European Commission's Public Consultation on Defining Criteria for Identifying Endocrine Disruptors (EDs) in the Context of the Implementation of the Plant Protection Product Regulation and Biocidal Products Regulation

Comments of the U.S. Government

January 16, 2015

Introduction

The United States Government appreciates this opportunity to comment on the European Commission Roadmap with respect to the "Defining Criteria for Identifying Endocrine Disruptors (EDs) in the Context of the Implementation of the Plant Protection Product Regulation and Biocidal Products Regulation". The United States strongly supports strengthening public health and environmental protection by properly identifying, understanding, and regulating the use of plant protection products[1] that may have endocrine disrupting properties. This U.S. commitment is longstanding one stretching back almost two decades to the enactment of legislation charging the U.S. Environmental Protection Agency (EPA) to develop a screening program for plant protection products based on their potential to be endocrine disruptors.[2] The U.S. experience in this area has emphasized that a principle applicable to all public health measures is particularly true and relevant with respect to regulating endocrine disruptors: the measures must be developed in accordance with scientific principles and based on the relevant scientific evidence. Plant protection products play a critical role in our lives. Imposing unnecessary restrictions could have far-reaching and particularly detrimental consequences. The following are just some of the key considerations that arise when considering plant protection products in the context of endocrine disruptor regulation.

- **Public Health**: Plant protection products serve an important public health objective by controlling pests and diseases. Notably, the pesticides used for plant protection not only prevent the spread of diseases and pests that impact plants, but also mitigate the risks of pest-borne diseases and carcinogens that directly affect humans.[3] As noted by the World Health Organization (WHO), "Vector control plays a key role in prevention and control of major vector-borne diseases… and often constitutes the first line of activity in case of epidemics of vector-borne diseases. *Chemical control (use of pesticides) is still the most important element in the integrated*

[1] Our use of the term "plant protection product" encompasses both pesticides and antimicrobial substances.

[2] Congress passed legislation back in 1996. *See* Food Quality Protection Act of 1996, 110 Stat. 489, 7 U.S.C. § 136 et. seq. & The Safe Drinking Water Act Amendments of 1996, 110 Stat. 1613, 42 U.S.C. § 300f.

[3] *See e.g.*, Eds. Hideo Ohkawa, Hisashi Miyagawa, et. al, Pesticide Chemistry: Crop Protection, Public Health, Environmental Safety (2007), p. 318 (noting one way of preventing the carcinogen aflatoxin from spreading is to control insect pests that feed on nuts.); M. Peraica, B. Radic, et. al., Toxic Effects of Mycotoxins in humans, Bulletin of the World Health Organization (1999); UK Food Standards Agency, Code of Good Agricultural Practice to Reuce Fusarium Mycotoxins in Cereals (Feb. 2007), available at http://www.food.gov.uk/sites/default/files/multimedia/pdfs/fusariumcop.pdf ("Recommended fungicides applied as an ear spray … at a robust rate can reduce ear blight and subsequent mycotoxin production. Growers should consider the use of fungicides and PGRs for fusarium mycotoxin reduction in conjunction with the Food Standards Agency's Pesticide Residue Minimisation Crop Guide for Cereals.")

approach to vector control."[4]

- **Environmental Protection and Climate Change:** Plant protection products help control invasive pests that can damage the environment and undermine ecological diversity. The European Food Safety Authority (EFSA) estimates that the cost to Europe to control and eradicate invasive species—and repair the damage wrought by them—is more than ten billion euros a year.[5] This figure, which excludes the costs of human pathogens and outbreaks of animal diseases, could rise significantly if plant protection products are removed from the market.[6] Moreover, these products make farming more efficient, reducing fuel and energy consumption. For example, crop protection products may allow for reduced conservation tillage, meaning less soil erosion as well as less fossil fuel consumption.[7]

- **Food Security:** Despite the current challenges presented by crop pathogens, it is important to recognize that modern crop protection products have resulted in drastic improvements that have strengthened food security. For example, the Irish Potato blight in the mid-19th century led to nearly one million deaths.[8] Today, advanced treatments prevent similar epidemics, although the head of research and development of the

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[4] World Health Organization, WHOPES: WHO Pesticides Evaluation Scheme, available at http://www.who.int/whopes/questions/en/ (last accessed January 9, 2015).

[5] EFSA, Invasive Species, available at http://www.efsa.europa.eu/en/topics/topic/invasivealienspecies.htm. (last accessed January 12, 2015).

[6] The Food and Environment Research Agency, Agronomic and economic impact assessment for possible human health and ecotoxicology criteria for endocrine disrupting substances, Sand Hutton, York UK. June 2013.

[7] *See* Jerry Cooper and Hans Dobson, The Benefits of Pesticides to Mankind and the Environment, CROP PROTECTION (2007) ("For example, the use of herbicides saves money or effort on mechanical weed control at the community level, brings medium term social benefits of reduced drudgery, improvement of the living environment on public and personal-use amenity or sports-use land at national levels, and longer term environmental benefits of reduced fossil fuel use, soil disturbance and moisture loss from tillage—a global scale benefit to us all."' University of Nebraska – Lincoln, CropWatch, available at http://cropwatch.unl.edu/tillage/advdisadv (last accessed January 12, 2015) (noting that while a disadvantage of a no till system is the increased need to rely on herbicides, benefits include erosion control. oil moisture conservation, and minimum fuel and labor costs; *compare* The Economist, Frankenfood Reduce Global Warming (May 4, 2013) ("GM crops in general need fewer field operations, such as tillage. Reducing tillage allows more residue to remain in the ground, sequestering more CO2 in the soil and reducing greenhouse gas emissions. Fewer field operations also means lower fuel consumption and less CO2.").

