William & Mary Environmental Law and Policy Review

Volume *44 (2019-2020)*
Issue 1

Article 6

November 2019

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THE DEFICIENCIES OF THE EUROPEAN UNION'S REGULATORY SYSTEM GOVERNING THE CLASSIFICATION OF ENDOCRINE DISRUPTING CHEMICALS

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INTRODUCTION

The European Union has issued a new regulatory scheme that proposes to identify and regulate endocrine disrupting chemicals with increased specificity.[1] However, its methodology and plan to carry out the new regulations are lacking in preventative approaches and will likely result in under-inclusion of the chemicals, to the detriment of the public health.[2] The United States has a similar program that is distinct in its approach to regulation of these toxins.[3] Endocrine disrupting chemicals are subjected to a heightened concern based on new and recent data that shows undesirable trends, including the increase of hormone-related cancers and an increase in fertility issues.[4] Other prevalent health issues

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[1] Commission Regulation (EU) 2018/605 of Apr. 19, 2018, Amending Annex II to Regulation (EC) No. 1107/2009 by Setting out Scientific Criteria for the Determination of Endocrine Disrupting Properties, 2018 O.J. (L 101), https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018R0605&from=EN [https://perma.cc/BJ27-TY37] [hereinafter Commission Regulation 2018/605].

[2] Press Release, Endocrine Society, EU Criteria Fall Short of Protecting Public from Endocrine Disrupting Chemicals (June 7, 2018), https://www.endocrine.org/news-room/2018/eu-criteria-fall-short-of-protecting-public-from-endocrine-disrupting-chemicals [https://perma.cc/7UXS-6Y2N].

[3] *Endocrine Disruptor Screening Program (EDSP) in the 21st Century*, EPA, https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-edsp-21st-century [https://perma.cc/3AP3-25CN] (last updated June 24, 2019) [hereinafter *EDSP in the 21st Century*]; *Endocrine Disruptor Screening Program (EDSP) Overview*, EPA, https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-edsp-overview [https://perma.cc/HTQ9-H64J] (last updated Feb. 22, 2017) [hereinafter *EDSP Overview*].

[4] *See* Gwynne Lyons, *Hazard Versus Risk within the context of the current debate on endocrine disrupting chemicals (EDCs) management in the EU.*, CHEMTRUST (Nov. 2013), http://chemtrust.org/wp-content/uploads/Hazard-v-Risk-a-CHEM-Trust-position-paper-Nov-2013.pdf [https://perma.cc/P2K9-UG4L]; Michael Warhurst, *EU action on endocrine disruptors:*

are affected by these widespread toxins, including diabetes, bone health, and obesity.[5] This Note argues that, while classifying these chemicals is difficult, for reasons that will be discussed, the European Union's system would be better off incorporating a more preventative approach with different burdens of proof in order to err on the side of caution and regulate as many of these harmful substances as possible.[6]

I. WHY ENDOCRINE DISRUPTING CHEMICALS NEED REGULATION: INTRODUCTION TO THE ENDOCRINE SYSTEM AND ENDOCRINE DISRUPTING CHEMICALS

The human body has extensive and physiologically complex systems that govern particular functions necessary to sustain life.[7] The endocrine system, by way of a general summary, is a delicate system that involves various glands and organs and governs hormone production.[8] Endocrine disrupting chemicals are a certain class of diverse and widespread chemicals that are detrimental to the human body due to their effects on the endocrine system.[9] These chemicals "act via nuclear receptors, nonnuclear steroid hormone receptors (*e.g.*, membrane ERs), nonsteroid receptors (*e.g.*, neurotransmitter receptors such as the serotonin receptor, dopamine receptor, norepinephrine receptor), orphan receptors . . . enzymatic pathways involved in steroid biosynthesis and/or metabolism, and numerous other mechanisms that converge upon endocrine and reproductive systems."[10] It is clear that these chemicals can impact the body and cause harm through a variety of pathways and physiological mechanisms.[11] For example, the type of cellular receptor is important because the receptor type is directly linked to the kind of substance that binds to the receptor.[12] One class of receptors, nuclear receptors, include a type of receptor

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some progress, many concerns, CHEMTRUST (Nov. 29, 2017), http://www.chemtrust.org/wp-content/uploads/chemtrust-edcs-fresenius-nov17.pdf [https://perma.cc/4XKF-3U73].

[5] Endocrine Society, *supra* note 2, at 1.

[6] *Id.*

[7] *What is the Endocrine System?*, EPA, https://www.epa.gov/endocrine-disruption/what-endocrine-system [https://perma.cc/3QMB-35JV] (last updated Jan. 24, 2017); *The Endocrine System*, HORMONE HEALTH NETWORK, https://www.hormone.org/hormones-and-health/the-endocrine-system [https://perma.cc/QBE9-P3YY] (last visited Oct. 28, 2019).

[8] HORMONE HEALTH NETWORK, *supra* note 7; *What is the Endocrine System?*, *supra* note 7.

[9] HORMONE HEALTH NETWORK, *supra* note 7; *What is the Endocrine System?*, *supra* note 7.

[10] Evanthia Diamanti-Kandarakis et al., *Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement*, 30 ENDOCRINE REV. 293, 294 (2009).

