PETROVA Nevyana (ENV)

From: HANSEN Bjorn (ENV)
Sent: 29 January 2013 18:04
To: Broun, Caroline N (USEU)
Cc: KORYTAR Peter (ENV)
Subject: RE: Endocrine Disruptors - interested in some EU perspective
Attachments: ED_AD-hoc-5_2012_04_Possible elements for the criteria for EDs.doc

Dear Caroline,

Peter (in copy) is the lead person on EDs in the Commission. I too would be very interested to meet with you on EDs (and other chemicals issues you may wish to raise), but my availability should not be an obstacle!

For your information I attach a thought starter for elements of criteria which we have discussed late last year with MSs and stakeholders which should give an indication of where we are in our debates and which difficulties we are having.

Greetings,

Bjorn

From: Broun, Caroline N (USEU) [mailto:BrounCN@state.gov]
Sent: Tuesday, January 29, 2013 4:00 PM
To: HANSEN Bjorn (ENV)
Subject: Endocrine Disruptors - interested in some EU perspective

Hi Bjorn:

We have corresponded, but I don't believe we have had a chance to meet, yet. I am the Environment officer at the US Mission to the EU. One of the issues we are looking at, as is the EU, are the endocrine disruptors.

I would like a chance to chat with the person with this portfolio at DG ENV to understand where the EU is on regulating these substances. I did attend the workshop last year, which was very interesting.

Would you or someone from your staff have time to meet? thanks

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SBU
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EUROPEAN COMMISSION
DIRECTORATE-GENERAL
ENVIRONMENT
Directorate D - Water, Marine Environment & Chemicals
ENV.D.3 – Chemicals, Biocides and Nanomaterials

Brussels, 22 November 2012
ED-AD-HOC-5/2012/04

THE COMMUNITY STRATEGY FOR ENDOCRINE DISRUPTORS

5TH AD HOC MEETING OF

COMMISSION SERVICES, EU AGENCIES AND MEMBER STATES

Centre de Conférence A. Borschette, room 4B, rue Froissart 36, Brussels
30 November 2012 (10:00 – 17:30)

Concerns: **Initial thoughts on the criteria for endocrine disruptors**

Agenda Point: **4**

Action Requested: **This paper sets out possible elements for the definition, identification and categorisation of Endocrine Disruptors (EDs) based on the discussions which have so far taken place in the Expert Group and the Ad-hoc Group. This document was developed by DG ENV for the 4th meeting of the expert advisory group to better steer and frame discussions at that meeting. The members of the expert group were asked to provide their comments which are summarised in the separate document.**

During the ad-hoc meeting the possible elements for the horizontal criteria for EDs as currently considered by DG ENV will be presented and the ad-hoc group may wish to provide comments (from the policy perspective).

The participants to the meeting are invited to:

- take note of this document

- provide comments (from the policy perspective)

Possible Elements for Criteria for Identification of Endocrine Disruptors

1. Definition

An *endocrine disruptor* is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations. (WHO/IPCS)

A *suspected endocrine disruptor* is an exogenous substance or mixture that may alter function(s) of the endocrine system and consequently may cause adverse health effects in an intact organism, or its progeny, or (sub)populations. (DK)

A *potential endocrine disruptor* is an exogenous substance or mixture that possesses properties that might be expected to lead to endocrine disruption in an intact organism, or its progeny, or (sub)populations. (WHO/IPCS)

2. Categories of Endocrine Disruptors

For the purpose of categorisation of endocrine disruptors, substances are allocated to one of three categories based on [weight of evidence] / [level of evidence] / [strength of evidence and additional considerations (weight of evidence)].

Categories for endocrine disruptors

- Category 1: Known or presumed endocrine disruptors
    - Category 1a: Known endocrine disruptors
    - Category 1b: Presumed endocrine disruptors
- Category 2: Suspected endocrine disruptors
- Category 3: Potential endocrine disruptors

3. Criteria for Placing Substances in Categories

<u>Category 1 – Known or presumed endocrine disruptors</u>

Substances are placed in category 1 when they are known to have caused ED mediated adverse effects in humans or [animal species living in the environment] / [population relevant effects on animal species living in the environment] / [ecosystem relevant adverse effects] or when there is evidence from [animal studies] / [experimental animal studies], possibly supplemented with other information, to provide a strong presumption that the substance has the capacity to cause ED mediated adverse effects in humans or [animals living in the environment] / [population relevant effects on animal species living in the environment] / [ecosystem relevant adverse effects].

The [animal studies] / [experimental animal studies] shall provide clear evidence of ED-mediated adverse effects in the absence of other toxic effects, or if occurring together with other toxic effects,

the ED-mediated adverse effects should be considered not to be a secondary non-specific consequence of other toxic effects. However, when there is e.g. mechanistic information that raises doubt about the relevance of the effect for humans or [animal species living in the environment] / [population of animal species living in the environment], category 2 may be more appropriate.