[8] Joel Mokyr, Irish Potato Famine, Encyclopaedia Brittanica (2014); John Reader, The Fungus That Conquered Europe, N.Y. Times (Mar. 17, 2008).

Potato Council in Great Britain has noted that the loss of a specific crop protection product identified in the EU endocrine disruptor proposal "would also lead to serious concerns over resistance management of potato blight as an increased numbers of applications of single mode of action active substances could be required in its absence."[9] Moreover, absent plant protection products, more land would have to be dedicated to cultivation even though most available farmland is already being farmed.[10]

- **Consumer Welfare:** Plant protection products are critical to maintaining current agricultural yields—and even the viability of some agricultural commodities for producers and possibly countries. For example, one study suggested that the production of apples in the United Kingdom—the most import tree fruit grown there on the basis of area, volume, and value—would not be commercially viable absent the use of pesticides. Thus, reducing plant protection products without developing substitutes would likely "reduce the availability, affordability and overall consumption of fruit and vegetables…." for consumers.[11]

- **Trade and Jobs:** Needlessly restricting plant protection products could have significant economic consequences for EU producers and the EU's trading partners. The Agriculture and Horticulture Development Board has expressed fears that if the EU were to reject a scientific risk based approach to regulating endocrine disruptors, the cost to UK agriculture alone could exceed £905 million. U.S. stakeholder analysis suggests the failure to adopt a scientific approach could impact €65.3 billion worth of imports into the EU (of which over €4 billion worth would be U.S. exports).

The particular options identified in the Roadmap seem to suggest that the Commission is inclined to adopt a hazard-based approach to regulating endocrine disruptors, whereby endocrine active substances would be identified—and then proscribed from use—on the basis

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[9] Potato Council, "Endocrine disruptor legislation 'could cost UK industry over £905 million" (December 9, 2004), available at http://23.253.170.141:16396/news/endocrine-disruptor-legislation-%E2%80%98could-cost-uk-industry-over-%C2%A3905-million%E2%80%99-ahdb

[10] Associated Press, UN: farmers must produce 70% more food by 2050 to feed population, The Guardian (Nov. 28, 2011), available at http://www.theguardian.com/environment/2011/nov/28/un-farmers-produce-food-population (last accessed January 12, 2015) ("The report found that climate change coupled with poor farming practices had contributed to a decrease in productivity of the world's farmland following the boom years of the "green revolution", when crop yields soared thanks to new technologies, pesticides and the introduction of high-yield crops.")

[11] Jerry Cooper and Hans Dobson, The Benefits of Pesticides to Mankind and the Environment, CROP PROTECTION (2007), citing Gattuso, D., Understanding the benefits of pesticides. Consum. Res.Mag. 83 (2000)

that they have a potential to impact the endocrine system or cause an impact on the endocrine system without any further examination.[12] In other words, the Commission's hazard-based approach would impose restrictions even if there is no risk from exposure.; without considering what impact the potential hazard has on health (including beneficial impacts),[13] and even if safe uses or mitigation techniques are available that might ameliorate the possibility of any adverse impacts.

It is unclear how a hazard-based approach could logically potentially advance a general objective identified in the Roadmap: "a high level of protection to human health and the environment." Staple agricultural products such as coffee, garlic, cherries, apples, and carrots contain naturally occurring endocrine active substances—and could be construed as hazards following the letter of the proposal.[14] As a practical matter, however, the "hazards" in these crops present negligible risks because individuals do not consume the amount necessary to incur any adverse impacts. No additional protection is afforded to the public by banning these products. Yet for reasons not stated, the options in the Roadmap envision such an approach with respect to plant protection products.

Further, the Commission has only provided information of a very general nature in the Roadmap regarding what could be covered by these options to regulate endocrine disruptors. Consequently, it is difficult to understand from the Roadmap how the Commission arrived at these four options and leaves much uncertainty regarding the impact on a particular sector, product, or chemistry. It would be helpful to know what other options were considered, or rejected and the reasons why. Also, if the Commission were to be provided with evidence supporting an option not among the four presented, would this be considered?

These comments are divided into two sections. Part I presents systemic concerns regarding the Commission's regulatory process with respect to endocrine disruptors to date. These comments include: process concerns, information concerning the U.S. approach, and a discussion of trade obligations and impacts. Part II of these comments review the four regulatory options listed in the Roadmap. In the U.S. view, selection of options 2 or 4, with certain modifications, as set out in more detail in our comments, could potentially allow for a suitable risk-based approach and foster continued U.S.-EU cooperation to increase transatlantic and global regulatory compatibility for endocrine disruptors in bilateral and intergovernmental fora.

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[12] Although we understand that the proposal may establish a default MRL of 0.01 PPM in lieu of complete market withdrawal, the reality is that an MRL at that level is a practically proscription on nearly all the substances at issue.

