What They're Saying about the EU Commission Criteria for Identifying EDCs

In the days before and after the **European Commission** published its **draft criteria for identifying endocrine disrupting chemicals (EDCs),** comments began flooding in from concerned scientists, EU and non-EU citizens, industry groups and companies with operations in Europe and around the world. Something critical was missing from the criteria, they noted – **a fundamental principle in toxicology** that could mean the difference between restricting substances with real potential to cause harm from substances like caffeine or cocoa, which may interact with the endocrine system but pose little to no health risk.

What did the Commission omit? **Potency** – an easy-to-understand, everyday phenomenon that helps to explain why highly potent substances can produce a given effect at low doses or exposures, whereas it may take other, less potent substances much higher doses and exposures to produce the same effect (e.g. why some chili peppers are spicier than others). Relative **potency** is a way of comparing the 'strength' of two chemicals in regard to their ability to produce an adverse health effect. It is at the core of how the biological effects of chemicals, including pharmaceuticals, are determined in the first place.

The omission of **potency** on the part of the EU was so concerning, in fact, that more than 70 scientists, EU and US citizens, industry groups and companies have either referred to it directly in the media or in their comments to the Commission, or they have expressed strong support for the only regulatory proposal that would include **potency as part of its criteria for identifying EDCs -- *Option Four*.**

Below is a small selection of quotes from those individuals and groups.

Daniel R. Dietrich

> "We are concerned that some of the European Union's processes for setting safety regulations for chemicals are being influenced by media and pseudoscience scaremongering. . . . Acting on hazard identification alone relieves the scaremongering party of the burden of proof, when harm is simply assumed. As a result, regulations can become unnecessarily restrictive. They may even be damaging, for example if an agricultural ban were to be imposed on triazole fungicides because of their endocrine-disrupting potential. The risk to humans at such levels of exposure would be negligible. It makes no sense to override such evidence with a blanket ban on potentially hazardous chemicals that ignores the public's demonstrable low level of exposure."

Gio Batta Gori, ScD, MPH, ATS & Wolfgang Dekant, Ph.D.

> "Initial discussion…needs to address why toxicology and regulation should adopt the exception of considering hazards as free standing entities without **potency** attributes. After all, the common rule is that natural events – including all physiologic ones – can only originate from stimuli or forces sufficiently potent to cause those events. Why bypass the rule when organisms can obviously thrive while being inevitably exposed to all infinite atoms and molecules, and thus to all putative hazards in the environment? Indeed, hazard-based regulations without dose-

potency attributes are lame propositions, likely to lean on the imaginary scenario of one cell, one molecule, one hit and one macroscopic pathology."

Gregory G. Bond, Ph.D., M.P.H.

"The only way the BfR could coax consensus from the scientists it had convened was to dupe them into thinking that identification of EDCs was merely the hazard identification step in risk assessment. The consensus statement argues that **potency** is critical to hazard characterization, but not to hazard identification. …this logic is flat out wrong because the WHO/IPCS definition of an EDC includes mode of action which itself is not usually included in hazard identification, but only in hazard characterization and/or later steps in a risk assessment. Furthermore… the BfR consensus statement would allow chemicals to be labeled endocrine hazards in the EU, despite lacking sufficient **potency** to affect anyone's endocrine system. By such standards, caffeine or cocoa would be endocrine hazards. This hardly seems helpful to regulators nor would consumers find it credible if it was explained to them in this manner."

Christopher Borgert

"Omitting **potency** did not create a more relevant standard of evidence as argued in the German Federal Institute consensus statement. **Potency** is the strength of a chemical's interaction with the endocrine system; toxicity refers to its strength in producing adverse effects. . . . High **potency** also distinguishes exogenous chemicals that can mimic hormones or interfere with their action from low **potency** chemicals that merely interact with the endocrine system without altering its function. . . . **Potency** evaluation is so powerful and reliable that it is the pharmaceutical industry's chief means of identifying hormonally active drug candidates and excluding low **potency** chemicals with no potential to produce endocrine effects. Thus, **potency** is the basic operating principle of the endocrine system that provides the critical link between an endocrine mode of action and an adverse effect."

Endocrine Policy Forum

"… the [draft] regulation provides no objective provisions for determining if adverse effects are produced by an endocrine mode of action, and it overlooks endocrine **potency**, even though **potency** is the property most important for making that determination. Most exposures (even to food such as caffeine and soy) elicit an endocrine response, and many chemicals are not sufficiently potent to elicit an adverse response at any reasonable level of exposure. Ignoring **potency** and exposure information will result in regulation of many chemicals as if they pose a health threat as EDCs when, in reality, they cannot."

