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AmCham EU general position on the need for thresholds to regulate endocrine disruptors

POSITION STATEMENT

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The American Chamber of Commerce to the EU (AmCham EU) welcomes the opportunity to provide input into the ongoing debate on whether thresholds could be determined for endocrine disruptors (hereafter EDs) in the context of the REACH review.

As an introductory remark, we fully support a science-based approach to legislation and were pleased to read the conclusions of the 29-30 May Competitiveness Council that reinforce the need for evidence-based regulations 'by means of a robust impact assessment'. We believe that the current discussion on thresholds has many ramifications and a very broad impact on EU industry and, therefore, requires a thorough impact assessment.

AmCham EU would like to share the following comments relevant to the questions raised in the 'thought starter on endocrine disruptors'.

A threshold as used in toxicology is the dose or exposure level at and below which no adverse effects are observed. Different substances have different thresholds and dose response curves based on differing effects depending upon their toxicological profile. Potency, threshold and dose response are key toxicological principles that are taken into consideration by agencies/regulators throughout the world to regulate chemical substances.

By definition, non-threshold effects are assumed to occur at any level of exposure to the substance. Whether the effect occurs is a function of probability, and although the probability will decrease as the level of exposure decreases, it is assumed that there is no level of exposure for which the probability is zero. Assessment of substances whose hazard action is assumed not to have a threshold requires a careful evaluation of the available information, including results from *in vitro* and *in vivo* biological assays and valid predictive SAR estimates, to determine the weight of evidence supporting the hypothesis that there is no mitigation possible for the adverse effect.

Compensatory mechanisms do exist to mitigate the adverse effects of the vast majority of substances suggested as being endocrine disruptive due to the very presence of systems for metabolic detoxification, physiological homeostasis, and cellular adaptation and repair. We request that, as for any other hazard endpoint, identification and classification of the hazard properties of substances suggested as being endocrine disruptive be made on a case-by-case basis.

We draw attention to the definition of an endocrine disrupter as suggested by the WHO/ICPS as 'an exogenous substance or mixture that alters function(s) of the endocrine system **and consequently causes adverse health effects**'. Indeed all substances entering the body are capable of inducing a plethora of alterations in a multitude of possible pathways (whether they have been consumed as food, taken as medication or absorbed unintentionally), thus all could be classified as endocrine disruptors unless the criteria of 'causing an adverse effect' is applied. If an adverse effect (rather than an alteration in one endpoint) is identified, then a given substance should be classified – in the same manner as for any other toxicological endpoint.

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The concept of alteration of physiological responses (as opposed to adverse outcome) is noted on page 6 of the thought starter in quoting the WHO/UNEP 2013 report that states:

> …these non-linear dose responses can be quite complex and often include non-monotonic dose responses. They can be due to a variety of mechanisms; because endogenous hormone levels fluctuate, no threshold can be assumed…

The body's natural method of metabolising substances is indeed via this 'variety of mechanisms'. It is not logical to then presume that the addition of a single molecule of a substance (non-threshold), in the presence of this highly functioning interactive system, would result in an adverse health effect.

Chemicals showing effects on hormone-receptor mediated endpoints require a certain dose to overcome the normal homeostatic mechanisms that regulate routine hormone functioning. **Applying a threshold assessment approach and using uncertainty factors (just as for other toxicological endpoints) can provide appropriate protection**.

Most EDs are far less potent in producing effects than natural hormones. Again the dose effect is key in defining their impact on health and the environment.

While we recognize that a case by case approach may entail additional substance-specific testing, we believe that it is the most appropriate route to evaluate and regulate EDs. The same principles of weight of evidence and read-across that have been successfully used in avoiding unnecessary testing for other toxicological endpoints should be applied.

The impact of adopting a no-threshold approach to EDs and their subsequent listing on the Substances of Very High Concern (SVHC) list will be a de facto phase–out of substances, as there is broad recognition that the Candidate List of SVHC can be considered a black list.

A no-threshold approach applied *a priori* to all endocrine disruptors would have implications that would go far beyond the REACH authorisation process. It would have implications not only for consumer products and the exposure of consumers, but also for any kind of manufacturing in Europe. For example, the whole body of EU worker protection legislation is based on reducing workers' exposure to hazardous chemicals to a threshold that is acceptable and does not lead to adverse effects.

Should a no-threshold approach be adopted *a priori* for all EDs, this would mean that for many substances unnecessarily stringent control and elimination of traces of substances would be required at all stages of the manufacturing, transportation or waste phase of a product. Such an approach would have major implications for these substances with little or no health and environmental benefit.

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The DG Environment list of potential endocrine substances for further evaluation (developed by BKH Consultants several years ago) includes many major commodity substances used in a wide variety of applications and sectors, bringing a wide range of benefits to EU society (including sustainability benefits). **If non-robust criteria and a non-threshold approach are applied *a priori* to identifying EDs on this list for regulatory action, then many substances will be captured which can and are being used safely based on risk assessment**.

Use of non-robust criteria and a non-threshold approach for EDs will therefore have a major impact on these substances, the chemical sector and the downstream user sectors with no benefit for health and the environment. The major commodity chemicals on the list have been developed through significant investment in all aspects of research, technology, manufacturing, distribution and applications with downstream users, over a period of decades. It is estimated that this has involved hundreds of billions of Euros of investment and impacts several million jobs in the EU economy. In addition to the potential impact on existing investments and employment, the uncertainty created will also impact new investment and innovation within the EU. The net impact would be to displace investment in the chemical industry, in new substances and downstream applications to countries outside the EU, with the associated impact for EU employment and the economy.

Based on the above AmCham EU urges the European Commission to ensure:

- That the criteria for identifying EDs are based on a robust scientific approach;
- That the evaluation of chemicals for ED properties is performed on a substance-by-substance basis; and
- That the categorisation as having a threshold or non-threshold mechanism of action be unique to each ED substance.

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AmCham EU speaks for American companies committed to Europe on trade, investment and competitiveness issues. It aims to ensure a growth-orientated business and investment climate in Europe. AmCham EU facilitates the resolution of transatlantic issues that impact business and plays a role in creating better understanding of EU and US positions on business matters. Aggregate US investment in Europe totalled €1.9 trillion in 2012 and directly supports more than 4.2 million jobs in Europe.

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