[13] For example, birth control pills, corticosteroids used to treat cancers, and medicines to treat psychiatric conditions are all endocrine disrupting substances. Canadian Centre for Occupational Health and Safety, Endocrine Disruptors, available at http://www.ccohs.ca/oshanswers/chemicals/endocrine.html (last accessed January 12, 2015).

[14] *See e.g.*, S. Ozen & S. Darcan, Effects of Encrine Disruptors on Pubertal Development, J. Clin. Res. Pediatric Endocrinology (March 2011).

I. Systemic Comments Regarding the Commission's Overall Regulatory Approach

A. Further Transparency to Promote Public Participation

The U.S. experience with respect to regulating endocrine disruptors, and regulating writ large, is that the regulatory development process needs to be transparent and predictable in order to fully leverage the public's expertise. Here though, the Commission has only provided the most general parameters of how it might regulate endocrine disruptors. Consequently, it is unclear from the Roadmap what evidence supports a particular option, how a potential option might impact a particular sector, product, or chemistry, or how each option would be put into effect. In the next revision of the Roadmap, the additional information detailed below will be important in ensuring that these ambiguities can be sufficiently resolved.

First, the Roadmap should precisely identify the scientific evidence that the Commission has considered in presenting each of the options and explain why the evidence led to the selection of a particular option. The Roadmap broadly notes that it convened expert groups and commissioned an EFSA scientific opinion, but there is no explanation what aspects of their work the Commission found relevant in arriving at these options. Indeed, the EFSA opinion appears inconsistent with the options listed in the Roadmap to identify endocrine disruptors. Specifically, the EFSA opinion recognizes that a risk-based approach is the scientifically sound basis for regulation:

> "to inform on risk and level of concern for the purpose of risk management decisions it is the opinion of the SC that risk assessment (taking into account hazard and exposure data/predictions) makes best use of available information. EDs can therefore be treated like most other substances of concern for human health and the environment, i.e. be subject to risk assessment and not only to hazard assessment."[15]

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> "It is the opinion of the SC that, if regulation of identified EDs is to be based on a level of concern, whether or not this level of concern is reached, can only be determined by risk assessment. This should take actual or predicted exposure into account, and consider the whole body of evidence in a combined manner to characterise the risk."[16]

The omission in the Roadmap of references to scientific evidence and the relationship of that evidence to the options is particularly striking considering the questions that are being asked in

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[15] EFSA Scientific Committee; 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., available at http://www.efsa.europa.eu/en/search/doc/3132.pdf, p. 3.

[16] *Id*. at 43.

the public consultation process. For example, the Commission is asking for stakeholders whether they "[h]ave … conducted or are … aware of an assessment of substances which would be identified as endocrine disruptors according" to each of the options. The public's ability to respond in an informed manner, to critique the options presented, and to provide relevant information would be greatly improved if the Roadmap indicated the initial evidentiary support that led to the formulation of these options.

Second, although the Roadmap identifies Member State impact assessments and provides links to them, there is no explanation of what aspects of those assessments were considered relevant—including who might be affected and how. Delineating that information will help the public know more precisely how their interests might be affected.

Third, the process should be transparent and accountable to the public moving forward. Transparency must be an ongoing process moving forward, particularly considering the limited information available in the Roadmap. In particular:

(i) Information should continue to be made available as it develops, and
(ii) the Commission should take steps to assure the public that their views on its proposals are being considered as the regulatory development process moves forward.

Furthermore, once the Commission has developed a draft text of its preferred option, it should be published in addition to the risk assessment and any impact assessments that are carried out. In addition, once the Commission takes a final decision it should explain in a public document how it took significant comments into account.

The Roadmap, and the request for consultations, seems to suggest that the only approaches to be considered are the ones identified in the Roadmap. To the extent there are legal or institutional impediments for consideration of alternatives, these impediments should be identified so comments can take them into account or suggest potential flexibilities. If the public can identify an alternative approach that is more effective in terms of public health and socio-economic costs, the consultation document should be open to that possibility.

B. Regulatory Compatibility and The U.S. Approach to Regulating Endocrine Disruptors

The *Final Report by the U.S.-EU High Level Working Group on Jobs, Growth*, issued in February 2013, cited "enhancing the compatibility of regulatory regimes" as a primary objective of a comprehensive T-TIP agreement. The June 2011 *United States-European Commission High-Level Regulatory Cooperation Forum Common Understanding on Regulatory Principles and Best Practices* also notes that "[r]egulatory measures should aim to avoid unnecessarily divergent or duplicative requirements between the U.S. and the EU, when appropriate." In this context, it is important that the Commission's approach to endocrine disruptors not foreclose U.S.-EU cooperation to increase transatlantic and global compatibility in the regulation of endocrine disruptors in bilateral and intergovernmental fora.