[11] *Id.*

[12] Stephen Tenbaum & Aria Baniahmad, *Nuclear Receptors: Structure, Function and Involvement in Disease*, 29 INT'L J. BIOCHEMICAL CELL BIOLOGY 1325, 1325 (1997).

that binds to hormones in the nucleus of a cell (intercellular) rather than being limited to the cell membrane.[13] Certain receptors do not have a corresponding ligand and this class is called orphan receptors.[14] Because the endocrine disruptors do not need a specific type of receptor or mechanism, but instead can affect multiple different types including intercellular and extracellular, they are particularly difficult to identify and regulate which, in turn, makes them all the more dangerous.[15]

The endocrine disrupting chemicals are a diverse group, not just because of how diversely they can impact the body, but also because they are so prevalent.[16] For example, these chemicals are naturally occurring but can also be synthetic, or man-made.[17] This again lends itself to the issue of identifying the chemicals and pinpointing the harm they inflict on public health.[18] The chemicals can alter, or disrupt, the delicate balance of the endocrine system "through environmental or inappropriate developmental exposures" and can be found in sources ranging from food to pharmaceuticals to plastics.[19] To elaborate on the previous introductory description of the endocrine system, it is one of the human body's main physiological systems that functions using glands that produce hormones that act as chemical messengers and internal regulators.[20] This complex system regulates many different physiological functions like respiration, metabolism, movement, sexual development, and sensory perception.[21] The hormones function as chemical messages and affect the different body systems by traveling through the bloodstream and sending chemical signals to the different tissues to direct them to perform various functions.[22] The type and amount of hormone secreted by each gland can have a huge impact on the functioning of the respective tissues.[23]

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[13] *Id.*
[14] *Id.* at 1325, 1335–36.
[15] *See generally* Thaddeus T. Schug et al., *Endocrine Disrupting Chemicals and Disease Susceptibility*, 127 J. STEROID BIOCHEMICAL & MOLECULAR BIOLOGY 204, 204–15 (2011); R. Thomas Zoeller et al., *Endocrine-Disrupting Chemicals and Public Health Protection: A Statement of Principles from The Endocrine Society,* 153 ENDOCRINOLOGY 4097, 4097–110 (2012).
[16] *See generally* Roland Solecki et al., *Scientific Principles for the Identification of Endocrine-Disrupting Chemicals: A Consensus Statement*, 91 ARCHIVES TOXICOLOGY 1001, 1001–04 (2017).
[17] Diamanti-Kandarakis et al., *supra* note 10, at 294.
[18] *See generally* Solecki et al., *supra* note 16.
[19] Diamanti-Kandarakis et al., *supra* note 10, at 294.
[20] HORMONE HEALTH NETWORK, *supra* note 7; *What is the Endocrine System?*, *supra* note 7.
[21] *What is the Endocrine System?*, *supra* note 7.
[22] *Id.*
[23] *Id.*

The endocrine system is constantly working to maintain a delicate balance and can be affected by many external and internal factors, including "aging, certain diseases and conditions, stress, the environment, and genetics."[24] This Note will focus mostly on the environmental factors that can impact the endocrine systems, and more specifically the exposure to toxins such as endocrine disrupting chemicals. The United States Environmental Protection Agency ("EPA") has stated that while this class of chemicals causes effects in the wild, there is limited knowledge regarding the effects of the chemicals on humans and what level of exposure causes harm.[25] This is largely due to the lack of testing done to find out the potential of this class of chemicals to harm the body.[26] The EPA acknowledges that the currently employed methods are not adequate to identify the potential risks of Endocrine Disruptors.[27] It is a truly strenuous task to identify what impacts the endocrine system because the physiological mechanisms that govern the system are extremely intricate and complex in addition to being incredibly sensitive to the delicate balance of internal and external conditions.[28]

To further emphasize why constructing a regulatory scheme of this nature is so difficult, this section will briefly discuss in greater detail how the system works and different examples of disruptors. "Endocrinology is the study of the mechanisms by which hormones coordinate and control the functions of multiple organ systems and processes . . . ."[29] A key concept in the study of the endocrine system is the idea that hormones function and communicate with the body via receptors, and endocrine disruptors can impact the efficiency of those receptors.[30] Sometimes the chemical disruptors even prevent hormone function entirely, but the level of disruption is hard to distinguish because the chemicals can replicate the response of the receptors.[31] The hormones act with a "lock and key" mechanism that binds to receptors within a cell and once this binding occurs, the receptor can act on the instructions of the chemical message which may be an alteration of existing proteins or building new materials.[32] The main producers of the

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[24] HORMONE HEALTH NETWORK, *supra* note 7.
[25] *See generally* HORMONE HEALTH NETWORK, *supra* note 7; *What is Endocrine Disruption?,* EPA, https://www.epa.gov/endocrine-disruption/what-endocrine-disruption [https://perma.cc/L67P-NPF6] (last updated Feb. 22, 2017); *What is the Endocrine System?*, *supra* note 7.
[26] *What is the Endocrine System?*, *supra* note 7.
[27] *See id.*; *see also EDSP Overview*, *supra* note 3.
[28] *See What is Endocrine Disruption?*, *supra* note 25.
[29] Zoeller et al., *supra* note 15, at 4099.
[30] *See What is Endocrine Disruption?*, *supra* note 25.
[31] *Id.*
[32] *What is the Endocrine System?*, *supra* note 7.

