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Policy Perspective on Endocrine Disruptors and Crop Protection Products

Endocrine disruption is a technically complex issue that garners public, political and scientific interest. As an important stakeholder, the crop protection industry addresses in this paper key scientific issues related to endocrine disruption and crop protection products.

What are Endocrine Disruptors?

The endocrine system is a set of glands that produce hormones (chemical messengers), which regulate processes such as growth, development, metabolism, reproduction and behavior. Hormones also maintain stability of the body's internal environment in response to changes in external conditions (homeostasis) as well as control changes at different stages throughout a lifetime (e.g., early development, onset of puberty).

Changes in the endocrine system can be caused by a variety of factors, including aging, certain diseases and conditions, stress, genetics and diet. Many substances, both natural and synthetic, can interact with the endocrine systems of humans and wildlife. Most **endocrine active substances (EASs)** will only produce biological changes within a living being's normal operating range (homeostatic capacity) or be detoxified by metabolism and therefore, do not cause adverse effects. However, substances that upset a normal biological range and cause adverse health effects are regarded as **endocrine disruptors (EDs)**. **Adverse effects** reduce a living being's functional capability that may result in a change in its shape, function, growth, development, reproduction or life span.

EASs can be found in a variety of chemical classes, including natural products from plants and other living organisms, pharmaceuticals, crop protection products, and consumer and industrial manufacturing products. A large number of EASs of natural plant origin are consumed as food or feed, such as estrogenic compounds in soy (e.g., genistein and daidzein) and goitrogens in cabbage (glucosinates). Other common EASs are caffeine and sugar.

Such EASs do not cause harm at doses commonly consumed and there are wide margins of exposure between the dose consumed and the dose required to cause an adverse effect. Similarly, chemical products commonly regarded as potential EDs may actually be EASs under normal use conditions and therefore, do not cause adverse effects. Hence, risk assessment that includes exposure is important.

Issues to Consider in Regulating Endocrine-Disrupting Crop Protection Products

For a substance to be regarded as an endocrine disruptor, it must cause an adverse effect in an intact organism or (sub)population by an endocrine mode of action. There is often confusion as to whether interaction of a substance with the endocrine system is in itself harmful or whether it could lead to harm under certain circumstances. Interaction with the endocrine system that leads to

adverse effects in humans or wildlife (i.e., **endocrine disruption**) is dependent upon the potency of a substance, its level (**dose**) and duration and timing of **exposure**.

Potency is a measure of a substance's strength to produce an adverse effect. A highly potent substance can produce a large effect at low doses, while a substance of low potency may have a small effect, even at higher doses.

Exposure describes to what extent an individual or population may come in contact with a substance (e.g., via food, water, inhalation or skin contact). The level, frequency and duration of exposure to a substance are all key determinants of whether or not, and to what extent, adverse effects may occur. Adverse effects may be observed in laboratory animal studies at very high doses; however, these levels are significantly above those to which humans and/or animals living in the environment may ever be exposed.

In regulatory decision-making, potency, dose and exposure must all be taken into consideration. In this context, it is important to remember that endocrine disruption is a mode of action, not an endpoint in itself. Chemical regulation is, and should continue to be, focused on adverse outcomes at environmentally relevant exposures rather than the mechanisms by which those effects occur. This is the approach used by the U.S., Canada, Japan and Australia.

The crop protection industry is very concerned with the European Commission's (EC's) newly proposed criteria to identify endocrine disruptors. This concern relates mainly to using the WHO/IPCS (2002) definition alone for criteria to identify EDs which are then subject to specific regulatory action, i.e., a ban based on hazard characteristics unless certain negligible risk derogations are met. Industry is of the view that further elements of hazard characterization, such as potency, should be incorporated into the criteria as these are essential to separate substances of high concern from those of no/little concern.

CropLife Canada View on the Regulation of EDs on Crop Protection Products

The continued protection of human health and the environment results from science- and risk-based policy-making. Regulatory decisions should incorporate scientific information considering exposure, potency, (eco)toxicological testing and mode of action in a transparent risk assessment framework. Using hazard-based decision-making fails to take into account all relevant scientific data and does not provide a rational basis for regulatory decision-making. Therefore, crop protection products should not be characterized as endocrine disruptors based on hazard alone without factoring in realistic conditions of use and exposure through risk assessment.

Current regulation of crop protection products ensures high levels of protection for human health and the environment. Substances are only made available to farmers if they are proven safe for their intended use following extensive evaluation by regulatory authorities. This includes testing for endocrine-mediated effects of crop protection products, which are scientifically strong and sufficient to support regulatory decision-making.

Ultimately, the ability of farmers to produce abundant, high-quality food relies on science-based, predictable and relevant regulation in all countries around the world. The crop protection industry is committed to staying on top of the latest science and best testing methods to ensure the safety of its products.

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