Establishing a transatlantic approach to endocrine disruptors would set the highest global standard for the protection of public health and the environment while ensuring that global trade is not unnecessarily disrupted. To that end, the Commission and EPA began a series of meetings in October 2014 to discuss opportunities and ideas to harmonize: (i) priority setting methodologies to identify potential endocrine disruption; (ii) screening methods to identify potential endocrine disruption, and (iii) assessment of potential endocrine disruption incorporating endocrine bioactivity, hazard, exposure, and risk. In future meetings, both parties will present case studies of potential endocrine disruption, in order to identify commonalities, understand differences, and discuss why such differences exist. Efforts to achieve greater regulatory compatibility can benefit from these ongoing scientific exchanges. Moreover, in the context of this Roadmap options more consistent with the risk-based approach to regulating chemicals would create opportunities for greater regulatory compatibility of the scientific approach for endocrine disruptor prioritization, screening, and testing between the Commission and the EPA.

A brief summary of the U.S. approach to regulating endocrine disruptors may be informative.

As noted, in 1996 Congress mandated that EPA develop the Endocrine Disruptor Screening Program (EDSP) to identify those pesticide chemicals which might be having undesirable effects. Under the Food Quality Protection Act, EPA must make a safety finding that a ”reasonable certainty that no harm” will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information. In the United States, EPA regulates chemicals using risk-based methods accounting for both hazard and exposure, including its EDSP.

The first compounds being put through this program are the crop protection products (hereinafter referred to as ‘pesticides’). This decision was made based on the amount of data available on pesticide products, which is generated as part of the registration process. In EPA’s experience, an appropriate regulatory definition of “endocrine disruptor” is one that causes harm, or an adverse effect; this regulatory definition would require: hazard identification, hazard characterization, exposure assessment, and risk characterization. Whereas the EU process employs only the first two, the U.S. regulatory definition of endocrine disruptors includes all four steps of a risk analysis.

In EPA’s experience, private sector participation in EPA’s EDSP can provide regulatory authorities the necessary data on which to base such an approach to chemical and plant protection products.

To that end, EPA is using a two-tiered screening and testing process. Tier 1 tests screen the pesticides in order to identify which, if any, have the potential to interact with the endocrine system. The current EDSP Tier 1 battery consists of 11 diverse, yet complementary in vitro and in vivo screening assays. The battery of assays was designed to be conducted as a whole to maximize sensitivity and reliability for determining the potential of a chemical to interact with the estrogen, androgen, or thyroid hormonal pathways. A detailed characterization of each Tier 1 screening assay, including its development, validation, strengths, and limitations, can be

found in EPA Integrated Summary Reports or OECD Final Reports for individual assays at the EDSP website (http://epa.gov/endo/pubs/assayvalidation/index.htm).

The subsequent Tier 2 tests are designed to determine whether or not that interaction has a negative impact on the performance of the organism—in much the same way current toxicological testing is already conducted. Specifically, there are three goals:

1. Determining whether a substance may cause endocrine-mediated effects through or involving estrogen, androgen, or thyroid hormone systems,

2. Determining the consequences to the organism of the activities observed in Tier 1; and

3. Establishing the relationship between doses of an endocrine-active substance administered in the test and the effects observed.

These tests will enable EPA to obtain a more comprehensive profile of the biological consequences of a chemical exposure and identify the dose or exposure that caused the consequences. Effects associated with endocrine disruption may not be expressed until later in the test subject's life, or may not appear until the reproductive period is reached. Therefore, Tier 2 tests usually encompass two generations and include effects on fertility and mating, embryonic development, sensitive neonatal growth and development, and transformation from the juvenile life stage to sexual maturity.

In addition, the EPA is seeking to develop rapid, non-animal based screening methodologies that ultimately—if deemed scientifically appropriate—will be used to replace the Tier 1 screens. Initially, however they will be used to whittle down the universe of chemicals that could potentially be evaluated to a more relevant and manageable number, before being submitted for Tier 1 screening and Tier 2 testing. Tier 2 test results will allow EPA to proceed with a full, science-based risk assessment which takes into account exposure to the chemical in the context of the effects at various dosage levels.

U.S. standards as set by the EPA are rigorous, extensive and ensure safe use of pesticidal and non-pesticidal chemicals. EPA has developed the EDSP framework to prioritize, screen and test pesticidal and non-pesticidal chemicals potential to disrupt endocrine systems in humans and wildlife in the United States. The EDSP has three stages of implementation:

- *Prioritization* determines which chemicals require further screening using high throughput and computational methods to quantify endocrine bioactivity, exposure, and thus potential endocrine disruption.

- *Screening* identifies potential endocrine bioactivity of chemicals utilizing a weight of evidence approach according to EPA and Organization for Economic Co-Operation and Development (OECD) guidance and test guidelines, and incorporating other scientifically relevant information from prioritization and testing stages of the program.

- *Testing* identifies potential endocrine-mediated adverse outcomes (i.e., hazard) and provides quantitative dose-response information that may be used for risk assessment. Testing consists of long-term reproductive tests across multiple generations for endocrine-mediated adverse effects relevant to humans and wildlife, using EPA and OECD test guidelines for mammalian and non-mammalian species.

Prioritization, screening and testing results from the EDSP are integrated within adverse outcome pathway frameworks, combined with exposure data and modeling, and used to strengthen quantitative hazard and risk assessments for both humans and wildlife.

As noted previously, this is only a very brief description of the U.S. approach. Below, please find a list of certain documents for your review and consideration that might provide further insight on some of the critical issues EPA has encountered in its work on endocrine disruptors.