chemical signals are the hypothalamus, which links the nervous system to the endocrine system; the pituitary gland; the thyroid gland, which is heavily involved in development and metabolism; the adrenal glands, which produce stress hormones and others that respond to glucose metabolism, blood pressure regulation, and salt levels in the body; the pancreas, which regulates the sugar concentration in the blood; and the gonads, which regulate reproduction and produce hormones like androgens, estrogens, and progestins.[33] By way of illustrative example, the thyroid gland makes thyroxine and triiodothyronine and these two hormones work together to control physiological processes like growth, metabolism, and development.[34] Disruption of hormones and their receptors can have detrimental effects on the body; specific examples include the function and development of the brain, reproductive system, and metabolic system.[35] Endocrine disrupting chemicals are particularly dangerous because exposure is widespread and subsequent harmful effects can be delayed, making it more difficult to find correlation between the substance and the detrimental results of exposure.[36]

To qualify as an endocrine disrupting chemical, the substance must actually physically interfere with the functioning of the endocrine system.[37] This physical interference usually occurs by disrupting the effectiveness of hormone receptors, or influencing and even halting hormone production.[38] This phenomenon again implicates the issue of pinpointing correlation, and it is for this reason that classification of the chemicals has posed such a difficulty.[39] There is a variety of ways a chemical can disrupt the endocrine system.[40] Sometimes the chemical mimics a hormone that is naturally produced in the body so the body will over-respond or under-respond.[41] Other endocrine disruptors can influence the body to respond to hormone production inappropriately.[42] They can also completely block certain receptors so that the hormone does not get to transmit its chemical message, and physiological processes will subsequently

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[33] *Id.*
[34] *Id.*
[35] *Id.*
[36] Warhurst, *supra* note 4.
[37] Robert Barouki, *Endocrine Disruptors: Revisiting Concepts and Dogma in Toxicology*, 340 COMPTES RENDUS BIOLOGIES 410, 411 (2017).
[38] *What is Endocrine Disruption?*, *supra* note 25.
[39] *Id.*
[40] *Id.*
[41] *Id.*
[42] *Id.*

be disrupted or prevented altogether.[43] Other chemicals can interfere with the receptors and glands that produce the hormones where the result is an underproduction or overproduction of hormones and this interference can, and often does, result in conditions such as hypothyroidism or hyperthyroidism.[44] Another reason the classification of these chemicals is difficult is because the harmful impact of the chemical is measured by "toxicity," which is a fluid entity and can really only be estimated, rather than quantifiably ascertained.[45]

For the purpose of further illustrating what an endocrine disrupting chemical is, a commonly known example is Bisphenol A, otherwise known as BPA, widely known for its use in plastic goods.[46] These substances are commonly used in everyday life and this widespread nature is another reason why regulation is so important.[47] Wide use of chemicals like alkylphenol ethoxylates ("APEO") is another example of how a lack of monitoring and variety of sources contribute to harmful exposure pathways.[48] Another example provided by the EPA is diethylstilbestrol ("DES"), which is a synthetic, or man-made, estrogen and it used to be prescribed to pregnant women to stimulate fetal development, but it was later discovered that the chemical caused damage in the children of the mothers who took the drug.[49] The effects of the drug included adverse effects on the reproductive system and also was linked to vaginal cancer.[50] Other chemicals that have been determined to cause adverse effects on public health include ethane and various metabolites, polychlorinated biphenyls, plant estrogen, and various organochlorine compounds.[51]

To add even further to the difficulty posed in classification and regulation of these chemicals, it turns out that it is not just the type of chemical that causes harm that may be hard to pinpoint but also the *source* of the chemical.[52] The EPA acknowledges that the chemicals may originate

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[43] *Id.*
[44] *See generally What is Endocrine Disruption?*, *supra* note 25.
[45] Warhurst, *supra* note 4.
[46] *See generally* Angela Simonelli et al., *Environmental and Occupational Exposure to Bisphenol A and Endometriosis: Urinary and Peritoneal Fluid Concentration Levels*, 90 INT'L ARCHIVES OCCUPATIONAL & ENVTL. HEALTH 49, 50 (2017); Warhurst, *supra* note 4.
[47] *See* Warhurst, *supra* note 4.
[48] Ismail-H. Acir & Klaus Guenther, *Endocrine-Disrupting Metabolites of Alkylphenol Ethoxylates—A Critical Review of Analytical Methods, Environmental Occurrences, Toxicity, and Regulation*, 635 SCI. TOTAL ENV'T 1530, 1530–33, 1535 (2018).
[49] *What is Endocrine Disruption?*, *supra* note 25.
[50] *Id.*
[51] *Id.*
[52] *See id.*

from a wide variety of sources like food, water, or the general environment.[53] Because the sources are so unknown, and yet incredibly widespread, the effects are unpredictable and harmful.[54] This Note argues that it is important to invest further research into identifying the link and causation of the chemicals and the impact on health, which in turn translates to stricter regulatory methodology.[55]

II. THE EUROPEAN UNION AND THEIR CLASSIFICATION SYSTEM

The issue of causation and unknown impacts on public health is what provides the basis for concern regarding the European Union's new regulatory scheme.[56] In the past, the European Union has tried to implement many different regulations in an attempt to phase out endocrine disruptors from numerous sources like water, other chemicals, and products like pesticides and biocides.[57] It is well-established that exposures to the chemicals cause an immense burden from a healthcare and disease standpoint.[58] The new regulations have a low burden of proof, and so the standard results in what amounts to an under-inclusive classification system that could potentially cost Europe millions in repairing the damage caused by both health repercussions and economic strain between Europe and the countries it trades with, such as the United States.[59] The United States has attempted to suggest that the European Union use a risk-based approach, much like the United States' Endocrine Disruptor Screening Program ("EDSP") rather than the European Union's current hazard-based

