PETROVA Nevyana (ENV)

From: HANSEN Bjorn (ENV)
Sent: 16 November 2012 15:34
To: KORYTAR Peter (ENV)
Subject: FW: Endocrine Disruptors - meeting request
Attachments: PlasticsEurope View Paper on Endocrine Disruption Nov 2012.pdf

Up to you to arrange a meeting – if possible I would like to be there too.

Bjorn

From: [redacted] [mailto:M[redacted]@plasticseurope.org]
Sent: Friday, November 16, 2012 3:08 PM
To: HANSEN Bjorn (ENV)
Cc: [redacted]@plasticseurope.org
Subject: Endocrine Disruptors - meeting request

Dear Mr. Hansen,

we in the Plastics industry, as part of the chemical industry, are very much engaged in the current debate on endocrine disruptors. We understand that the Commission's updated strategy will be released early next year, together with proposed criteria for identifying endocrine disruptors. Cefic has shared with us the document presenting the *Possible Elements for Criteria for Identification of Endocrine Disruptors* which we considered thoroughly.

The identification of endocrine disruptors raising concerns is a challenging task, both at scientific and regulatory level. The Plastics industry has invested considerable resources in this field and gathered quite some knowledge. We would therefore very much like to share with you our views on the proposed categorisation and its potential implementation within current regulatory frameworks such as REACH.

We are happy to make ourselves available at your convenience.

Meanwhile, you can find attached to this mail the Plastics Industry's View Paper on Endocrine Disruptors.

Best wishes

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View Paper on Endocrine Disruptors

November 2012

Key Messages:

1. Understanding science is key
Just because a substance interacts with the hormonal system does not mean it is an endocrine disruptor. This requires an adverse effect caused by the substance via the hormonal system.

2. Risk-based regulation should focus on potency and exposure
To identify endocrine disruptors of regulatory concern from those which present no actual risk, potency of the substance and how much humans and the environment are/can be exposed to is key.

3. Need for responsible risk communication
Contradictory and imprecise information about certain risks unnecessarily increases the emotional risk perception of the public. Therefore, we urge all scientists and authorities to communicate accurately and scientifically about endocrine disruptors.

Introduction

Who hasn't read an article or watched a documentary on endocrine disruption lately? Who hasn't heard stories about chemicals reportedly linked to, for instance, decrease in sperm counts?
Endocrine disruption has received growing attention over the past years and is now very high on the political agenda in Europe. A lot of questions as well as concerns are raised; including by media whose headlines are often quite alarming: Obesity, precocious puberty, diabetes, decreases in male fertility, lower IQ, behavioural changes ...

Endocrine disruption is a complex issue which deserves an honest and constructive debate.

The plastics industry is fully committed to the safe use of its products and therefore considers questions and concerns very carefully. In this matter, understanding science is key and the investment in testing and research is considerable (e.g. Cefic LRI-EMSG 56: Combined Low-dose Exposures to Anti-androgenic Substances).
Also, endocrine disruption cannot be tackled if not put in a broader perspective. Indeed, the endocrine system maintains a balance in the body by responding and adapting to (changing) environmental conditions. Therefore, all distinctive aspects of our lifestyle which eventually impact on these conditions - e.g. eating & drinking habits, smoking habits, lack of exercise, late pregnancy, etc - must be taken into consideration in a holistic approach.

Finally, one should not forget that living conditions have greatly improved over the past decades and continue to improve, to a large extent thanks to chemicals in general and plastics in particular. Food conservation and preservation, clean water, modern health care, sustainable transport solutions, to name but a few; none of these would be possible without the benefits brought by plastics.

Legislative and regulatory responses must fit this complexity; i.e. result in targeting actual problematic substances rather than spread undue concerns on numerous safe and beneficial products. Such outcome is possible on the condition that legislation relies on solid data and proven facts.

1. Understanding science: What is an endocrine disruptor?

The human body is a place of constant endocrine activity: the body naturally secretes hormones such as testosterone (sex hormone) or adrenaline (stress hormone); while at the same time being exposed to natural or man-made hormones and hormone-like substances such as caffeine, contraceptive drugs or specific synthetic chemicals.
Endocrine active substances are part of our daily life and not all - including synthetic chemicals which have drawn most attention in this debate - should be confused with endocrine disrupting substances that have adverse effects.

What is the difference between an endocrine active substance and an endocrine disruptor?