1. *Scientific Issues Associated with Prioritizing the Universe of Endocrine Disruptor Screening Program (EDSP) Chemicals Using Computational Toxicology Tools*
   http://www.epa.gov/scipoly/sap/meetings/2013/012913meeting.html

2. *Endocrine Disruptor Screening Program (EDSP) Tier 1 Screening Assays and Battery Performance*
   http://www.epa.gov/scipoly/sap/meetings/2013/052113meeting.html

3. *Endocrine Disruptor Screening Program (EDSP) Tier 2 Ecotoxicity Tests*
   http://www.epa.gov/scipoly/sap/meetings/2013/062513meeting.html

4. *Weight-of-Evidence: Evaluating Results of EDSP Tier 1 Screening*
   http://www.epa.gov/scipoly/sap/meetings/2013/073013meeting.html

5. *New High Throughput Methods to Estimate Chemical Exposure*
   http://www.epa.gov/scipoly/sap/meetings/2014/072914meeting.html

C. EU Principles Applicable to the Regulation of Endocrine Disruptors

Adoption of a risk-based approach for regulating endocrine disruptors is consistent with long-standing EU policy. We understand elements of the EU policy include:

- The analysis of risk … comprises three elements: risk assessment, risk management, risk communication.

- Risk can rarely be reduced to zero, but incomplete risk assessments may greatly reduce the range of options open to risk managers.

- Any assessment of risk that is made should be based on the existing body of scientific and statistical data.

- Risk assessment consists of four components - namely hazard identification, hazard characterization, appraisal of exposure and risk characterization …

- Measures should be proportional to the desired level of protection.

- The measures envisaged must produce an overall advantage as regards reducing risks to an acceptable level.

The risk assessment should consist of four components, including considerations of exposure and risk characterization, and be based on the existing science. Any resulting regulation should be proportionate, which means reducing risk—as opposed to reducing or eliminating hazard—to an acceptable level (i.e., not zero, which will likely be impossible). A hazard-based approach, which is based on *a more limited set of* data than a risk-based approach, would not improve the protection of public health and the environment as much as a risk-based approach since such an approach ignores risk from exposure.

To that end, great care should be taken that any measure adopted should not create the unintended effect of taking products—which can be safely used—off the market (e.g., by creating lists of "suspected" endocrine disruptors). This would not only disrupt global supply chains, but could inadvertently increase the probability of exposure to other risks and deprive the public of the health, safety, and environmental benefits (e.g., disease reduction, crop protection, increased yields) provided by certain substances.

Taking a risk-based approach would also be consistent with the report of the EC's Endocrine Disrupters Expert Advisory Group.[17] The report recommends the use of a Weight of Evidence approach for assessing endocrine disruptors, examining both whether a substance interacts with the endocrine system and whether it causes adverse effects. In addition, the report recommends that any approach taken consider data quality, study reliability, and reproducibility of reported effects, which the United States also supports.

D. Trade Obligations and Impact

1. Trade Obligations

The regulation of endocrine disruptors is intended to protect human and animal health and will undoubtedly have a significant impact on trade. Accordingly, the EU's measures on endocrine disruptors must comport with the EU's obligations under the WTO Agreement on the Application of Sanitary and Phytosanitary Measures ("SPS Agreement"). As the EU is aware, the SPS Agreement recognizes that governments have the right to set their appropriate level of protection and to adopt appropriate measures that achieve those levels of protection. We

[17] "Key scientific issues relevant to the identification and characterization of endocrine disrupting substances," European Commission, JRC Scientific and Policy Reports, Report of the Endocrine Disrupters Expert Advisory Group (March 2013).

strongly concur as reflected by the high level of protection for endocrine disrupting substances in the United States.

To ensure, however, that such measures are not a disguised barrier to trade, the SPS Agreement requires measures grounded in science. Specifically, Article 2.2 of the SPS Agreement provides that:

> Members shall ensure that any sanitary or phytosanitary measure is applied only to the extent necessary to protect human, animal or plant life or health, is based on scientific principles and is not maintained without sufficient scientific evidence, except as provided for in paragraph 7 of Article 5.

Article 5.1 of the SPS Agreement further provides:

> Members shall ensure that their sanitary or phytosanitary measures are based on an assessment, as appropriate to the circumstances, of the risks to human, animal or plant life or health, taking into account risk assessment techniques developed by the relevant international organizations.

The WTO Appellate Body has found that the requirement for a risk assessment is a specific application of the basic obligation in Article 2.2 and that these provisions should be read together as a result.[18] Thus, undertaking a risk assessment is an integral part of having science based measures; this is not a formality but a careful exercise. To that end, "one of the basic principles of a risk assessment appears to be that it needs to be carried out for each individual substance."[19] These principles counsel against the adoption of a hazard-based approach to regulating endocrine disruptors, since such an approach categorically reject examining available scientific evidence regarding whether an endocrine disruptor will have an adverse impact in light of exposure, dosage, and intrinsic properties. Moreover, Article 5.2 of the SPS Agreement requires Members to take into account the risk assessment techniques developed by the specialist agencies. Although their techniques vary, all—as recognized by EFSA—promote asking the same five questions:

- What can cause an adverse effect?
- How can it cause an adverse effect?
- What is the probability of an adverse effect occurring (i.e. what is the risk)?
- What are the consequences?