American Chemistry Council

"**Potency** is a fundamental principle of toxicology and hazard characterization. Without it, substances that have been demonstrated to pose no unacceptable risks to humans or wildlife in the U.S. may be banned from commerce in the EU. While the WHO/ICPS definition is an

appropriate starting point for the proposed criteria, without the addition of **potency** and other elements of hazard characterization it will not enable European authorities to differentiate for regulatory purposes between substances that are likely and unlikely to cause harm."

Cefic

"Without **potency** built-in, substances present in everyday food and drinks which are safe for consumption such as caffeine or soy bean proteins could be identified as ED. . . . So the inclusion of **potency** does not negatively impact health but helps ensure that only substances with the potential to cause harm are identified by the criteria."

CropLife America

"Using the WHO/IPS definition for ED as proposed, would result in many substances, both natural and synthetic, which present little or no risk, being 'identified' as ED; **potency** and exposure must be considered prior to assessment of potential impact on human health and wildlife populations."

CropLife Canada

"The diversity and range of chemicals, both natural and synthetic, that exhibit endocrine activity is huge and speaks to the need to consider all elements of hazard characterization (severity and (ir)reversibility of effect, **potency**, and lead toxicity) and potential exposure in the evaluation. We strongly urge the EC to adopt a risk-based approach to the regulation of endocrine-active compounds."

European Crop Protection Association

"… **potency** and other hazard characterisation elements (severity, reversibility, lead toxicity) must be built into the criteria. Hazard characterisation is an essential step in hazard assessment and these elements are critical to enable regulators to distinguish between substances which pose a real danger to health and the environment and those that do not."

Crop Protection Association (CPA)

"By failing to distinguish between substances dangerous to the environment and health and those that are not, the criteria fail to be fit for purpose as a regulatory tool. CPA objects to the proposal on this basis and urges the Commission and Members States to include hazard characterisation elements in the criteria. These should include not only **potency**, which was considered in the roadmap, but also severity, reversibility and lead toxicity."

U.S. Soybean Export Council (USSEC)

"USSEC does not agree with the hazard-based approach underlying this proposal. Whereas we agree that regulation should guarantee adequate food safety and appropriate environmental

protection, it should be based on realistic exposure scenarios and therefore take into account **potency** factors."

Gowan Italia

"**Potency**, severity and hazard characterization elements have to be taken into consideration to build a comprehensive risk assessment to distinguish between substances really dangerous to health and environment and those that do not."

BASF FE

"The present proposal ignores the reality of **potency**, despite the fact that physiologic hormones trigger responses depending on hormonal concentration directly linked to **potency**. Considering **potency** in a hazard assessment of a substance is mandatory to judge on whether a substance potentially poses harm to human health and the environment or not. Otherwise purely hypothetical high-dose effects exceeding the maximum tolerable dose would drive a regulatory decision without real-life relevance and lead therefore to false and not justified decisions."

Syngenta International AG

"Without the addition of hazard characterisation elements, such as **potency**, severity of effect, reversibility and lead toxicity…the criteria do not allow the separation of compounds that are of concern from those of that are of little or no concern. Under the criteria as written, products such as soya, caffeine and chocolate would likely be classed as endocrine disruptors if the key elements of hazard characterisation were to be ignored."

UK Chemical Industries Association

"The Commission's opinion that **potency** in particular should not be part of hazard characterisation is opposed by the experts involved in the recent scientific meeting in Berlin who concluded that there is a logical **potency** cut-off for hazard identification purposes."

Covestro AG

"The rationale [of the European Commission] seemed to have been based on the interpretation of the recent Berlin consensus that **potency** should not be considered in the identification of endocrine disruptors. However the consensus clearly states that **potency** is part of the hazard characterisation, and not the risk assessment. Therefore including **potency**, and all other hazard characterisation elements, is fully in line with the current legal framework and should not be excluded."

Union des Industries Chimiques

"UIC regrets that **potency** was not retained by the European Commission as a criterion, as it would have helped make the case for substances which in a small dosage do not cause harm. This approach will result in the regulation of many substances whose benefits largely outweigh

their hypothetical risks. . . . Furthermore, while the Berlin scientific consensus statement refers to **potency** not being required to identify EDs, it does clearly refer to the use of **potency** and risk assessment for the regulation of ED substances."

H.L. Hutchinson LTD

"We ask the EU and members states to ensure that any definition of ED properties includes a risk assessment of **potency** and potential exposure. A hazard based approach if applied to caffeine would lead to a ban of a very useful product that is safe if consumed in moderation i.e. the exposure is considered. Any assessment of essential agrochemicals needs to consider both the **potency** and the actual exposure using Good Agricultural Practice."