The World Health Organisation (WHO) defines an endocrine disruptor as a *"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 2002)

According to this internationally agreed definition, it is the occurrence of adverse health effects caused by the interaction of the substance with the hormonal system (i.e. endocrine mode of action) which indicate disruption.

There are then three characteristics to be taken into consideration:

- **Adverse health effects in intact organism**: The occurrence of an effect does not equal health hazard. The adversity of the effect must be identified; i.e. there must be 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)

- **Endocrine mode of action**: the adverse effect must be directly induced by an alteration of the endocrine system.

- **A causal link between both**: the simultaneity of the presence of a chemical and the occurrence of an adverse effect does not mean the former causes the latter or that the adverse effect has been triggered via an endocrine mode of action. A causal link must be identified. It has to be demonstrated that the chemical being evaluated is the trigger for the effect.

PlasticsEurope supports the WHO definitions because it provides clear, objective and scientifically based characteristics. However, this definition alone is insufficient to identify which substances should be regulated due to their endocrine disruptive activity.
The occurrence of adverse effects shows only the **hazard** (potential source of danger) of a substance but the definition says nothing about the conditions under which the hazard would

actually occur; i.e. the **risk whose analysis requires both a hazard and an exposure assessment**.
The consideration of risk is indeed crucial because it enables the identification of substances which would have an endocrine adverse effect in the organism exposed to real-life concentrations; substances one could call endocrine disruptors of regulatory concern.

2. Assessing the risk: What is an endocrine disruptor of concern?

The identification - in a laboratory - of a substance with intrinsic endocrine properties causing adverse health effects does not necessarily mean that endocrine disruption would actually occur. It does not mean that the substance has to be considered of concern and regulated as such.
For two reasons:

- **Not all endocrine disruptors have the same potential for endocrine disruption**

Endocrine disruptors are not all the same and cannot be treated in the same manner. Some have a high endocrine potency; i.e. high potential for endocrine activity, while others have only a weak potency.
Let's draw a parallel with bikes and motorcycles to make the distinction clearer: both have two wheels and are used as modes of transport. However, because their potential for harm in case of accidents differs very much, different rules apply. Contrary to bikes, motorcycles must be insured and registered. It is the same logic with substances qualifying as endocrine disruptors according to the WHO definition. They all are endocrine disruptors but their "likelihood" for endocrine disruption differs.

In the case of high endocrine potency, the substance triggers adverse effects at rather low doses and regulatory risk management measures may be necessary if there is relevant exposure. *Estradiol* (natural sex hormone), for instance, is one of the most potent natural hormone.
In the case of weak endocrine activity on the contrary, adverse effects due to changes in endocrine function would only be seen at doses no organism would be exposed to in 'real life'. Caffeine is a good example in this regard as it has a weak endocrine activity but presents no risk at doses people typically consume.

It is therefore crucial to distinguish amongst endocrine disruptors.

- **Humans or organisms in the environment are not necessarily exposed to levels of concern**

Once chemicals highly potent endocrine disruptors have been identified, exposure to such chemicals must be evaluated in order to determine whether people or the environment are exposed to levels of concern in real life.
This is a very important step. While laboratory studies might suggest that chemicals could interact with the endocrine system and cause adverse effects, exposure assessment indicates whether such adverse effects would actually happen. Indeed they may never occur under real-life conditions.
The key is therefore to define the safety threshold below which no adverse effects are observed and make sure that exposure to levels above do not occur via uses which are made of the substance.

The regulatory response to endocrine disruptive chemicals must therefore consider potency and exposure as key criteria. Otherwise, day-to-day products such as caffeine or soybeans, both of which are known for their endocrine activity could be considered as endocrine

disruptors of regulatory concern even though they pose no risk to human health at doses we consume.

3. It is the dose that makes the difference.

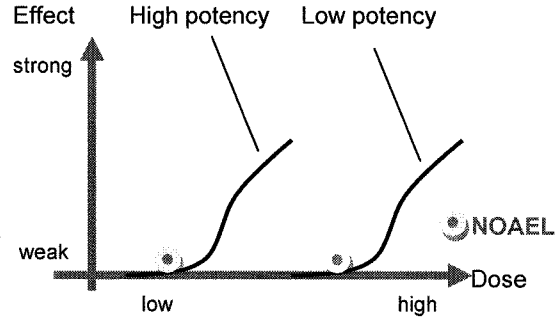
Certain natural substances present in the diet (e.g. soybeans, carrots, coffee, red wine, hops, etc.) can interact with the endocrine system but would only cause adverse effects at doses that are never reached in real life. Below these doses, these products can be consumed without concern. The same applies for synthetic substances which have similar effects: for these substances, the acceptable daily intake (= safe dose) is set far below the level at which any effect can be measured.