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[18] Appellate Body, *EC – Hormones (US)*, para. 180.

[19] Panel Report, *EC – Hormones (US)*, para. 8.257.

- What are the prerequisites for an adverse effect to indeed occur? [20]

To the extent one argues there is a paucity of scientific data on endocrine disruptors that might call for an exception, two points are notable. First, the WTO Appellate Body has found that "the existence of unknown and uncertain elements does not justify a departure from the requirements … for a risk assessment."[21] Second, the summary of the EFSA opinion is instructive:

> The SC considers that a reasonably complete suite of assays is (or will soon be) available to identify and characterise the important hazards of EATS substances in mammals and fish, with fewer tests available for birds and amphibians. Furthermore, these evaluation methods should, in principle, be fit for the purpose of establishing safe doses/concentrations of EDs if (1) certain aspects (e.g. follow up of exposure in critical windows of susceptibility to later life stages) are addressed and (2) used with all available information in a weight-of-evidence approach.
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> Furthermore, to inform on risk and level of concern for the purpose of risk management decisions it is the opinion of the SC that risk assessment (taking into account hazard and exposure data/predictions) makes best use of available information. EDs can therefore be treated like most other substances of concern for human health and the environment, i.e. be subject to risk assessment and not only to hazard assessment.[22]

There is no reason to believe that a risk-based approach to regulating endocrine disruptors is unavailable. EU scientific experts believe it feasible, and U.S. regulators have twenty years of experience doing it in practice. Accordingly, in the United States experience it is possible to regulate to the highest levels of protection in accordance with our trade obligations.

2. Trade Impact

The European Union and the United States have realized substantial economic benefits as a result of the stable agricultural trade relationship between our countries. The EU is the fifth largest export market for U.S. agricultural products, while the United States is the largest export market for EU agricultural products.

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[20] EFSA Scientific Committee; Scientific Opinion on Risk Assessment Terminology. EFSA Journal2012;10(5):2664, p. 9.

[21] Appellate Body, *Australia – Salmon*, para. 130.

[22] EFSA Scientific Committee; 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., available at http://www.efsa.europa.eu/en/search/doc/3132.pdf,

Implementation of any hazard-based "cut off" option, as outlined in the EC roadmap, that removes the requirement for conducting a full risk assessment could have severe implications for EU imports of U.S. agricultural goods. U.S. agricultural producers rely on a variety of plant protection products to control pests and plant diseases, improve quality and yield, and limit human disease outbreaks associated with rodent and insect populations. Without the availability of viable pest mitigation alternatives, the elimination of important pesticides could significantly limit the quantity and quality of U.S. agricultural goods intended for export to the EU.

In 2013, the United States exported approximately €4.4 billion worth of fresh and processed plant products to the EU that could be potentially impacted if hazard based criteria are applied by the EU.

EU Imports of U.S. Fresh and Processed Plant-Based Products in 2013[23]	
Commodity	*Value in Euros*
Edible Fruits and Nuts	€ 1,836,384,000
Edible Vegetables and certain roots and tubers	€ 253,421,000
Cereals	€ 402,388,000
Oilseeds and Oleaginous fruits; Miscellaneous grains, seeds and fruit	€ 1,975,156,000
Total	**€ 4,467,349,000**

This data does not include potential changes in trade flows in active pesticide ingredients exported from the United States to the EU, nor does it estimate total economic effects that may be caused by these changes in trade flows. Non-trade effects may include disruption in production, marketing, and prices for U.S. commodities and development of resistance to remaining acceptable active substances. For this reason, these trade impact estimates are conservative.

II. Specific Comments Regarding the Options in the Commission's Roadmap

A. Options for Criteria for Determination of Endocrine Disrupting properties

The preamble to the roadmap states:

> "There is general consensus on the WHO/IPCS (2002) definition of an Endocrine Disruptor. It is defined 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*."

The roadmap focuses on making a determination of the first condition of altered function (hazard analysis), and not on the second condition of adverse health effects (risk assessment). If this definition of endocrine disruptors is the "general consensus," then why would the roadmap not allow for a full risk assessment?

The preamble further states:

> "The BPR and the PPPR also set the regulatory consequences for substances considered as ED: Annex II, Section 3.6.5 of the PPPR and Article 5 of the BPR stipulate that ... substances having *endocrine disrupting properties . . . which may cause adverse effects* will not be approved for the respective use […]"

A hazard analysis may be able to determine "endocrine disrupting properties," but only a risk assessment can determine "which may cause adverse effects." Full risk assessment for agriculture chemicals is not a component of an option set forth in the roadmap.

[23] *European Commission Trade Market Access Database* http://madb.europa.eu/madb/indexPubli.htm accessed: January 14, 2015

Our understanding on this point is shaped by the relevant EU legislation referenced in the Roadmap. Specifically, the two different EU regulations that respectively govern plant protection products (PPP) and biocidal products (BP). For BP (non-food), the consideration is "risk;" for PPP, the consideration is only "exposure." This relegates the consideration of chemicals protecting crops to a less rigorous process than regulating disinfectants. Both should consider risk, and only then the socio-economic impacts of having or not having these products available.