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[53] *Id.*
[54] *See* Diamanti-Kandarakis et al., *supra* note 10, at 295.
[55] *See* Almudena Veiga-Lopez et al., *Obesogenic Endocrine Disrupting Chemicals: Identifying Knowledge Gaps*, 29 TRENDS ENDOCRINOLOGY & METABOLISM 607, 618–19 (2018).
[56] *See* Commission Regulation 2018/605, *supra* note 1, at 33, 34; *Defining Criteria for Identifying Endocrine Disruptors in the Context of the Implementation of the Plant Protection Products Regulation and Biocidal Products Regulation,* at 6, 15, 39, 40, COM (2016) 350 final (June 15, 2016), https://ec.europa.eu/health/sites/health/files/endocrine_disruptors/docs/2016_impact_assessment_en.pdf [https://perma.cc/8FGU-ZASY].
[57] *Latest Updates of Endocrine Disruptors Regulations and Lists in EU*, CHEMSAFETYPRO, https://www.chemsafetypro.com/Topics/EU/Endocrine_Disruptors_Regulations_and_Lists_in_EU.html [https://perma.cc/NK8E-3LWB] (last visited Oct. 28, 2019).
[58] Gregory G. Bond & Daniel R. Dietrich, *Human Cost Burden of Exposure to Endocrine Disrupting Chemicals, a Critical Review*, 91 ARCHIVES TOXICOLOGY 2745, 2745–47 (2017).
[59] *See generally* USDA, 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 (Jan. 16, 2015), https://www.usda-eu.org/wp-content/uploads/2015/01/United-States-Submission-Endocrine-Disrupters-2015-01-20.pdf [https://perma.cc/VFN5-Z6JB].

approach.[60] This Note will argue in favor of the type of regulatory scheme found in the EDSP because it is a more inclusive approach and in application it will be more preventative of more chemicals, which translates into the minimization of environmental harm and danger to the public health.[61] First, this Note will cover the European Union's new classification system and their reasons for adopting it, then identify issues with the system and suggest ways to improve it based on the system used by the United States.

Since this Note will focus on the regulatory system of the European Union, it is important to note that the European Union defines endocrine disrupting chemicals as "exogenous substance[s] that cause[] adverse health effects in an intact organism, or its progeny, secondary to changes in endocrine function" and potential endocrine disrupting chemicals as "substance[s] that possess[] properties that might be expected to lead to endocrine disruption in an intact organism."[62] The World Health Organization has declared endocrine disrupting chemicals to be "a global threat."[63] Health complications as a result of these chemicals, including diagnostics and treatment, have been estimated to cost Europe over 150 billion pounds annually.[64] The new regulatory scheme impacts not just Europe but the rest of the world due to implications on international trade and agriculture.[65] The United States has taken measures to provide guidance and constructive criticism, discussing the impact of inadequate regulation from a public health perspective, but also from the international trade perspective where there is concern that trade could be adversely affected.[66] The United States has pointed out that the key to preserving public health is identifying and controlling products that may have adverse effects on the endocrine system and emphasized that "measures must be developed in accordance with scientific principles and based on the relevant scientific evidence."[67] The United States also noted in their input to the European Union that plant protection is vital, and "[i]mposing unnecessary restrictions could have far-reaching and particularly detrimental consequences."[68]

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[60] *Id.* at 3–4, 14, 16.
[61] *Id.* at 7–9.
[62] Zoeller et al., *supra* note 15, at 4098.
[63] Alyssa Alfonso, *What's More Hazardous—Endocrine Disruptors or the EU's Proposed Criteria?*, CTR. INT'L ENVTL. L., https://www.ciel.org/endocrine-disruptors-criteria/ [https://perma.cc/8VU3-5RZD] (last visited Oct. 28, 2019).
[64] *Id.*
[65] *See* USDA, *supra* note 59, at 3, 12–13.
[66] *Id.* at 17.
[67] *Id.* at 1.
[68] *Id.*

For example, pesticides that are employed for plant protection function in various ways, including preventing the spread of diseases that affect the plants and diseases that could impact humans, such as diseases that originate from the pests themselves or carcinogens from other sources.[69]

Getting greater control on the exposure of the chemicals is very important in this context because 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."[70] This is an important consideration because the regulatory structure of the pesticides and biocides and the control and exclusion of these products will directly impact the agricultural sphere and, subsequently, the international trade between the United States and the European Union.[71] In addition, pesticide regulation is critical, as well as biocide regulation, because pesticides are used to protect the public from diseases.[72] These diseases can impact both the agricultural community and the subsequent products involved in international trade, and the chemicals may also have a direct adverse impact on human health in the form of human-specific diseases and carcinogens.[73] The additional concern of inadequate pesticide regulation is that plants can serve as vectors, or nonhuman carriers of disease.[74] As it stands, the European Food Safety Authority estimates that it could cost Europe more than ten billion euros annually to both control invasive species and remedy the damage caused.[75] This cost does not even account for the cost of human disease.[76] There are other economic concerns in food production; for example, certain food products may not be as available without the use of pesticides, which in turn means that the agricultural yield could be adversely affected.[77] If the agricultural yield is adversely affected, it could affect the cost of the products, and subsequently, consumer welfare; plant-based dangers reach concerns regarding food sources, which have

