European Commission

Report on

Public consultation on defining criteria for **identifying endocrine disruptors** in the context of the implementation of the Plant Protection Product Regulation and Biocidal Products Regulation

Health and Food Safety

EUROPEAN COMMISSION

DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Brussels, 22th of July 2015
Ares (2015)3022734

Subject: **Report on public consultation on defining criteria for identifying endocrine disruptors in the context of the implementation of the Plant Protection Product Regulation and Biocidal Products Regulation**

Executive summary

Open public online consultations are systematically part of the consultation strategy for initiatives subject to impact assessments. A public consultation on defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and the biocidal products regulation took place from 26 September 2014 to 16 January 2015 by on-line consultation questionnaire. The usual consultation period (12 weeks) has been extended to provide stakeholders with sufficient time for comments. Submissions were accepted in any official EU language. Responses could be transmitted through the online questionnaire, as well as via e-mail. The public consultation generated over 27 000 responses which illustrates the significant public interest in the EU endocrine disruptors policy. The submissions received on line can be found at the website of Directorate-General for Health and Food Safety[1].

Respondents came from various parts of society and included doctors, farmers, non-governmental organisations, chemical, electronic, food and medical devices industry, water companies and scientists) showing the diversity of use of these chemicals. This shows how widely these chemicals are used. Individual responses (as opposed to responses of behalf of organisations) accounted for more than 90% of the responses received. Of these individual responses, 88% came from seven Member States (Austria, Denmark, France, Germany, Spain, Sweden and the United Kingdom). 863 responses were made on behalf of an organisation and 64% of these came from one Member State (United Kingdom). Almost 26% of the responses on behalf of an organisation came from of industry or trade organisations and 5% from consumer/non-governmental organisations. Only two health institution and hospitals responded. Three EU-governments as well as 18 authorities have sent comments. Six public authorities and six governments from non-EU countries gave their comments.

The objective of this consultation was to gather information for the impact assessment on the establishment of criteria to identify endocrine disruptors. This objective was reached as there were many respondents that provided information. The public consultation generated a great deal of data consisting of scientific articles, studies, reports, views and legal opinions. The Annex provides an overview of the type of impacts that respondents indicated and the articles and studies they referred to.

[1] https://ec.europa.eu/info/consultations/public-consultation-defining-criteria-identifying-endocrine-disruptors-context-implementation-plant-protection-product-regulation-and-biocidal-products-regulation_de#consultation-outcome.

Commission européenne/Europese Commissie, 1049 Bruxelles/Brussel, BELGIQUE/BELGIË - Tel. +32 22991111
Office: DM24 2/44 - Tel. direct line +32 229-02 2950178

The opinions of respondents varied significantly on the options for criteria for determination of endocrine disrupting properties (options 1-2-3-4) and for approaches to regulatory decision making (options A-B-C). The public consultation report provides an overview on the submitted arguments by respondents in favour and against the options as included in the roadmap. In general, respondents expressed diverging views on how to define criteria and how endocrine disruptors should be regulated. Overall, responses suggested that there is a need for the EU to establish definitive criteria by the European Union for endocrine disruptors. Option 1 (no policy change, the interim criteria set in the plant protection products and biocidal products regulations continue to apply) is not therefore supported by the consultation.

Many respondents raised issues in relation to food safety, the threat that endocrine disrupting substances might pose to human health and/or the environment and the impact of the different options proposed in the roadmap on agriculture, industry, health and environment. In particular farmers and agri-business highlighted the potential high implications of setting criteria to identify endocrine disruptors on agriculture. Authorities from non-EU countries stressed the potential impact on trade. A risk-based approach for regulating endocrine disruptors was proposed by many respondents who identified themselves as farmers, private companies, industrial or trade organisations, or authorities in non-EU countries. Many respondents supported the use of the WHO/IPC 2002 definition as a starting point for defining an endocrine disruptor. Authorities in non-EU countries noted that any decision on endocrine disruptors must respect the principles of the World Trade Organisation.

The public consultation provided an overview on the type and size of impacts that may occur if a chemical would be identified as an endocrine disruptor, the methodologies that may be used to obtain this type of information and also data and references to studies and articles to be considered in the impact assessment. The outcome of the public consultation provided useful input for impact assessment process that addresses the economic, environmental and health impacts of the different policy options.

Contents

1. INTRODUCTION

The Plant Protection Products Regulation (EC) 1107/2009[2] and the Biocidal Products Regulation (EU) 528/2012[3] provide for the establishment, by December 2013, scientific criteria to identify substances with endocrine disrupting properties3.

The European Commission is carrying out a comprehensive impact assessment to analyse different options for defining the criteria to identify endocrine disruptors following standard rules for impact assessments as part of policy making.

This impact assessment is considered a key element supporting the decision-making in this area as to date there is no consensus on how to address endocrine disruptors scientifically. Besides, from a regulatory perspective, the definition of the criteria may also impact on other pieces of legislation (e.g. REACH Regulation, Cosmetics Regulation, Water Framework Directive), and the potential health, environmental and socio-economic impacts of the different options for defining the criteria are not yet fully known and might be significant.