Risk Assessment is the scientific gold standard as set forth by all three WTO SPS organizations (OIE, IPPC, CODEX). To abandon this standard weakens scientific credibility, creates confusion, makes regulatory harmonization and risk communication very difficult, and in the end produces an inferior product. The simplest solution to the broad range of policy and regulatory options is to standardize the use of risk assessment in all cases. The roadmap itself states that: "These criteria have to be operational, i.e. they have to allow for science-based regulatory decision-making." Risk assessments present results that are more complete and informative. Conversely, hazard based assessments may result in decision-making that neglects relevant science and results in poor outcomes from a variety of perspectives including public health, environmental protection, and socio-economic interests.

In the event the Commission is not so amenable, in the U.S. view, selection of options 2 or 4, with certain modifications (as set out in more detail below) could potentially allow for a risk-based approach. Utilizing such an approach would also reduce the potential for unwarranted trade impacts.

1. Option One

This option only determines if a certain chemical can have an effect on an endocrine system in some animal—irrespective of whether in the real world there is a situation where this would actually happen. We can agree with the EC's own initial rejection of Option 1 and its assessment that Option 1 would not meet objectives 2 and 3 as set forth: 2) scientific criteria and regulatory operability, and 3) "horizontal" application to all legislation.

Under this policy, the accepted science-based risk assessment process found in international standards and guidelines would not be followed. Rather, regulatory policy would be based on the existence of a hazard—irrespective of exposure to the hazard, the risk of the hazard to human health, or whether safe uses can be identified. Products would be removed from the market, and maximum residue levels (MRLs) in commodities produced with active crop protection substances identified under this categorization system could either be withdrawn entirely or set at a default level of 0.01 ppm, which is effectively a ban.[24]

A proposed EU rule taken pursuant to Option 1 would also discriminate among end uses of the same chemical product, by differentiating among the following uses: cosmetic, industrial, biocide, and pesticide. Agriculture use falls under pesticides, and this is the class

[24] Achieving such a low MRL is difficult, and testing to this low level is subject to false positives.

with most draconian restrictions proposed: no exposure assessment, no socio-economic assessment, and no registration.

2. Option Two

Policy Option 2 for Aspect I of the EU criteria is based on the WHO/IPCS definition to identify endocrine disruptors (hazard identification). In addition, Option 2 includes scientific issues in articles (a) through (e) that the EPA relates to endocrine bioactivity (including potency), hazard, exposure, and risk in the context of a systematic consideration of whether a substance has the capacity to cause endocrine-mediated adverse effects in humans or population-relevant endocrine-mediated adverse effects on animal species living in the environment, which EPA interprets to mean capacity under an assumption of ordinary exposure. In the U.S. view, Option 2 appears to have some potential consistency with a risk-based approach to regulating chemicals. However, Option 2 does not explicitly mention potency, exposure or risk in any direct terms.

Taking a risk-based approach would also be consistent with the report of the EC's own Endocrine Disrupters Expert Advisory Group.[25] That report recommends the use of a Weight of Evidence approach for assessing endocrine disruptors, examining both whether a substance interacts with the endocrine system and whether it causes adverse effects. In addition, the report sensibly recommends that any approach taken consider data quality, study reliability, and reproducibility of reported effects, which the United States also supports.

3. Option Three

The EC's own initial assessment that there are inconsistencies within Option 3 is sound, as stated in the roadmap: "for sectors with decision making mainly based on hazard identification (PPPR, BPR general public uses), the impact on number of identified substances are expected to be higher as compared to the sectors with decision making based on risk or on socioeconomic considerations (BPR, REACH, MDR, WFD)."

Indeed, it is unclear why a chemical/class of chemicals would be differently classified, depending on what form of analysis one uses (hazard vs. risk). Specifically, chemicals are expected to have the same effect at the same concentrations in the same situation. The different classifications of the same chemical/class of chemicals are an artifact of the system of analysis, not a scientific quality of the chemical itself or its effects. Also we note two references in Option 3 to "mode of action." A chemical could have a mode of action which under some circumstances could disrupt endocrine systems, but would the chemical use in the real world (as per label), and at the actual concentration found in the environment, cause an adverse effect in a specific exposed organism? This is a defect which could be remedied by a full risk analysis.

[25] "Key scientific issues relevant to the identification and characterisation of endocrine disrupting substances," European Commission, JRC Scientific and Policy Reports, Report of the Endocrine Disrupters Expert Advisory Group (March 2013).

4. Option Four

Policy Option 4 for Aspect I is also based on the WHO/IPCS definition to identify endocrine disruptors, with the inclusion of potency as an element of hazard characterization (hazard identification and characterization). In the U.S. view, the mention of potency in Option 4 is related to endocrine bioactivity, hazard, exposure and risk in the context of a systematic consideration of whether a substance has the capacity to cause endocrine-mediated adverse effects in humans or population-relevant endocrine-mediated adverse effects on animal species living in the environment.

However, it is not clear that Option 4 includes articles (a) through (e) associated with Option 2. If Option 4 includes articles (a) through (e), similar to Option 2, and explicitly adds potency as an element of hazard characterization relevant to dose-response and critical for comparisons to exposure for risk-based methods, then Option 4 would be more consistent with a risk-based approach to regulating chemicals, including its approach to endocrine disruption in the EDSP.