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[69] *Id.*
[70] *Id.* at 12.
[71] USDA, *supra* note 59, at 3.
[72] *See generally* Commission Delegated Regulation (EU) 2017/2100 of Sept. 4, 2017, Setting Out Scientific Criteria for the Determination of Endocrine-Disrupting Properties Pursuant to Regulation (EU) No. 528/212 of the European Parliament and Council, 2017 O.J. (L 301) 2, https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R2100&from=EN [https://perma.cc/M52D-Q52J] [hereinafter Commission Delegated Regulation 2017/2100]; Commission Regulation 2018/605, *supra* note 1, at 33.
[73] *See* Commission Delegated Regulation 2017/2100, *supra* note 72.
[74] USDA, *supra* note 59, at 1–2.
[75] *Id.* at 2.
[76] *Id.*
[77] *Id.* at 2–3.

obvious implications for public health.[78] Pesticide treatments work to reduce epidemics, like the well-known Irish Potato Blight, which are a potential concern in Europe seeing as a loss of crop protection could potentially introduce diseases, and maybe even epidemics, back in to the modern world.[79] In addition, the Agriculture and Horticulture Development Board has expressed their concern 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" and in turn could impact billions worth of imports, including United States exports.[80]

III. THE PROBLEM WITH THE NEW REGULATORY SYSTEM: UNDER-INCLUSION AND OVER-EXCLUSION

On April 19, 2018, the European Union launched a new regulatory scheme for the classification of endocrine disrupting chemicals.[81] There were supporting documents, including a guidance document developed in part by the European Food Safety Authority and the European Chemicals Agency, and a "roadmap" was published that detailed the impact assessment of the regulations.[82] Specifically, the guidance documents serve the regulatory authorities on the "implementation of the scientific criteria for the determination of endocrine-disrupting properties pursuant to [the regulations]."[83] The purpose of the new criteria was to ensure a "high level of protection of both human and animal health and the environment, in particular ensuring that substances or products placed on the market have no harmful effect on human or animal health."[84] The European Union stated that the point of the new criteria is to "allow [the identification of active substances] having endocrine disrupting properties more accurately."[85] The 2018 version of the EU regulation still operates by a weight of evidence evaluation that functions by defining whether a substance has endocrine disrupting properties if: (1) there is an adverse effect in an

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[78] *Id.* at 1, 3.
[79] *Id.* at 2–3.
[80] USDA, *supra* note 59, at 3.
[81] Commission Regulation 2018/605, *supra* note 1, at 33.
[82] *Process to set scientific criteria to identify endocrine disruptors*, EUR. COMMISSION, https://ec.europa.eu/health/endocrine_disruptors/process_en [https://perma.cc/44PF-4DZ5] (last visited Oct. 28, 2019).
[83] Niklas Andersson et al., *Guidance for the Identification of Endocrine Disruptors in the Context of Regulations (EU) No. 528/2012 and (EC) No. 1107.2009*, 16 EUR. FOOD SAFETY AUTHORITY J. 1, 5 (2018).
[84] Commission Regulation 2018/605, *supra* note 1, at 33.
[85] *Id.* at 34.

organism, (2) the mode of chemical action is via the endocrine system, and (3) the adverse effect is causally related to the endocrine action.[86] The main issue is that the new regulations have not addressed the prior and ongoing problem with endocrine disrupting chemical classification.[87] The issue is that the burden of determining if a chemical is one from the class of endocrine disrupting chemicals is the aforementioned weight of the evidence approach.[88] This burden of proof is too high and therefore allows too many substances to go by unregulated.[89] The hazard identification process is not extensive, and the EU's deficiencies are centered on data collection, evaluation of the data, and the integration of the data in order to assess the endocrine disrupting properties of various chemicals.[90]

In addition to the weight of the evidence approach, the new regulatory scheme also employs a nontarget approach in conjunction with the weight of the evidence standard.[91] The nontarget approach provides that the effects of the chemicals will be assessed in relation to organisms of the same taxonomic phylum.[92] This approach, when practically applied, means the effect on nontarget organisms will not be considered unless there is special showing that it should be assessed with consideration given to nontarget organisms.[93] This approach is based on the concept that "[o]rganisms belonging to different taxonomic phyla differ biologically on essential traits, involving different endocrine modes of action."[94] There is an additional caveat where if the intended endocrine method of action produces the same effect on organisms of the same phylum as the targeted one, such a method should not be considered when the intent is to identify endocrine disruption as applied to organisms that belong to a different taxonomic phylum.[95]

Requiring a special approach to show that the chemical should even be given further consideration for analysis beyond the threshold consideration is a high burden and results in most chemicals not being regulated if it cannot be shown that they will have an adverse effect on