The roadmap for the impact assessment was published in June 2014. It sets out different options for setting EU criteria for identifying endocrine disruptors (outlined as "EU criteria to

[2] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:309:0001:0050:EN:PDF.

[3] Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:167:0001:0123:EN:PDF.

identify ED"), including the baseline (interim criteria), and approaches to regulatory decision making[4].

From 26 September 2014 to 16 January 2015, a public consultation took place on defining criteria for identifying endocrine disruptors as part of implementing the Plant Protection Products Regulation and the Biocidal Products Regulation took place by on-line consultation questionnaire. The standard consultation period (12 weeks) was extended to provide stakeholders with sufficient time for comments.

Open public online consultations form a systematical part of the consultation strategy for measures that require an impact assessment. Stakeholder consultation helps to make EU law making transparent, well targeted and consistent. It is enshrined in the Treaties. Consultations - together with impact assessments, evaluations and expertise - are a key tool for transparent and informed policy making. They help make decisions that respect principles of proportionality and subsidiarity and that are based on evidence, including the experiences and views of those affected by the policy and those involved in implementing the policy. The Commission consults widely, at each stage of the policy cycle, respecting principles of openness and transparency and following minimum standards that are generally acknowledged as appropriate and in line with international best practice.

Given the complexity and the sensitivity of the issue, the European Commission was particularly interested in gathering data to inform its impact assessment through this public consultation. Open questions also allowed respondents to submit comments, data or information.

More than 27,000 responses were received (about 22, 000 responses via the online questionnaire and about 5,000 replies via the functional mailbox), which were published on DG SANTE website at the beginning of February. Respondents that asked to keep anonymity were not published. Over 25,000 of the responses received (i.e. more than 90%) were received via two NGO campaigns.

It should be noted that this public consultation resulted in one of the highest number of responses among the public consultations launched so far by the European Commission. The amount of participation clearly underlines the significant interest from stakeholders and the general public in this issue.

This consultation was different from other public consultations in that respondents were asked to provide data (for example methodologies used to select endocrine disrupting substances or to identify the socio-economic impact of identified endocrine disruptors). No specific questions were included that asked respondents' opinions. This report cannot, therefore, provide quantitative information on the views held by different stakeholders.

This report sets out an analysis of the responses received by the Commission services during the consultation and complements the full responses published on DG SANTE website[5].These views in the report should not be regarded as the views of the European Commission or its staff.

[4] For the roadmap see: https://ec.europa.eu/info/consultations/public-consultation-defining-criteria-identifying-endocrine-disruptors-context-implementation-plant-protection-product-regulation-and-biocidal-products-regulation_en.

[5] https://ec.europa.eu/info/consultations/public-consultation-defining-criteria-identifying-endocrine-disruptors-context-implementation-plant-protection-product-regulation-and-biocidal-products-regulation_en.

2. HISTORIC AND LEGAL SETTING

2.1. EU policy on endocrine disruptors

In the middle of the 1990s, scientific discoveries about endocrine disruption, and the fact that commonly occurring contaminants can interfere with the natural hormonal signals controlling foetal development, started to attract worldwide attention.

In 1999 the Commission Scientific Committee for Toxicity, Ecotoxicity and the Environment (SCTEE)[6] stated that endocrine disruptors posed a 'potential global problem for wildlife and this opinion formed the basis for the 1999 Community strategy for endocrine disruptors[7]. The Strategy sets out 11 actions to address the problem of endocrine disruptors, ranging from soft measures, such as communication activities, to hard measures, taking legislative action.

The Strategy still governs the EU actions on endocrine disruptors: in recent years, it has led to the inclusion of specific provisions on endocrine disruptors in various pieces of EU legislation. In chronological order, these are: the Water Framework Directive[8], the chemicals regulation REACH[9], the Plant Protection Products Regulation and the Biocidal Products Regulation. Provisions governing endocrine disruptors are also included in the Regulations on Cosmetics[10] and EC proposal of the EC for Medical Devices[11].

The Plant Protection Products Regulation and the Biocidal Products Regulation provide for the establishment, by December 2013, of scientific criteria to identify substances with endocrine disrupting properties by December 2013. Until these scientific criteria are defined, protective interim criteria defined in the legislation apply. Exposure to residues of endocrine disruptors in food must be reduced at or below the analytical limit of detection.

It is important to note that the criteria that the Commission will draw up will apply directly to the Plant Protection Products Regulation and the Biocidal Products Regulation but they may have repercussions to other EU legislation containing specific provisions governing endocrine disruptors.

2.2. The on-going impact assessment

During the preparatory work to set scientific criteria for defining endocrine disruptors, the European Commission realised that diverging views still exist on many points within the scientific community and amongst regulators worldwide. Stakeholders also indicated diverging views on the potential impacts of setting criteria and there are no legally-binding criteria in

---

6 http://ec.europa.eu/food/fs/sc/sct/out37_en.pdf.

7 http://ec.europa.eu/environment/chemicals/endocrine/strategy/index_en.htm.

