European Crop Protection

BRIEFING PAPER
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ECPA View on Endocrine Disruptors

On 15 June 2016 the European Commission published its draft proposal **for criteria for** ***endocrine disrupting properties,*** **for both** the Pesticides Regulation 1107/2009 (on plant protection products), and the Biocides Regulation 528/2012. Once the final criteria are adopted the Commission may consider applying similar or identical criteria to General Chemicals (REACH) and Cosmetics.

The goal we all share is to safeguard human health and the environment and to ensure a high level of protection for both. However, the way the final criteria are defined could have profound consequences for the agricultural sector, the availability of safe food, and international trade. It is essential that the final criteria continue to maintain high levels of protection while ensuring European farmers continue to have access to essential crop protection products.

The Commissions draft proposal, related impact assessment and overall communication can be found at this link: http://ec.europa.eu/health/endocrine_disruptors/policy/index_en.htm

Key Messages

- **ECPA strongly opposes the Commission's proposal in its current form.** The proposal fails to take into account all available and relevant scientific evidence, including potency, when evaluating a substance for its potential endocrine-disrupting properties.
- **The proposal for the criteria is based almost solely on the WHO/IPCS definition which by itself does not provide criteria suitable to support regulatory decision making.** Many substances, both natural (e.g. caffeine) and synthetic, which present little or no risk, would be "identified" as endocrine disruptors by using the WHO/IPCS definition (e.g. iodine (wound disinfectant) will be identified as an endocrine disruptor under the proposal but would not be if potency was taken into account). For the purposes of regulatory decision making it is essential that regulators be provided with the necessary tools to separate out those substances which pose a real concern, from those that don't.
- **The criteria must incorporate all elements of hazard characterisation, including potency, severity and lead toxicity.** Hazard characterisation is an essential step in hazard assessment. The strength of a substance (its **potency**) and the levels to which humans and the environment come in contact with it (**exposure**) are key determinants as to whether a substance will actually cause adverse effects and lead to harm.
- **Questions have been raised regarding the potential impact of exposure to chemicals on human health,** for example on the incidences of certain endocrine related human diseases such as some hormonal cancers. Incidences of disease are influenced by many factors, such as age, and lifestyle choices. Changes in disease rates may also reflect improvements in screening and diagnosis (e.g. prostate cancer screening).
- In a comprehensive review commissioned by EFSA[1] on pesticides and health, the authors found **no evidence of an association between pesticide exposure and hormonal related cancers**. In fact, the most consistent finding in large epidemiological studies on agricultural communities (e.g. Agrican study in

[1] http://www.efsa.europa.eu/en/supporting/pub/497e.htm

France[2]), **is that farmers, the group most exposed to pesticides, are healthier than the general population.** Here, farmers have lower mortality and lower incidences of almost all cancer related illness. These findings underline the effectiveness of the regulatory framework in place for pesticides, a point highlighted in the Commission's own impact assessment on the criteria for endocrine disruptors.

- **The Commission's Impact Assessment, concludes that all options under consideration offer the same high level of protection for human health and the environment.** However, Option 2 and 3 were assessed as having the highest impact on sectorial competitiveness, agriculture and trade. Therefore, we fail to understand why the Commission has selected Option 2, the option that will have the greatest impact on the availability of products for farmers,[3] is not in line with the Commission's own political commitment to better regulation and the principle of proportionality, and would fail to meet the EU commitments with WTO, established under the SPS Agreement.
- **Furthermore, the impact assessment highlights the potential risk of resistance development in pests.** The loss of some critical chemical classes due to the proposed criteria could result in pest, weed and disease resistance with many unintended and potentially dangerous consequences for food safety, and would further reduce the size of the farmer's toolbox.
- The Commission has proposed certain derogations for substances triggering the hazard based approval criteria, by considering some elements of risk and exposure. **Relying entirely on regulation by derogation signals a fundamental flaw in the basic regulation.** Our first priority is to have in place the right criteria. Regulating substances based on risk assessment provides a more predictable framework and better supports product development and innovation.
- **The Commission must adopt workable, proportionate and science based criteria for endocrine disrupting properties which maintain the existing high levels of protection for human health and the environment,** and ensure regulators have the necessary tools to make informed regulatory decisions.
- **It is our firm view that endocrine disruptors can and must be regulated like most other substances of potential concern and be subject to risk assessment which considers both hazard and exposure.** This is the conclusion of the EFSA Scientific Committee[4], and the Scientific Committee on Consumer Safety (SCCS)[5].