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[86] Melanie Gross et al., *Weight of Evidence Approaches for the Identification of Endocrine Disrupting Properties of Chemicals: Review and Recommendations for EU Regulatory Application*, 91 REG. TOXICOLOGY & PHARMACOLOGY 20, 21 (2017).
[87] *See id.*
[88] *See id.*
[89] Warhurst, *supra* note 4.
[90] Gross et al., *supra* note 86, at 21.
[91] Commission Delegated Regulation 2017/2100, *supra* note 72, at 1–3.
[92] *Id.* at 2.
[93] *See id.*
[94] *Id.*
[95] *Id.*

nontarget organisms, even if they very well may have an adverse effect.[96] The vague nontarget evidentiary approach, combined with the equally vague weight of the evidence approach provides a weak and under-inclusive regulatory scheme.[97] In addition to the under-inclusivity concern, the United States also expressed an over-inclusivity concern with the hazard-based approach where "[s]taple agricultural products such as coffee, garlic, cherries, apples, and carrots contain naturally occurring endocrine active substances—and could be construed as hazards."[98] This over-inclusion is obviously a concern since these hazards are a negligible risk as they are not inherently harmful to humans unless they are consumed in massive quantities, which is unlikely.[99] This is a key distinction between a risk-based approach and a hazard-based approach.[100]

Based on the evidentiary defects of the regulatory scheme, more research should be developed at the earlier stages to try and obtain a more comprehensive understanding of the impact of the chemicals on other organisms besides just the target species, since causation and correlation are difficult to prove.[101] This is an aspect of the program that the United States noted in their commentary, stating "[t]he omission in the [program] of references to scientific evidence and the relationship of that evidence to the options is particularly striking."[102] Based on the inherent difficulty of this task, these are inappropriate standards to determine whether a chemical is harmful and should therefore be regulated. The key to maximizing protection from endocrine disrupting chemicals is to continually try to understand them and how they function, so that it will be easier to not just prevent exposure from known endocrine disruptors, but also to predict what effects other chemicals may have that are not already classified as endocrine disruptors. The weight of evidence and the target/nontarget approaches are too broad and vague, and do not invest enough exploration into determining as much as possible about the scope of the types of potentially harmful chemicals and unknown impacts on public health.[103] If a chemical is suspected to be a potential endocrine disruptor, the initial response should be to attempt to determine the response with organisms, not just target organisms, but nontarget as well. The weight of evidence

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[96] *See id.* at 2.
[97] *See* USDA, *supra* note 59, at 17.
[98] *Id.* at 4.
[99] *Id.*
[100] *Id.* at 10.
[101] *Id.* at 15.
[102] *Id.* at 5.
[103] USDA, *supra* note 59, at 5.

approach was the issue with the European Union's former regulatory scheme and, because the new scheme still uses the same burden of proof, the underlying issue of under-inclusion and inadequate protection from the chemicals has yet to be addressed by the new classification scheme.[104]

Another criterium that gives cause for concern, for much the same reason, is that "presumed and suspected EDCs are excluded from the criteria," which implicates the notion that only the "EDCs that have been *proven* to have adverse effects on humans" are included in the regulatory scheme.[105] This standard of inclusion obviously excludes many unknown hazardous chemicals and allows for these substances to go unregulated since it limits "the scientific evidence considered."[106] Again, the result of this overly high burden of proof is that chemicals will be excluded from classification despite "the high likelihood they are harmful to human health."[107] Despite the concerns that were voiced from other countries, including the United States, during the drafting of the new regulations, the current standard for a chemical to be considered as having endocrine disrupting properties is if "it shows an adverse effect in [an intact organism . . .] which is a change in the morphology, physiology, growth, development, reproduction or life span of an organism . . . that results in an impairment of functional capacity . . . ."[108] The main issue that remains unaddressed is the "adverse effect" language. This "adverse effect" language implies that the chemical in question needs to have *already* demonstrated harmful impacts on the endocrine system.[109] The criteria does not allow for the possibility that a chemical may be harmful and so there is not any research done into potential harms, since it is just assumed that if the chemical is not known to show adverse effects then it will not be considered in the classification system.[110] This system is still based on a hazard approach, rather than a risk assessment approach, where the aforementioned weight of the evidence approach is used to determine if a chemical is a hazard or not for the purposes of classification and subsequent regulation.[111]

Overall, the issue with the new regulation is the hazard-based approach, which utilizes the weight of the evidence approach rather than a risk assessment–based approach, and uses a lower burden of proof where

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[104] *Id.* at 15–16.
[105] Alfonso, *supra* note 63.
[106] *Id.*
[107] *Id.*
[108] Andersson et al., *supra* note 83, at 7.
[109] *See id.*
[110] *See id.*
[111] *See id.*

chemicals that may have the potential to be harmful are assessed.[112] These concerns are shared with other countries, including the United States, and public health organizations in Europe and across the globe.[113] The United States has attempted to advise the EU that their hazard based approach would impose limitations without a solid basis of risk and would also be lacking in evaluating potential impacts on health, which includes beneficial impacts as well as adverse impacts.[114] Further, the United States pointed out that the EU's overall plan for their regulatory scheme should first identify the scientific evidence that serves as the basis for each classification and provide an explanation of the evidence and methodology.[115] The United States' report emphasizes that the EU has failed to do so, in addition to also failing to provide adequately supported impact assessments in a way that is transparent so that the public can remain informed and easily access the information.[116] The risk assessment approach would likely employ more resources devoted to scientific research at the initial stages of screening the chemicals, and would therefore require a budget restructuring to account for the investment.[117] This Note argues that the investment would pay off in terms of increasing the general health and well-being of the public by decreasing exposure to these toxic materials that are found everywhere and can have dramatic effects on our bodies.