8 http://ec.europa.eu/health/endocrine_disruptors/docs/wfd_200060ec_directive_en.pdf.

9 http://ec.europa.eu/health/endocrine_disruptors/docs/reach_1907_2006_regulation_en.pdf.

10 http://ec.europa.eu/health/endocrine_disruptors/docs/cosmetic_1223_2009_regulation_en.pdf.

11 http://ec.europa.eu/growth/sectors/medical-devices_old/documents/revision/files/revision_docs/proposal_2012_542_en.pdf.

non-EU countries to identify endocrine-disrupting chemicals. This adds to the complexity of the link between scientific and regulatory aspects making decision-making on endocrine disruptors particularly challenging. As a result, the Commission decided it needed to develop a better understanding of the health, environmental and socioeconomic of endocrine disruptors.

The Commission decision to launch an impact assessment is in line with the standard procedure for all Commission measures or decisions which are expected to have significant impacts. It is also in line with the 7th Environment Action Programme (EAP).

The roadmap for the impact assessment was published in June 2014. The first studies supporting the impact assessment are currently underway and others are planned. In the autumn of 2014, the Commission carried out a public consultation, which is part of a broader transparency and stakeholders' involvement exercise. In 2015, several events (three round tables and one public conference held on the 1st of June 2015) were organised to update stakeholders, Members of the European Parliament, Member States and non-EU countries on the progress made on the impact assessment on criteria to identify endocrine disruptors and to give them the opportunity to express their views and discuss the issue. More targeted events, meant to update and inform interested parties on specific points of the impact assessment, may be organised later in the process. The Commission has also launched a webpage focussing on the impact assessment on criteria to identify endocrine disruptors on the Health and Food Safety section of the Commission's website[12]. This webpage is updated regularly with relevant information concerning the impact assessment.

The Commission will take a decision on the criteria when the impact assessment has been carried out.

3. METHODOLOGY OF PUBLIC CONSULTATION

The on-line consultation questionnaire on defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and the biocidal products regulation was provided in English. The public consultation took place from 26 September 2014 to 16 January 2015 by on-line consultation questionnaire[13]. Participants were invited to read the roadmap for background information before answering the questionnaire. This on-line consultation was open to all interested parties. In order to ensure all relevant stakeholders were informed the Commission published a press-release[14] at the launch of the public consultation and the questionnaire was available on DG SANTE website and "Your voice in Europe"[15].

The usual consultation period (12 weeks) has been extended to provide stakeholders with sufficient time for comments. Responses were accepted in any official EU language, as well as via e-mail. Participation to the consultation was acknowledged.

---

12 https://ec.europa.eu/health/endocrine_disruptors/overview_en

13 For the consultation document see: https://ec.europa.eu/info/consultations/public-consultation-defining-criteria-identifying-endocrine-disruptors-context-implementation-plant-protection-product-regulation-and-biocidal-products-regulation_en

14 For the press-release see link: https://ec.europa.eu/commission/presscorner/detail/en/IP_14_1057.

15 http://ec.europa.eu/yourvoice/consultations/2015/index_en.htm.

Respondents could indicate how the contribution would appear: under the name supplied (and consent to the publication of all the information in the contribution), anonymously (and consent to the publication of all the information in the contribution, except the name/the name of the organisation) or ask for confidential treatment of the contribution and do not give consent for publication.

It is important to note the objective of the public consultation was to gather data (for example methodologies used to select endocrine disrupting substances or the socioeconomic impact of identified endocrine disruptors) and not the views of stakeholders. As a result, no specific questions were included asking the opinion of respondents.

The online consultation questionnaire was composed of four parts.

The first part was to gather information about the respondents. They had to identify themselves and indicate whether they were replying as a(n) 'individual/citizen/consumer' or 'on behalf of an organisation'.

If they were replying on behalf of an organisation, they had to specify whether they were representing:

(1) 'a public authority';

(2) 'an academic/research institution';

(3) 'a hospital/health institution';

(4) 'a private company';

(5) 'agricultural producers';

(6) 'consumer/ non-governmental organisation';

(7) 'industrial or trade association'; or

(8) 'other'.

The second part of the online consultation questionnaire contained questions on the options for criteria for determining endocrine disrupting properties (options 1, 2, 3 and 4 as outlined in the roadmap).

For each of the four options, there were four sets of questions. Respondents were first asked whether they had conducted or were aware of an assessment of substances which would be identified as endocrine disruptors according to each of the four options. They were then asked whether they were aware of any assessment(s) of substitutability of these substances. Finally, they were asked if they were aware of any assessment(s) of the socioeconomic impact of regulating these substances without further risk assessment. For each of these first three sets of questions, they were invited to describe the methodology(ies) and the outcome(s) of the assessment(s) and to provide reference(s) whenever possible.

The last question enabled them to add any other comment they may have had regarding each option.

The third part of the online consultation questionnaire contained questions on options for approaches to regulatory decision making (options A, B and C as outlined in the roadmap).