Remmers Baustofftechnik GmbH

"Taking into account the **potency** of chemical substances in hazard-based regulations already is a well established principle for example in the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures. Without **potency** built-in, substances present in everyday food and drinks which are safe for consumption – such as e.g. caffeine or soy bean Proteins – could be identified as ED and thus would be banned from the use in biocidal products."

DuPont

"By adopting the WHO definition as the sole identifier of substances to be regulated as endocrine disruptors (EDs), the Commission ignores the wide **potency** range that exists across chemicals, whether synthetic or natural, and makes no attempt to keep substances of low concern (low **potency**) out of the regulated category. **Potency** differences can be considerable. For example the estrogenic **potency** of diethylstilbestrol (DES) is 25 million (25,000,000) times greater than for benzylparaben. Such a reality must not be overlooked out of political convenience. In a system in which intrinsic properties (hazards) lead to prohibition, taking into account how much of a substance is required to cause an adverse effect (**potency**) is the only practical way to avoid the loss of numerous products of low concern."

Japan Chemical Industry Association

"We believe that regulating endocrine disruptors requires identifying and more quantitatively assessing their adverse effects. To that end, their **potency** must be considered. Otherwise, there is a possibility that substances whose existing usage has no risk of damaging human health or the environment may be prohibited, thereby seriously affecting the agriculture, public health, trade, industry, and economy of Europe as a whole."

American Chamber of Commerce to the EU

"This omission [of **potency**] will have major unintended consequences with many substances, which pose no risk in normal use, being identified as EDs. . . . The inclusion of **potency** in the ED

criteria, for example, would allow for the continued safe use of azole fungicides, maintaining their benefits to EU food production and to society as a whole. If azole fungicides were no longer used for disease control, both the quality and quantity of wheat production would drop. The EU, who is currently a net exporter of wheat, would become a net importer. The global wheat supply would be disrupted, and price volatility would increase, with likely global adverse consequences on availability and affordability of basic food and feed."

Agricultural Industries Confederation (AIC)

"Inclusion of **potency** in the WHO / IPCS definition will allow the continued use of active substances (ais) used to control weeds, pests and diseases in crops contributing to the production of safe, wholesome, affordable food for consumers. Some ais used to protect human and animal health (e.g. fungicides used to control mycotoxins in grain), could be classified as endocrine disruptors without the inclusion of **potency** in the criteria."

Duncan Brown

"The proposed definition (option 2 WHO/IPCS) is not risk based. Hazard characterisation factors must be included in the definition, especially **potency**, severity and reversibility. . . . If **potency** is not included some AS's used to protect human health could be classified as ED's. Inclusion of **potency** will allow the continued use of critical and vital AS's to control weeds, pests and diseases without which the production of healthy and affordable food will be threatened. The likelihood of increased resistance as control methods will have to rely on fewer modes of action."

Slovak Crop Protection Association

"We call on the Commission and Member States experts to amend the proposal by hazard characterisation elements, especially **potency** and other (severity, reversibility, lead toxicity) must be inbuilt into the criteria. Only by referring to precise and full hazard characterisation it is possible to clearly assess and distinguish whether the substance can pose a real danger to health and further damage the environment and thus needs to be regulated and consequently eliminated from food production chain."

Soy Canada

"The [European Commission's] proposal relies too heavily on intrinsic hazards and fails to take into account scientific evidence when studying substances for possible endocrine disruptor properties. All characteristics including **potency**, severity of effect, irreversibility, lead toxicity, dose and exposure are important factors that must be taken into account as part of a risk assessment and are critical to distinguishing between substances with real potential for harm and those that pose little or no risk. We believe that crop protection products should not be characterized as endocrine disruptors based on hazard assessments alone and must factor in realistic conditions of use as well as thorough science-based risk assessments."

Bayer Crop Science

> "Many substances, both natural and synthetic, which present little or no risk, would be 'identified' as EDs by using the WHO/IPCS definition alone (e.g. the impact assessment shows that iodine will be identified as an endocrine disruptor under the proposal but would not be if **potency** was taken into account). We call on the Commission and Member States to amend the proposal. In particular, **potency** and other elements of hazard characterisation (severity, reversibility, lead toxicity) must be built into the criteria."

UEAPME (Union Européenne de l'Artisanat et des Petites et Moyennes Entreprises)

> "We share the view of the European Commission that no categories within the ED-criteria are necessary. However, in our view also further parameters as severity and **potency** should be included. In our opinion this would make the criteria clearer and more useful for regulatory actions."

Association of the Austrian Chemical Industry

> "In order to identify endocrine disruptors of concern it is of utmost importance to include the severity and the **potency** in the identification of an active substance as having endocrine disrupting properties. Only substances with high **potency** that lead to severe adverse effects on the endocrine system should be addressed in the frame of Regulation (EC) 1107/2009 and of Regulation (EU) No 528/2012."