IV. THE UNITED STATES ENVIRONMENTAL PROTECTION AGENCY'S ENDOCRINE DISRUPTOR SCREENING PROGRAM IS A BETTER MODEL FOR CLASSIFICATION AND REGULATION

A better example of a classification scheme for the EDC's can be found in an EPA regulatory program, the Endocrine Disruptor Screening Program, that is "designed to screen and test chemicals for potential endocrine bioactivity, and the risk of endocrine disruption in humans and wildlife."[118] This program is designed to operate the way the critics of the

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[112] *See id.*
[113] *See generally* USDA, *supra* note 59.
[114] *Id.* at 4.
[115] *Id.*
[116] *Id.* at 4–6.
[117] *See generally* Lyons, *supra* note 4 (providing background to the method and costs of the risk assessment approach).
[118] Natalia Garcia-Reyero & Cheryl A. Murphy, *Advancing Adverse Outcome Pathways for Risk Assessment*, *in* A SYSTEMS BIOLOGY APPROACH TO ADVANCING ADVERSE OUTCOME PATHWAYS FOR RISK ASSESSMENT 5 (Natalia Garcia-Reyero & Cheryl A. Murphy eds., 2018).

EU regulations want it to work.[119] The purpose of the EDSP is to allow the EPA to assess the risks associated with the chemicals and take subsequent remedial measures to address the risk.[120] In 1996, the United States Congress mandated that the EPA develop the program primarily to identify pesticides that had detrimental effects.[121] The Food Quality Protection Act states that the EPA needs to make safety finding of "reasonable certainty that no harm" would come from an "aggregate exposure" to the chemicals.[122] The EPA regulates the chemicals utilizing a risk-based approach, and one of these methodologies is the Endocrine Disruptor Screening Program.[123] The EDSP is an intensive screening process that assesses potential risks of chemicals, and uses an "Adverse Outcome Pathway ("AOP") framework" that focuses on the toxicity pathways of potential toxins and to assess them, uses linkages of biologically likely mechanistic relationships to show biological pathways or emphasize a lack of understanding of certain pathways.[124] In more concise terms, the proper regulation requires "hazard identification, hazard characterization, exposure assessment, and risk characterization."[125] This approach is based on the general distinction between the risk-based and hazard-based approaches.[126] The EU's regulatory scheme uses the first two criteria, while the U.S. regulations use all four steps of risk analysis.[127] The EDSP has three stages of implementation: prioritization, screening, and testing.[128] The screening process is described in further detail below, as well as deficiencies in the system.

The United States' risk assessment approach consists of a two-tiered screening process where the first phase screens chemicals to test for potential interactions, adverse or otherwise, with the endocrine system.[129] Tier 1 screening data is the threshold for determining a chemical's

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[119] *Id.* at 16.
[120] National Archives and Records Administration, Endocrine Disruptor Screening Program, Policies and Procedures for Initial Screening, 74 Fed. Reg. 17,560, 17,561 (Apr. 15, 2009), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2007-1080-0029 [https://perma.cc/G8HE-N7WF].
[121] USDA, *supra* note 59, at 7.
[122] *Id.*
[123] *Id.*
[124] *Id.* at 7–9.
[125] *Id* at 7.
[126] Lyons, *supra* note 4.
[127] USDA, *supra* note 59, at 7.
[128] *Id.* at 8–9.
[129] *Id.* at 7–8.

potential to interact with the endocrine system.[130] This phase requires the development of a chemical screening program where the testing used is appropriately validated and the results are meant to indicate the presence of hormonal effects.[131] The specific systems that are examined include the thyroid, estrogen, and androgen hormone systems.[132] If a chemical is found to show potential interaction, the chemical is moved to the second phase.[133] The second phase consists of looking further into the interactions, determining exactly what kind of interaction occurs, and what dose or amount of the chemical constitutes the threshold amount to cause the interaction.[134] The Tier 2 testing phase also sets out a qualitative correlation between the dose, or amount, of the chemical and the resulting adverse effect.[135] This information is combined with information regarding exposure and this produces a risk assessment to support mitigation measures and subsequent regulatory decisions.[136] Specifically, this information is used to assess if a certain chemical or other substance found in sources accessible to humans, like sources of drinking water, poses a risk to the environment and public health.[137] This kind of method employs high throughput assays that allow for a variety of chemicals to be efficiently evaluated for bioactivity and biochemical interactions with the chemicals.[138] In addition, there are advanced computational methods used to measure

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[130] *Endocrine Disruptor Screening Program Tier 1 Assessments*, EPA, https://www.epa.gov/ingredients-used-pesticide-products/endocrine-disruptor-screening-program-tier-1-assessments [https://perma.cc/TE79-YLRC] (last updated June 14, 2017).

[131] Endocrine Disruptor Screening Program; Final Second List of Chemicals and Substances for Tier 1 Screening, 78 Fed. Reg. 35,922, 35,922 (June 14, 2013), https://www.federalregister.gov/documents/2013/06/14/2013-14232/endocrine-disruptor-screening-program-final-second-list-of-chemicals-and-substances-for-tier-1 [https://perma.cc/YPP9-SDGA].

[132] *Id.*

[133] *Id.*

[134] USDA, *supra* note 59, at 8.