For each of the three options, there were two sets of questions. Respondents were first asked whether they had conducted or were aware of an assessment applying any of the three different options for regulatory approaches to decision making (option A-C) to substances identified as endocrine disruptors by any of the options for defining criteria (option 1-4). They were then asked whether they had conducted or were aware of an assessment of the socio economic impact of the three different options for regulatory approaches to decision making (option A-C) for substances identified as endocrine disruptors using any of the options for defining criteria (option 1-4). For each of these sets of questions, they were invited to describe the methodology(ies) and the outcome(s) of the assessment and to provide the reference(s) whenever possible.

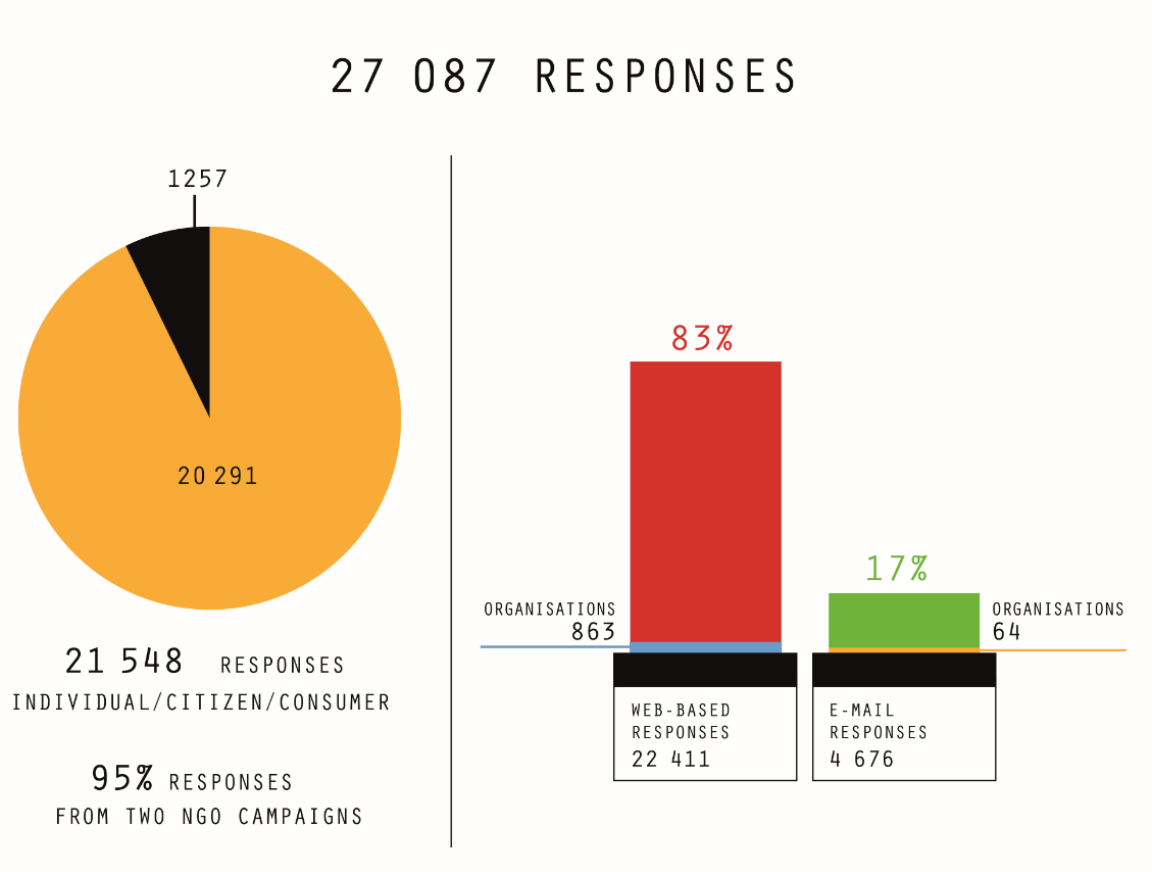
The fourth part of the online consultation questionnaire invited respondents to provide any other data or information that could help the Commission to conduct its impact assessment.

4. STATISTICS FOR CONSULTATION RESPONSES

The Commission received a total of 27.087 responses, consisting of 22.411 web-based responses and 4.676 email responses. Please note that affiliation (public authority, academic/research institution, hospital/health institution, private company, agricultural producers (farmers), consumer/non-governmental organisation, industrial or trade association) is based on self-identification by respondents and has not been validated.

Respondents were asked if they were responding on behalf of an organisation or as an 'individual/citizen/consumer' (see figure 1). The public consultation received 21548 and 863 web-based responses from those identifying themselves as 'individual/citizen/consumer' and organisations, respectively (see figure 1). Of the 4676 email-responses 64 could be considered as being on behalf of organisations. It is important to note that verification for email-responses was limited as many respondents did not include information about the type of organisation they represented (see figure 1).

Figure 1. Distribution of responses of 'individuals/citizens/consumers' and 'organisations' to the public consultation.



Of the 863 web-based responses on behalf of organisations many respondents identified themselves as farmers, private companies, and industry and trade organisations (see figure 2).

