidance document. Further, it would also imply that substances with a short biological half-life but continuous exposure like bisphenols and phthalates would not require additional data generation, hindering their identification as EDs. In addition, the introduction of the term 'potent toxicity' is unclear and not appropriate here as the identification of inherent hazard properties does not include potency aspects. Furthermore, hormones and EDs often act very specifically in certain tissues and a focus on potency based on available data bears the risk that

effects in other tissues are overlooked.[4] Therefore, we do not support this waiver for human health, nor for the environment.

- In this context it would be important to see the proposed changes to Annex XI, so the general approach on adaptation and waiving options can be discussed together.

3) **Emissions to the environment need to be minimized via strict controls if testing for the environment is to be waived (slides 4-5)**

The adaptation proposed on slide 4 is contradictory (bullet 1 says that further testing for ED properties with regard to the ENV might still be required, and bullet 2 introduces a waiver for *in vivo* follow-up studies on ED for the ENV). This should be clarified.

The proposal foresees to waive the specific investigation for the ED environment for Annex VII substances in case the substance is classified as ED Cat. 1 for human health and if appropriate risk management measures (RMM) are implemented. This raises several issues:

- It is problematic to deprioritize the identification of EDs for the environment solely based on the availability of data that allows classification as Cat. 1 ED for human health. Fish, birds and amphibians may be more sensitive to endocrine disrupting effects compared to rodents and environmental emissions across sectors are not automatically stopped by the human health classification.

- Waiving of environmental testing should be allowed only if the substance is also classified **as ED Category 1 for the environment** based on the human health data set. In the supply chain communication the substance should be officially referred to also as an ED for the environment.

- How will it be ensured that the RMM would stop all uses leading to environmental releases? In our view the legal text should stipulate that that the substance can only be used under strictly controlled conditions, excluding all emissions into the environment. Usually a non-threshold approach is taken for EDs for the environment – as no safe threshold can be applied with sufficient certainty. Can we assume this approach would also be taken for RMM for human health EDs in view of the data gaps?

4) Additional specific comments

Introduction of 4 *in vitro* tests: These activity assays are important and necessary additions, since the ED definition includes evidence for endocrine activity. As they do not cover the metabolism, also measurements with metabolic activation are needed. We recommend to consider introducing High Throughput Screening instead of individual tests to save resources, as well as to use a more comprehensive battery of tests, including the recently endorsed OECD tests that would better inform the decision for further data generation.

Omission of information for effects on the thyroid hormonal system: We strongly recommend including at least a placeholder in the current text to prepare the inclusion of *in vitro* assays for several thyroid modes of action without further delay once they have been validated and endorsed by the

[4] https://www.env-health.org/infographic-more-than-one-potency/

OECD. In addition, it should be clearly stated that all indications of effects that may be related to the thyroid hormonal system should be thoroughly assessed and further investigated.

Omission of non-EAS modalities: The proposal neglects non-EAS modalities of endocrine disruption, including metabolic disorders like diabetes, obesity and non-alcoholic fatty liver disease and certain types of cancer. The legal text should reflect that all indications of effects that may be related to non-EAS modalities should be assessed and further investigated.

On Toxcast ER Bioactivity Model: The Toxcast ER Bioactivity model will only catch ED substances that interacts with the hormonal receptors which means it will not identify EDs acting via other modes of action. Further, many scientists and regulators have questioned whether Toxcast has been adequately validated. We also wonder about including information from this US database in an EU legal proposal, as it is currently unclear how Toxcast will be continued in the future. More importantly: it should be clearly stated that Toxcast results can only be relied on if they are positive, but not if they are negative. This is due to uncertainties, including in relation to applicability domain, and metabolism and validation issues.

On the Uterothrophic and Hershberger bioassays: These assays are not very sensitive. It must be emphasized that only positive results are to be relied on, and in case of negative results, a follow-up is needed to carefully evaluate whether this may be a false negative result considering the positive WoE, and whether other investigations should be carried out. It is not entirely clear to us whether a positive result in an *in vitro* assay should be followed up with the Uterothrophic/Hershberger assay. However, if this is the case, we would question why a positive *in vitro* result must be followed up with these *in vivo* mechanistic studies, which are quite insensitive. Maybe it would be more effective to use other tools/options to investigate bioavailability etc., and also applying read-across and grouping, before moving from positive *in vitro* test results to higher tier testing? This should be reconsidered.

Testing proposals: Based on the discussions during the meeting, we understand that testing proposals will be required for *in vivo* testing at all tonnage levels. This is a new element for Annex VII and VIII, what are the implications in terms of time and resources needed?

Enforcing the ED assessment: It would be important to provide clarity on timelines for the updates of the registration dossiers of company assessments.

Comprehensive testing strategies: Clarification is needed on testing strategy for the environment, for example on the need for further data generation in the hypothetical example that WoE and *in vitro* tests were positive, but FSDT test, Uterotrophic or Hershberger assays are negative.

Conclusion:

We strongly support updating the information requirements for the identification of EDs. However, the current proposal still leaves many open questions, uncertainties and loopholes (potential false-negatives, non-EATS modalities, WoE determination) which we hope can still be addressed. Acknowledging that some of the complex issues warrant more discussion, we also urge the Commission to support an overall EU test methods and validation strategy so that the regulatory uptake of test methods and discussion on regulatory decisions on different (and more predictive) evidence including from grouping, read-across and QSAR modelling will be addressed in a more systematic way.