April 2013

CHEM Trust & HEAL's view on the report of the ED Expert Advisory Group (ED EAG): *Key scientific issues relevant to the identification and characterisation of endocrine disrupting substances -*

http://ihcp.jrc.ec.europa.eu/our_activities/food-cons-prod/endocrine_disrupters/jrc-report-scientific-issues-identification-endocrine-disrupting-substances

General comments on context of the report and role of this group:

The report presents the results of the work of the Endocrine Disrupters Expert Advisory Group (ED EAG), which was set up in 2011 to provide advice on scientific criteria for the identification of endocrine disrupting substances. The Expert Advisory Group was designed as a sub-group to provide this advice to the Ad Hoc Group of Commission Services, EU Agencies and Member States under the Community Strategy for Endocrine Disruptors. The Ad Hoc Group works on the interface between Endocrine Disruptor science and EU chemicals policy and is intended to exchange information, combine ED science and policy, discuss horizontal aspects of ED regulation, and provide orientation to the Commission on development and implementation of EU policy on EDs. The Expert Advisory (sub) Group was composed of toxicologists and ecotoxicologists, nominated by Member State authorities, relevant industry associations and non-governmental health, consumer and environmental protection organisations as well as representatives from EFSA and ECHA.

The results will feed into the discussions on science and policy issues relating to the Community Strategy for Endocrine Disruptors (EDs) and the requirements in EU legislation to establish the criteria for the identification and assessment of EDs in the above mentioned Ad Hoc Group.

The EAG group met 5 times over 1.5 years and was set up as the main expert advisory group for input into the European Commission development of the EDC criteria. In contrast, EFSA

received their mandate in August 2012 and their report [1] "is of a specific nature and focused on food safety." (See EU Commission response to NGO letter[2] (8.1.2013).

Main comments:
CHEM Trust and HEAL are pleased that the experts reached almost unanimous agreement that potency does not play a part in the identification of an ED: The identification is comprised of the endocrine mode of action linked to an adverse effect.

CHEM Trust and HEAL both noted that another important issue in the identification of an endocrine disruptor is the level of proof that will be required to link the endocrine activity with the adverse effects. They stressed that the relevant EU legislation does not require full certainty in the link with adverse effect as the phrasing is "may cause adverse effect" (e.g. in the pesticides legislation).

They welcomed this expert group's acknowledgement that proof of causation might be too high a requirement in establishing a substance as an endocrine disrupter. However, it remains to be seen what data the regulators will consider sufficient and necessary to demonstrate what constitutes an ED.

Like the EFSA report the EAG report does acknowledge that existing tests may miss some effects that endocrine disruptors have, and that there is no current test which investigates early life/*in utero* exposure for effects which may appear in later life stages, such as cancer incidence, impact on menopause etc. CHEM Trust and HEAL highlight the need for both additional test methods and for adequate testing requirements in EU legislation in order to close the gaps which undermine the ability to currently identify EDs.

Important issues in more detail

Definition
The EAG report uses the WHO/IPCS definition as a starting point. However, the EU laws speak of "endocrine disrupting properties ….which may lead to adverse effects", i.e. requiring less burden of proof for regulating substances with endocrine disrupting properties. Thus CHEM Trust and HEAL are very concerned the burden of proof for identifying EDCs may end up being too high and too few relevant EDCs will be regulated. Moreover, we think it is wrong that the WHO/IPCS definitions for suspected and potential EDs were deleted from the report during in the final version.

[1] http://www.efsa.europa.eu/en/press/news/130320.htm
[2] http://www.env-health.org/policies/chemicals/letters-43/article/joint-ngo-letter-to-commissioners

Proof of causality

CHEM Trust and HEAL welcome that the expert group acknowledged that proof of causation might be too high a requirement in establishing a substance as an endocrine disrupter (section 2.5). However, it remains to be seen how much data will really be required to demonstrate a biologically plausible linkage between the activity of the chemical in producing the alteration of the endocrine system and the observed adverse effect. A lot of this will be left for a case by case evaluation and discussed further in the guidance development.

Scope of the ED system

CHEM Trust and HEAL support the conclusion that the EDs should not be limited to substances which disrupt the estrogen, androgen, or thyroid hormones, or those effecting steroidogenesis – the so called EATs pathways. Thus, we agree with that "the definition of the endocrine system must include the existing knowledge (EAT pathways and steroidogenesis), but must be relatively open and flexible in order to cover less known and newly or still to be discovered endocrine system elements in several taxa."

ED Identification

The report highlights that the decisive step, the identification of an endocrine disrupter, is only comprised of the endocrine mode of action linked to an adverse effect. Factors such as potency and lead toxicity are not part of the ED identification but rather factors to be used in priority setting for subsequent regulatory action.

Adversity

The issue of adversity is very tricky to resolve in general terms. While the IPCS/WHO definition is usefully relatively broad[3], the discussions in the report show that the interpretation varies a lot and can easily include value judgments instead of purely scientific issues. Importantly, it must clearly be established that EDC effects cannot be equated with traditional toxicological testing "adversity", where for example weight loss is considered an adverse effect, a gain in weight on the other hand is not.

We concur with the Endocrine Society which has emphasized that the ability of a chemical to interfere with hormone action is a reliable predictor of adverse outcomes.

Relevance for humans/ Relevance for wildlife

We agree that assuming relevance for humans from studies in mammalian animals should always be the default. Only when non relevance for humans can be conclusively proven should this not apply. However, we are still concerned that this can and may be abused, and bogus arguments that findings in animals are not relevant for humans can take up the regulators' time and resources to evaluate, and might be accepted .

[3] WHO/IPCS definition of adverse effect: "Change in the morphology, physiology, growth, development, reproduction, or, life span of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other influences.

Factors relevant for the characterization of ED
CHEM Trust and HEAL agree that in the context of a human health assessment factors such as severity and irreversibility of the observed effect as well as lead toxicity and potency may provide useful additional information for a prioritization of the identified EDs. For the ecotoxicological assessment these factors play a minor role.

No risk assessment for identified EDs under PPPR and BPR
The report rightly states on page 18 that no risk assessment is carried out for identified EDs under PPPR and BPR (the EU's laws on pesticides and biocides).

Use of non-GLP data
CHEM Trust agrees with the need to adequately consider non-guideline studies, as stated on page 22:

"Nevertheless, it was proposed that non-guideline data (e.g. from academic laboratories) following good scientific principles in design, conduct and reporting and employing appropriate statistics, should be judged on their scientific merit and not automatically considered of lower quality to a Test Guideline conducted by a GLP accredited facility".

Need for new test methods to enable ED identification
CHEM Trust and HEAL welcome that the report acknowledges that existing tests may miss some effects that endocrine disruptors have, and that there is no current test which investigates early life/*in utero* exposure for effects which may appear in later life stages, such as cancer incidence, impact on menopause etc. We do stress the urgent need for both additional test methods and for adequate testing requirements in EU legislation in order to close the gaps which undermine the ability of identifying EDs.

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