Figure 2. Web-based responses on behalf of organisations.

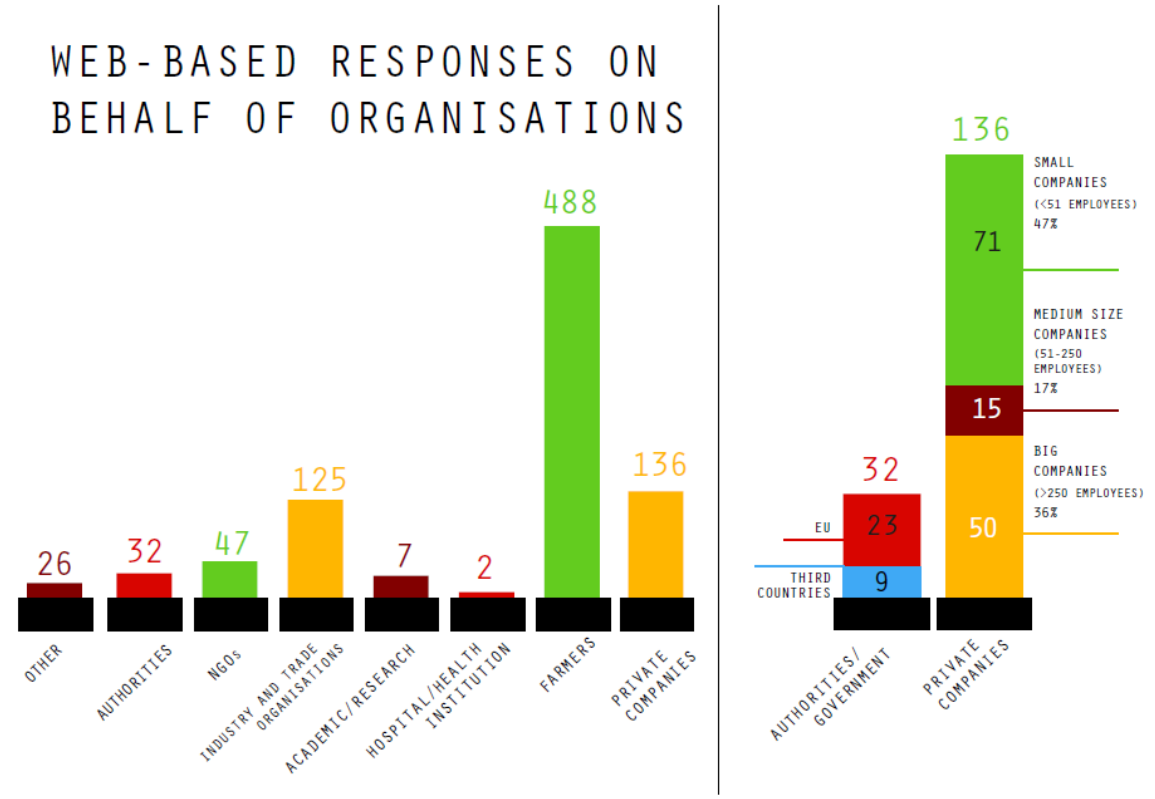
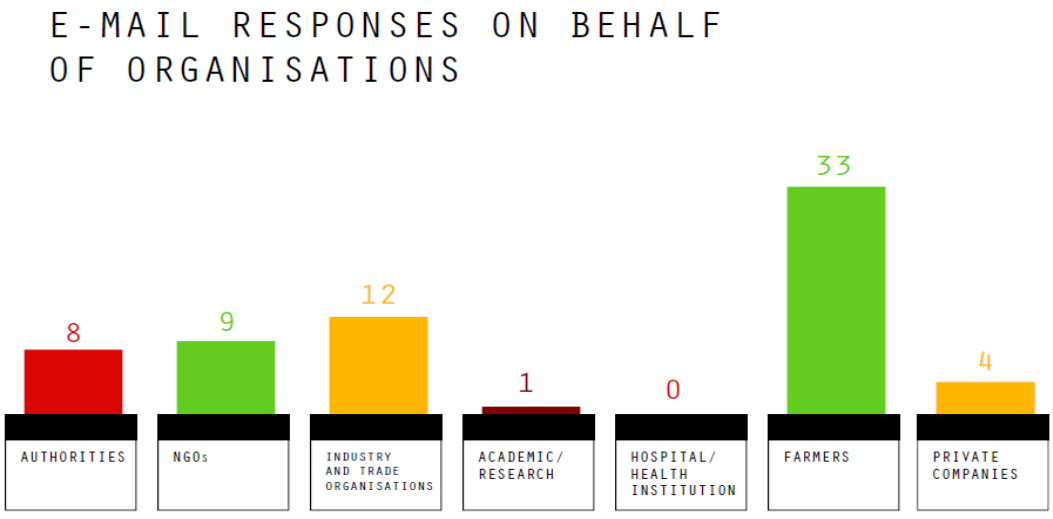
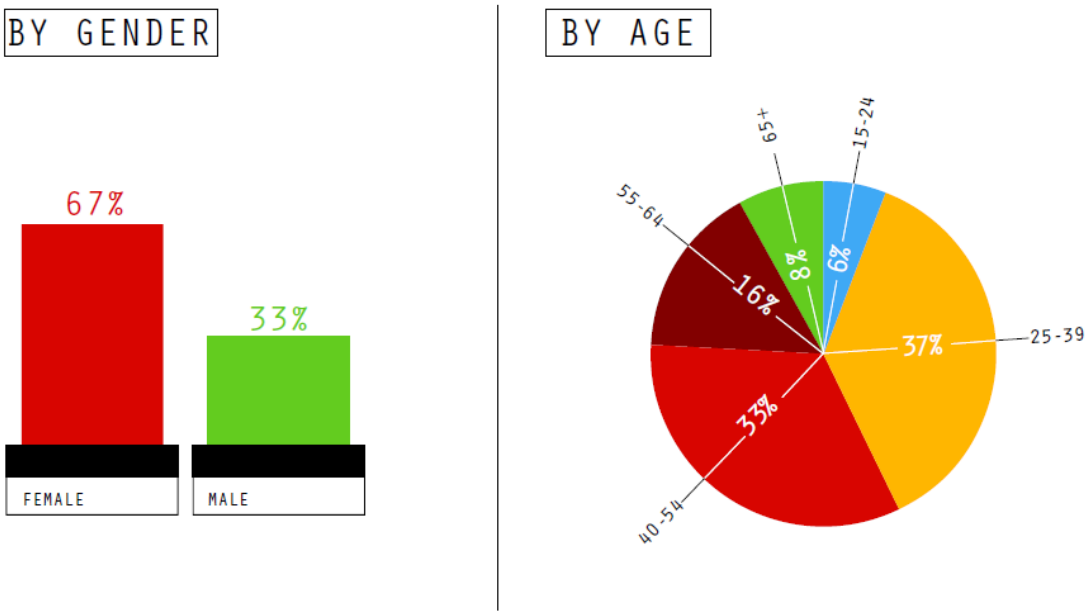