B. Approaches for Regulating Endocrine Disruptors

The roadmap asserts the possibility of three approaches for regulating endocrine disruptors. It is unclear why the Commission identifies only these three approaches, but the following comments outline specific concerns regarding those approaches.

With respect to Option A, "no policy change," the Roadmap explicitly characterizes this option as not meeting the requirements of the BPR and PPPR or any of the other objectives listed). Accordingly, despite being mentioned, it does not seem to be an option under consideration.

Option B provides the introduction of additional elements of risk assessment into sectoral legislation. Here, the document gives the example of the exemption in the BPR for cases where negligible risk can be demonstrated. It says such an exemption could be introduced into the PPPR. While this is a positive step, it insufficient. In the U.S. view, it would be preferable to modify Option B to ensure that risk assessment is a core and fundamental component with respect to endocrine disruptors writ large. Option C demonstrates well why such should be the case.

Option C, proposes the introduction of further socio-economic considerations, including risk-benefit analysis, into sectoral legislation. The Roadmap says such an approach is needed if banning an endocrine disruptor would have a disproportionate negative effect. The Roadmap does not define what a disproportionate negative effect would be or what socio-economic costs would be considered. That information would be helpful in being able to intelligently comment on this provision. But put plainly, the United States has no issue with the EU seeking the highest level of protection possible—and is <u>not</u> suggesting that the level of protection be compromised. On the contrary, what the United States has noted is that it is possible to regulate intelligently and effectively to raise public health without unnecessarily impeding commerce. The U.S. system for example does not allow chemicals unless there is reasonable certainty of no harm—a very high level of protection. The U.S. system avoids unnecessary detrimental effects

by applying a risk-based system to chemical management. In short, the U.S. view is that Option C is a false choice—the Commission can limit negative socio-economic benefits by applying a risk-based approach to endocrine disruptors.

C. Horizontal Issues

It is concerning, that within this consultation for identifying EDs for implementation and application in the PPPR and BPR, there is discussion about the horizontal application of the criteria to medical devices, cosmetics, workplace products, pharmaceuticals and food contact materials. This secondary objective is not clearly stated in the in the announcement of the initiative. Further, each of these product categories has a different uses for chemicals and different levels of risk associated with their use.

In particular, the language in the Roadmap referring to "the general calls on the Commission to establish horizontal hazard-based scientific criteria to identify endocrine disruptors…", which then goes on to mention: 1) a 1999 Commission Strategy which calls for "horizontal criteria for identifying endocrine disruptors," and 2) two Commission expert groups established in 2010 to provide "advice/orientation on scientific criteria for the identification of endocrine disrupting substances." Neither of these refers to "hazard based" assessment as the preferred form of scientific analysis to be used.

The potential scope and ramifications of this measure beyond food and agriculture are unclear from the Commission roadmap. In addition to pesticidal and biocidal products, which are specifically referenced in the subject line, such a measure could also impact—whether directly or indirectly—other economic sectors, or parts thereof, including: chemicals and products containing chemicals and cosmetics. Thus, depending on its content the impact of a measure could be very dramatic. For example, endocrine disruptors may be included in Annex XIV of REACH (Regulation 1907/2006) as Substances of Very High Concern (SVHCs), pursuant to article 57f. Consequently, if certain substances were identified as endocrine disruptors as part of this exercise, they could potentially be listed in Annex XIV of REACH as well; as a result, companies would need to expect to incur costs similar to other SVHCs to obtain an authorization for such substances.

To the extent this horizontal application is not intended to protect plant, animal health or food safety, any such measures that constitute technical regulations could still be subject to disciplines under the Agreement on Technical Barriers to Trade (TBT Agreement). Article 2.2 & Article 2.4 of the TBT Agreement are particularly relevant:

> Article 2.2: Members shall ensure that technical regulations are not prepared, adopted or applied with a view to or with the effect of creating unnecessary obstacles to international trade. For this purpose, technical regulations shall not be more trade-restrictive than necessary to fulfil a legitimate objective, taking account of the risks non-fulfilment would create. Such legitimate objectives are, inter alia: national security requirements; the prevention of deceptive practices; protection of human health or safety, animal or plant life or health, or the environment. In assessing such risks, relevant elements of consideration are, inter alia: available scientific and technical information, related processing technology or intended end-uses of products.

> Article 2.4: Where technical regulations are required and relevant international standards exist or their completion is imminent, Members shall use them, or the relevant parts of them, as a basis for their technical regulations except when such international standards or relevant parts would be an ineffective or inappropriate means for the fulfilment of the legitimate objectives pursued, for instance because of fundamental climatic or geographical factors or fundamental technological problems.

Creating technical regulations on the basis of hazard based criteria are often (i) more trade restrictive than necessary because risk based mitigation measures exist and because (ii) they do not fulfill a legitimate objective as they are not supported by scientific evidence.

III. CONCLUSION

The United States Government fully supports measures to protect public health and the environment. We urge the Commission to take the U.S. comments into account and to adopt an approach that fully considers the vital role that pesticide chemicals play in food safety and security, while promoting strong levels of protection, inspiring public confidence, and avoiding unwarranted burdens. Such consideration is critical to accomplishing our joint purpose and to ensuring that any decisions are informed by risk assessments.