Category 1 is further divided into two sub-categories on the basis of whether the evidence for classification is primarily from human data or data from [animals living in the environment] / [field studies] (Category 1A – Known Endocrine Disruptors) or from [laboratory animal studies] / [experimental animal studies] (Category 1B – Presumed Endocrine Disruptors).

Substances can be allocated to the sub-category 1A based on evidence from humans or from [animal species living in the environment] / [field studies] where it is plausible that the observed adverse effect is ED-mediated.

Substances can be allocated to the sub-category 1B based on:

- [Animal studies] / [experimental animal studies] where it is plausible that the observed adverse effects are caused by an ED mode of action
- [Animal studies] / [experimental animal studies] showing an ED activity *in vivo* which is clearly linked to adverse effects *in vivo* (e.g. through read-across)

Category 2 – Suspected endocrine disruptors

Substances are placed in category 2 when there is some evidence for ED mediated effects from humans or experimental animals, and where the evidence is not sufficiently convincing to place the substance in category 1. If, for example, limitations in the study (or studies) make the quality of evidence less convincing, category 2 could be more appropriate. Such effects should be observed in the absence of other toxic effects, or if occurring together with other toxic effects, the ED mediated effect should be considered not to be a secondary non-specific consequence of other toxic effects.

Substances can be allocated to this category based on:

- Experimental animal studies where it is suspected that the observed adverse effects are caused by an ED mode of action
- Experimental animal studies showing endocrine activity *in vivo* which is suspected to be linked to adverse affects *in vivo* (e.g. through read-across)
- *in vitro* studies showing endocrine activity, combined with toxicokinetic *in vivo* data which is suspected to be linked to adverse effects *in vivo* (e.g. through read-across, chemical categorisation and QSAR predictions).

Category 3 – Potential endocrine disruptors

Substances are placed in Category 3 when there is some *in vitro/in silico* evidence indicating a potential for endocrine disruption mediated adverse effects in intact organisms and where the evidence is not sufficiently convincing to place the substance in category 1 or 2.

The evidence could also be observed effects *in vivo* where there is general but not specific evidence relating those to ED mediated adverse effects (i.e. that may, or may not, be ED-mediated).

4. Further issues for consideration to be part of the criteria

4.1 Endocrine system

Should the endocrine system be defined and if so, what definition should be used?

Human health

Option 1: In humans, endocrine glands include the pituitary, thyroid, adrenal glands and gonads, and parts of the kidney, liver and heart. The three important endocrine axes are the Hypothalamus-pituitary-gonad (HPG) axis, Hypothalamus-pituitary-adrenal (HPA) axis, Hypothalamus-pituitary-thyroid (HPT) axis. These axes describe the boundaries within which the endocrine system and endocrine disruption have been confined from the perspective of classical endocrinology.

Option 2: Signalling pathways considered under OECD DRP ENV/JM/MONO(2012)23: Hypothalamus-pituitary-adrenal (HPA) axis, Hypothalamus-pituitary-gonad (HPG) axis, Hypothalamus-pituitary-thyroid (HPT) axis, Somatotropic axis, Retinoid signalling pathway, Vitamin D signalling pathway, Peroxisome proliferator-activated receptor (PPAR) signalling pathway, epigenomic regulatory mechanisms

Option 3: Any type of receptor-mediated signalling pathway

Option 4: Does any general definition exists for endocrine system in humans (e.g. in endocrinology)?

Environment:

Does any suitable definition exist for endocrine system across all animal species?

4.2 Route of exposure

Should the route of exposure be specified in the definition, categories, criteria or possibly guidance?

Human health and environment

Option 1: Any route of exposure is relevant

Option 2: Only physiological routes of exposure are considered relevant

4.3 Adversity

Should adversity be defined in greater detail in the definition, categories, criteria or possibly guidance?

Human health

Option 1: No specific consideration

Option 2: A change in morphology, physiology, growth, reproduction, development or lifespan of an organism which results in impairment of functional capacity or impairment of capacity to compensate for additional stress or increased susceptibility to the harmful effects of other environmental influences. (WHO/IPCS)

Option 3: More detailed description

Environment

Adverse effect should be observed or presumed at the population level.

4.4 Mode of action

Should the mode of action be elaborated or better defined in the definition, categories, criteria or possibly guidance?

4.5 Proof of causality

Does what we mean with causality need to be elaborated further?

4.6 Data

Categorisation of a substance as an endocrine disruptor is made on the basis of evidence from reliable and acceptable studies. The evaluations shall be based on all existing data, peer-reviewed published studies and additional acceptable data.

4.7 Potency

Option 1: No potency consideration

Option 2: Potency cut-off

Option 3: Potency as part of weight of evidence

4.8 Lead toxicity

Should the consideration of the lead toxicity be included?

4.9 Severity

Should the consideration of severity be included?

4.10 Irreversibility

Should the consideration of irreversibility be included?

4.11 Specificity

Should the consideration of specificity be included?

4.12 Step by step procedure

1. Gather all available data
2. Consider adversity and mode of action in parallel
3. Evaluate human and wildlife relevance

4. Final (eco)toxicological evaluation, classification and categorisation