Figure 3. Email responses on behalf of organisations.



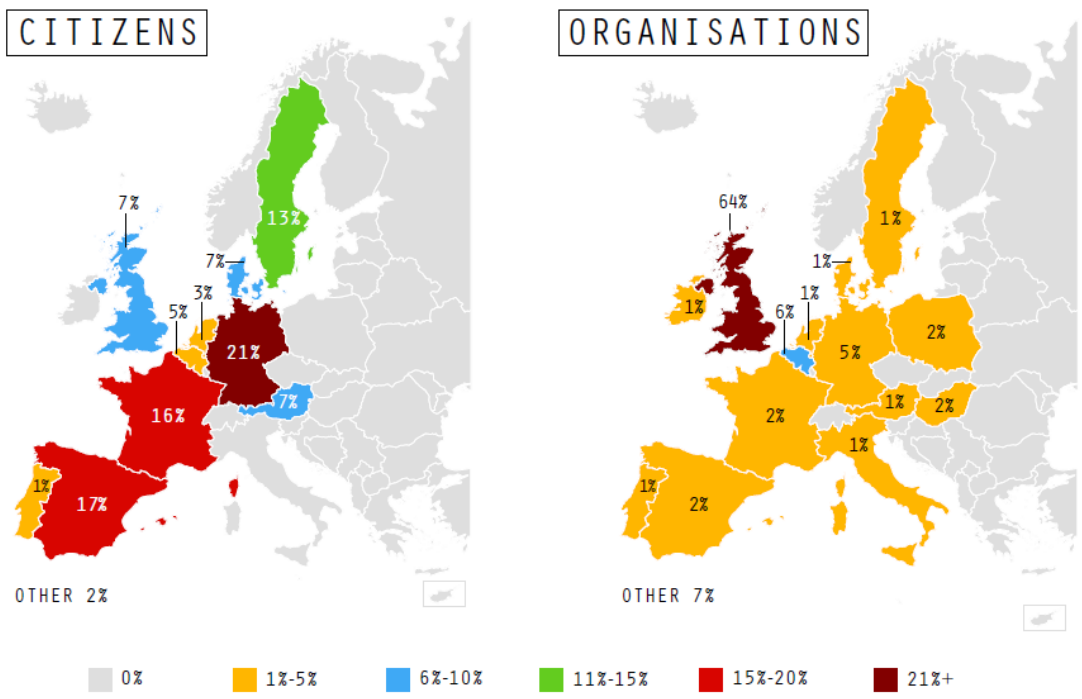
A similar picture appeared for email-responses (see figure 3). Of the responses of authorities most originated from within the EU (78%) and a minority from third countries (22%, see figure 2). Most of the companies (63%) classified themselves as small companies (see figure 2).

Figure 4. Distribution of replies of citizens by gender and age.