[135] *See generally EDSP Overview*, *supra* note 3; *Endocrine Disruptor Screening Program (EDSP) Universe of Chemicals*, EPA, https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-edsp-universe-chemicals [https://perma.cc/53QV-LDBY] (last updated Feb. 22, 2017) [hereinafter *EDSP Universe of Chemicals*] (providing background information about Tier 2 testing related to the EDSP and Risk Assessment Approach).

[136] *See generally EDSP Overview*, *supra* note 3; *EDSP Universe of Chemicals*, *supra* note 135.

[137] *How Does EPA Use Information from the Endocrine Disruptor Screening Program?*, EPA, https://www.epa.gov/endocrine-disruption/how-does-epa-use-information-endocrine-disruptor-screening-program [https://perma.cc/FKX8-WN3X] (last updated Aug. 30, 2016).

[138] *Use of High Throughput Assays and Computational Tools in the Endocrine Disruptor Screening Program*, EPA, https://www.epa.gov/endocrine-disruption/use-high-throughput-assays-and-computational-tools-endocrine-disruptor [https://perma.cc/YP3N-5K9U] (last updated Feb. 22, 2017).

bioactivity.[139] The computational modeling, combined with molecular biology, is used with in vitro methodologies that allow for detection of endocrine-specific events and pathways, an entire process that helps prioritize the information found in the Tier 1 phase of the research.[140]

While the EDSP is a more preventative approach, it is not without its deficiencies.[141] Firstly, the program sometimes fails to validate the Tier 1 and Tier 2 testing, which is an issue because the process of validation is what determines if the information is reliable.[142] Secondly, some of the Tier 1 tests often result in false positives where the results say the endocrine system is impacted when it may not actually affect it at all.[143] However, even though the methodology is not perfect, the EPA has made efforts over the recent years to reevaluate it and now employs new computational methods to estimate the risk to humans and the environment.[144] Specifically, "pathway frameworks may be used to evaluate the predictive performance of one or more computational models to predict downstream key events."[145] These computational approaches may be able to serve as an alternative to the typical Tier 1 screening approach at some point.[146] This kind of proactive, research-heavy, and focused approach is what the current EU criteria is missing, and this kind of approach would address the widespread critique of the overly high burden of proof and over-exclusion of potential toxins while improving detection and identification of endocrine disrupting chemicals.[147]

CONCLUSION

The endocrine system is a complex and delicate physiological network that is easily corrupted by both internal and external factors,

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[139] *Id.*
[140] *EDSP in the 21st Century*, *supra* note 3.
[141] *The EPA's Endocrine Disruptor Screening Program*, PETA, https://www.peta.org/issues/animals-used-for-experimentation/epa-edsp/ [https://perma.cc/GKN6-25ME] (last visited Oct. 28, 2019).
[142] *Id.*
[143] *Id.*
[144] *Id.*
[145] Patience Browne et al., *Use of High-Throughput and Computational Approaches for Endocrine Pathway Screening*, *in* A SYSTEMS BIOLOGY APPROACH TO ADVANCING ADVERSE OUTCOME PATHWAYS FOR RISK ASSESSMENT 15 (Natalia Garcia-Reyero & Cheryl A. Murphy eds., 2018).
[146] *Id.*
[147] *See generally* USDA, *supra* note 59, at 17 (providing background information as to why the United States follows a risk-based approach and why the EU does not).

including toxins like endocrine disrupting chemicals which are both naturally occurring and synthetic, and can originate from a variety of sources.[148] Because of the complexity of the interactions within the endocrine system, it is difficult to pinpoint exactly what chemicals harm the endocrine system, and even once a toxin is identified, it is difficult to measure the scope of the impact or confirm causation.[149] There is additional complexity given that there is often a disconnect between the scientific research and methodology used in policy implementation.[150]

The EU's new regulatory scheme is a hazard-based approach that does not provide enough specificity and will continue to allow too many potential toxic chemicals to go unregulated, or will over-regulate chemical sources that are not a real concern. The United States' Endocrine Disruptor Screening Program, overseen by the EPA, is a more inclusive and preventative approach that provides for a more comprehensive level of protection and screening that utilizes the same initial approach as the EU, but adds several additional steps to further assess risk.[151] The EU should incorporate aspects of this program into its own regulatory scheme, with emphasis on an elevated burden of proof, as opposed to the current "weight of the evidence" standard. The elevated burden of proof will place the focus on more preventative screening, which in turn will ensure more chemicals will be regulated and exposure to harm will be minimized. This minimization will cut the cost of medical expenses, prevent disease, preserve the agricultural markets, and will further protect the health of international trade. The EU should revise their regulatory scheme of endocrine disrupting chemicals, and look to the EPA's Endocrine Disruptor Screening Program for guidance. A regulatory scheme for substances such as these chemicals, that are difficult to identify and trace, should have a more prevention-based focus so as to avoid any under-inclusion and overly harmful exposure.

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[148] For further explanation, *see supra* Part I.
[149] *Id.*
[150] Marlene Agerstrand et al., *An Academic Researcher's Guide to Increased Impact on Regulatory Assessment of Chemicals*, 19 ENVTL. SCI.: PROCESSES & IMPACTS 645, 651 (2017).
[151] *See generally* USDA, *supra* note 59, at 7–8 (providing additional support for why the EDSP might be more comprehensive and successful than the EU's approach).