2 AGRICAN - Étude Agrican - Centre François Baclesse, University of Caen, France, http://cancerspreventions.fr/

[3] While more substances are impacted by option 1, page 295 of the IA concludes that more commercial products would be impacted by the application of option 2.

[4] "Scientific Opinion on the hazard assessment of endocrine disruptors: Scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment", EFSA Journal 2013;11(3):3132, doi: 10.2903/j.efsa.2013.3132.

[5] Scientific Committee on Consumer Safety (SCCS) Memorandum on Endocrine Disruptors. Retrieved from: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_009.pdf.

Background and Timeline

Under the Plant Protection Products Regulation 1107/2009[6] (Pesticides) and the Biocidal Products Regulation 528/2012 (Biocides) ***"endocrine disrupting properties"*** have been introduced as a hazard-based approval criterion and substances considered to have these properties will not be authorised (i.e. will be banned). A definition was not included during adoption of these regulations, but the European Commission was required to develop a set of scientific criteria by 14 December 2013 to determine what these properties are. Until the final criteria are adopted **a set of interim criteria**[7] apply.

In February 2013, the Directorate General for the Environment of the European Commission (DG ENV) presented a draft proposal[8] for a set of horizontal criteria for Endocrine Disruptors intended to be applied to Pesticides and Biocides, but also to general chemicals (REACH) and Cosmetics[9]. However, agreement was not reached on this proposal and the European Commission resolved to undertake **an impact assessment** to evaluate the possible impacts of several different policy options for the Endocrine Disruptor criteria. The policy options are described in the Commission's Roadmap published in June 2014.

On 26 September 2014 the European Commission launched a Public Consultation to gather input from **stakeholders** on the options as laid out in the Roadmap. A report on the public consultation responses was published in July 2015.

During the process for preparing the criteria the Commission has organised a number of events, including a series of roundtable meetings (for MEPs, Member States and other stakeholders) and open stakeholder conferences in June 2015 and November 2015, in line with its agenda for ***Better Regulation, Openness and improved Transparency.***

On 15 June 2016 the Commission came forward with a draft proposal for the **Endocrine Disruptor Criteria**, alongside the final Impact Assessment report for biocides and pesticides. The proposal was then presented to the Standing Committee on Plants, Animals, Food and Feed – Phytopharmaceuticals (SCoPAFF) and the Biocides standing Committee on 22 June, with further detailed discussions expected in July, with voting likely in October. Alongside this the Commission hosted a stakeholder workshop to present the criteria on 30 June.

The final criteria are likely to be formally adopted in early 2017.

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[6] Regulation 1107/2009, Annex II, point 3.6.5 and point 3.8.2

[7] Substances classified as C2 and R2 under CLP Regulation 1272/2008 shall be regarded as endocrine disruptors. Substances classified as R2 and which are toxic to the endocrine organs may be considered to be endocrine disruptors.

[8] DG Environment document: *Revised version of possible elements for criteria for identification of endocrine disruptors* (ED-AD-HOC-6/2013/02), 19 February 2013

[9] REACH (Regulation 1907/2006) & Cosmetics (Regulation 1223/2009).

Glossary of ED Terminology

Endocrine System

The endocrine system is a complex set of glands which release hormones (chemical messengers) into the body that control the regulation of important processes such as growth, development, puberty onset and behaviour. The endocrine system also maintains stability of the body's internal environment in response to changes in external conditions (homeostasis).

Endocrine Disruptor

Endocrine disruption occurs when a substance has an adverse effect by altering the functioning of the endocrine system, causing irreversible change and/or illness. In other words, an endocrine disruptor interferes with the endocrine system to cause a harmful effect. WHO/IPCS (2002) has defined an endocrine disruptor as *"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".*

Severity

Severity describes the magnitude of an adverse effect and/or the qualitative nature of the adverse effect induced by a substance as observed in laboratory animal studies. Severe adverse effects would contribute to a greater overall level of concern.

(Ir)reversibility

Consideration of reversibility or irreversibility contributes to evaluation of severity. Reversibility implies that recovery of the individual or population (in laboratory animal studies) may occur after exposure to the substance in question has stopped. Reversible adverse effects would provide a lower overall level of concern.