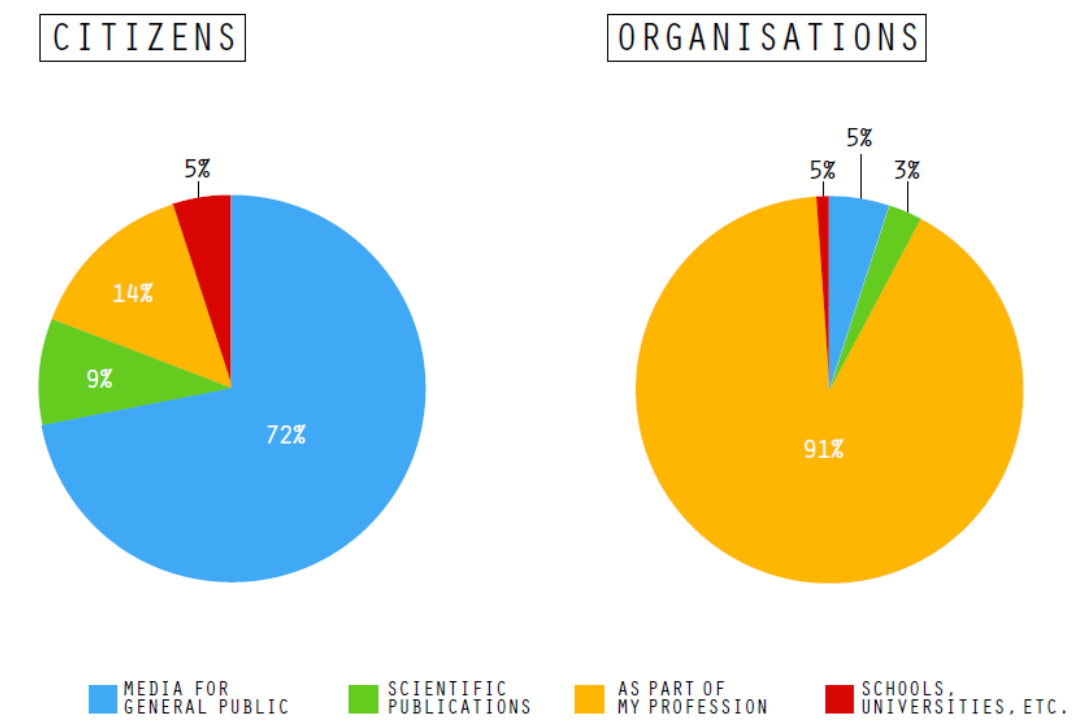
Of the web-based responses from 'individual/citizen/consumer' 95% originated from a campaign encouraging individuals to participate in the public consultation (see figure 1). Most respondents were female and in the age between 25-54 years (see figure 4).

Figure 5. Geographical distribution of web-based responses.



The largest number of web-based responses from 'individual/citizen/consumer' came from Germany, Spain, France and Sweden. Together these countries accounted for almost 70% of the responses (see figure 5). The high response in those countries was likely due to the popularity of the campaigns encouraging people to respond. Of the web-based responses for organisations 64% of the responses came from the United Kingdom (see figure 5). Most of these respondents identified themselves as farmers.

Figure 6. Source of information leading to pariticpation in public consultation.



Of the web-based responses from 'individual/citizen/consumer' the respondents indicated to have become aware of the discussions about endocrine disrupting chemicals by media for the general public (see figure 6). Organisations indicated to be mostly informed as part of their profession (see figure 6).

Figure 7. Involvement of respondent in EU legislation the last 3 years before the public consultation took place and the type of NGO.