These principles - and the consideration for potency and exposure which follows - are challenged by some scientists who claim that endocrine disruptors should be treated differently because they would show adverse effects at very low doses (the *Low Dose* hypothesis), even far below the so-called No Observed Adverse Effect Level (NOAEL).
It would then be impossible to set a limit - a safety threshold - below which an endocrine active substance can be considered safe.

The *"Low Dose" hypothesis* has become a focal point in the Endocrine Disruption debate and has led to much controversy, both at the scientific and the political level.

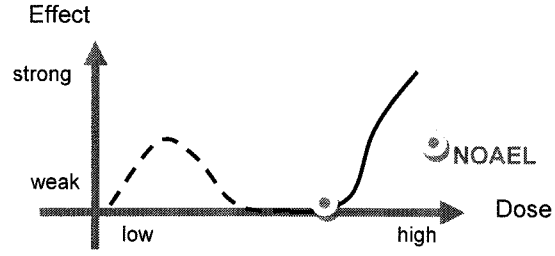
In toxicology, one defines the level at which a substance does not produce adverse effect and calls it the No Observed Adverse Effect Level (NOAEL). At this concentration, the substance does not produce a harmful effect.
Based on indicators such as the NOAEL, a safety threshold; i.e. an acceptable daily intake, is set.
Due to their high potency, some substances can show adverse effects at low levels. This is a well-known fact that does not challenge the relevance of the well-established dose-response approach. However, it does means that the NOAEL can sometimes be very low with the corresponding threshold being even lower.

1. Dose-Response curves



Some scientists claim on the contrary that there are no thresholds below which an endocrine active substance can be considered safe because it could cause (adverse) effects at some point below the NOAEL while, in between, no effect would be observed.
Should this hypothesis be verified, it would become impossible to set a safety threshold and all endocrine active substances would become of regulatory concern.

2. "Low Dose" hypothesis



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The endocrine system responds to many different factors as part of its normal functioning. Changes happen constantly and it is important to differentiate between a temporary adjustment of the endocrine system and a disruption causing adverse effects. The fact that - in some cases - adverse effects occur at rather low level does not mean that a safety threshold cannot be set. It means that for these chemicals, adversity must be carefully assessed and the threshold correspondingly low.

Despite years of research to prove the opposite, there is no real-life proof demonstrating the validity of the *"Low Dose"* hypothesis. Results of exploratory studies that reported so called low dose effects could not be reproduced or confirmed by more comprehensive studies.
Data gathered so far remain inconsistent and often lack statistical significance: for example, studies have been conducted at such a small scale (using a very limited number of animals or cells) that in fact no valid conclusions can be drawn from these.

Regulation cannot be based on a hypothesis with no basis of solid proof. Doing further research is a logical approach but one should keep in mind that it is still a theory whose validity has not been verified.

4. Management of endocrine disruptors: A consistent approach

If a substance of regulatory concern is identified, then appropriate measures can be applied through existing legislation.
The European Union has already extensive Regulatory Frameworks governing chemicals. Legislations such as REACH, the Plant Protection Products and the Food Contact Regulation or the Toys directive provide an arsenal of technical guidance and potential measures (from targeted restrictions to total bans) that can and should be applied to substances which will eventually be identified as endocrine disruptors of concern based on the assessment process the EU will define.

It is important that already existing regulations apply the same approach for identifying endocrine disruptors. Risk management measures may vary from one to another but the same definition and criteria should be applied when it comes to the identification of endocrine disruptors of concern.

Concluding remarks

The complexity of endocrine disruption, both in terms of science and policy, is challenging. If one is interested in developing solutions which will effectively improve the protection of human and the environment, such debate cannot be separated from a broader consideration of our life style in general and must rely on sensible science.

The Plastics industry is ready to cooperate with policy makers on setting science-based criteria to identify and manage endocrine disruptors of regulatory concern.

We urge regulators in Brussels and in all Member States to develop a regulatory framework that targets substances of actual regulatory concern and avoid jeopardizing the manufacture of substances which present no risk for people or the environment.

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