Specificity

For a substance to be considered to have endocrine disrupting properties, the adverse effect should manifest as a direct consequence of a primary endocrine mode of action[10], and not indirectly as a result of secondary non-endocrine mediated systemic toxicity.

Potency

Potency is a factor of both the dose level at which adverse effects are induced and the duration required to cause those effects. A highly potent substance produces a large effect at low concentrations, while a substance of low potency leads to a small effect at even higher concentrations. Also, a potent substance may cause an adverse effect after a short exposure duration, whereas a less potent substance may require a longer exposure duration to elicit the same effect. Potency is therefore a measure of a substance's strength to produce an adverse effect. It is a routine part of the dose response considerations in the hazard characterization (see below) of a substance and is an essential element to discriminate between substances of high regulatory concern (those of high potency) from those of lower concern (those of low potency).

Lead Toxicity

The lead toxic effect considers the dose response relationship of all effects observed in the toxicity dossier of a substance. It is considered to be the adverse effect that occurs at the lowest dose. The lead toxic effect describes the most sensitive toxicological endpoint (i.e. critical effect) and "drives" the risk assessment of a substance. Any

[10] The inherent ability of a substance to interact or interfere with one or more components of an endocrine system.

risk management measures based on the lead toxic effect will be protective of all other adverse effects which occur at higher dose levels (including effects occurring via endocrine modes of action).

In ECPA's view, a substance should only be considered of regulatory concern (i.e. considered to have endocrine disrupting properties), when the endocrine mediated adverse effect is the lead toxic effect and occurs at doses lower than those that cause other types of toxicity.

Human and population relevance

The endocrine mediated adverse effects observed in laboratory studies must be relevant to humans or non-target populations (the environment). For human health, relevance to humans is generally assumed by default in the absence of scientific data demonstrating non relevance. For the environment, effects observed in studies must be relevant at the species population level.

Hazard

The ***intrinsic properties*** of a substance having the ***potential*** to cause an adverse effect when humans or wildlife (environmental) species are exposed to that substance.

Risk

The ***probability*** of an adverse effect in humans or wildlife (environmental) species caused by exposure to a substance, i.e. risk describes the chance of harm being done, in terms of both the likelihood of harm, and the extent of that harm.

Hazard assessment

The process to determine the **possible** adverse effects of a substance to which humans or wildlife (environmental) species could be exposed. The process includes *hazard identification* **and** *hazard characterization* (see below). The process focuses only on the intrinsic properties (hazard) of a substance and does not consider real-life conditions of exposure of humans or wildlife (environmental) species to that substance.

Risk assessment

The process to calculate the **risk** to humans or wildlife (environmental) species, following exposure to a particular substance, taking into account the intrinsic properties of the substance (hazard) as well as the susceptibility of humans or wildlife (environmental) species, i.e. risk assessment examines the inherent properties of a substance (hazard), and determines if this substance could cause adverse effects to human health or wildlife (environmental) species *under real-life conditions of exposure*.

The risk assessment process includes four steps: (1) hazard identification, (2) hazard characterization (Dose–response assessment), (3) exposure assessment, and (4) risk characterization.

(1) Hazard identification

The identification of the type and nature of adverse effect(s) that a substance has the inherent capacity to cause in humans or wildlife (environmental) species. Hazard identification is the first stage in hazard assessment and the first of four steps in risk assessment.

(2) Hazard characterization

The qualitative and, wherever possible, quantitative description of the intrinsic properties of a substance that have the potential to cause adverse effects. This includes a detailed description of the adverse effect (i.e. observed in laboratory animal studies), a quantitative assessment of the relationship between the dose of the substance and

the incidence of the adverse effect (dose–response relationship), the potency and consideration of the lead toxic effect (critical effect). Hazard characterisation also includes a qualitative description of the adverse effects, looking at the severity and irreversibility of the effect.

Hazard characterization is the second stage in the process of hazard assessment and the second of four steps in risk assessment. Related terms: *Dose–effect relationship, Effect assessment, Dose–response relationship, Concentration–effect relationship*

(3) Exposure assessment

Evaluation of the likely or predicted level of exposure of humans or wildlife (environmental) species to a substance. Exposure assessment is the third step in the process of risk assessment.

(4) Risk characterization

The qualitative and, wherever possible, quantitative determination, of the **probability** of the occurrence of known and potential adverse effects of a substance in humans or wildlife (environmental) species, under expected conditions of exposure. Risk characterization is the fourth step in the risk assessment process.