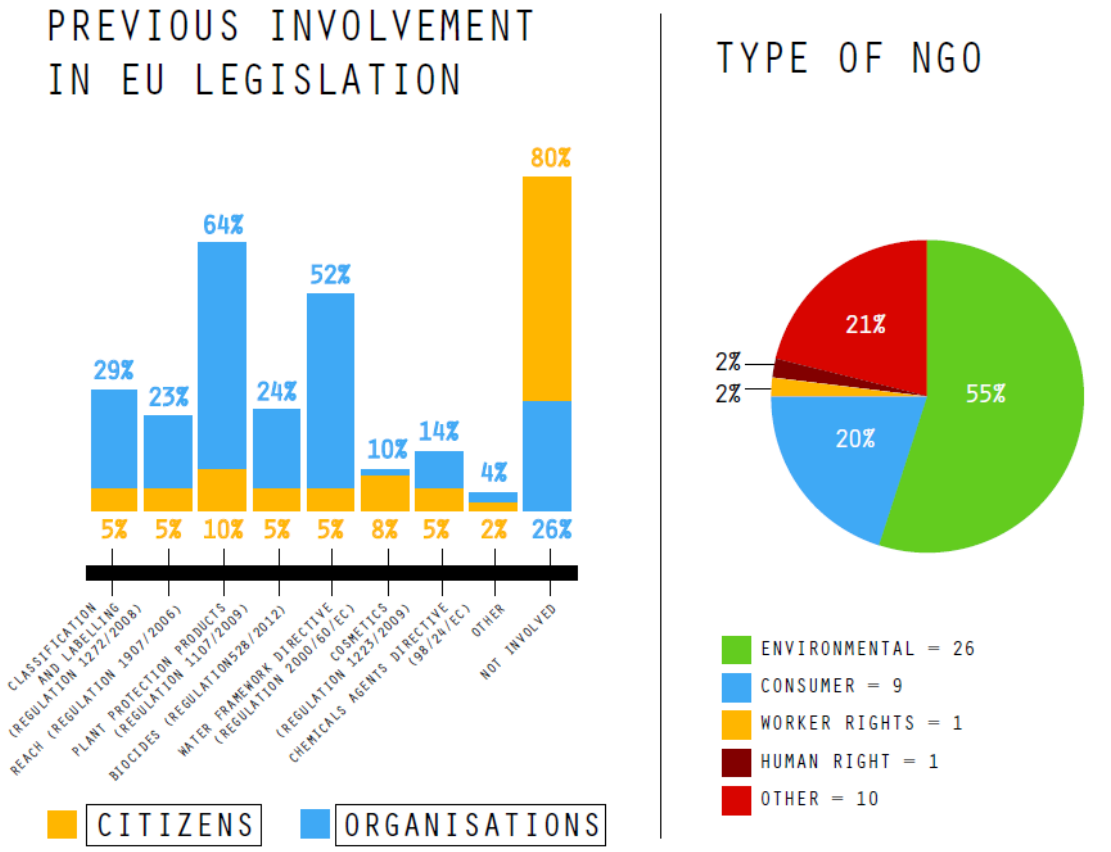


Figure 6

Of the web-based responses from 'individuals/citizens/consumers' 80% of the respondents indicated that they had not previously been involved in EU legislation. Many organisations indicated that they had been involved in EU legislation on plant protection products (64%) and in the Water Framework Directive (52%) (Figure6). Consumer/non-governmental organisations from all sectors participated in the consultation providing 47 web-based responses. However, the scope of the activities of consumer/non-governmental organisations (47 web-based responses) appeared to be mostly focussed on environmental (55%) and consumer (22%) concerns.

All web-based responses have been published, unless a contributor requested otherwise, at https://ec.europa.eu/info/consultations/public-consultation-defining-criteria-identifying-endocrine-disruptors-context-implementation-plant-protection-product-regulation-and-biocidal-products-regulation_en.

5. ANALYSIS OF RESPONSES

The public consultation generated over 27,000 responses which illustrates the significant public interest in the EU endocrine disruptors policy. The submissions received on line can be found at: https://ec.europa.eu/info/consultations/public-consultation-defining-criteria-identifying-endocrine-disruptors-context-implementation-plant-protection-product-regulation-and-biocidal-products-regulation_en.

The public consultation report sets out the results of the consultation focussing on qualitative rather than quantitative terms. Organisational affiliation (public authority, academic/research institution, hospital/health institution, private company, agricultural producers (farmers), consumer/non-governmental organisation, industrial or trade association) is based on self-identification by respondents and has not been checked. It is important to underline that this analysis does not provide an exhaustive overview of all contributions because of the high number received contributions.

5.1. Individual/citizen/consumer

The public consultation attracted a large response from individuals /citizens/consumes (21548 web-based responses of a total of 22411). This volume appears to be a result, to a large extent, of two mobilisation campaigns that took place in particular the following Member States: Austria, Denmark, Germany, France, Spain, Sweden and the United Kingdom (in total 88% of the responses originated from these seven Member States). The two campaigns were organised by a group named EDC-Free Europe. They provided two on-line platforms with pre-prepared consultation responses in several languages (for further details of these on-line platforms please see Annex to this report). EDC-Free Europe is a coalition of public interest group representing more than 50 organisations across Europe (for further details of participants please see link: http://www.edc-free-europe.org/about-us/). According to their website the organisations have come together through a concern about endocrine disrupting chemicals and efforts to raise public awareness and urge quicker governmental action. It is noted that many of the organisation participating in the coalition did provide also an individual response (for example Health and Environment Alliance, Pesticide Action Network Europe, Women in Europe for a Common Future, ChemSec, Friends of the Earth Germany). When searching through the web-based responses received, 20291 could be identified as originating from EDC-Free Europe, i.e. about 95% of all responses in the category of 'individuals /citizens/consumers'. EDC-Free Europe also provided the option of responding to the consultation by email through their on-line platform. In total 4,499 email responses could be identified as originating from EDC-Free Europe, which represents about 97% of all email responses. One of the effects of these on-line platforms is that a significant number of pre-programmed responses were submitted to the public consultation.

The responses through EDC-Free Europe support options 3 and A. For further details of these responses, please see Annex 9.2.

5.2. Public authorities

The public consultation received 32 web-based and 5 email responses respectively from authorities. Of these, two requested that they remain anonymous. T**hree EU governments and 18 public authorities have sent comments:** the Technical and Scientific Association for Gas and Water (Germany); the Agriculture and Horticulture Development Board - AHDB (United Kingdom); the Swedish Chemicals Agency (KEMI); the City of Stockholm (Sweden), the City of Vasteras (Sweden), the Danish Environmental Protection Agency (EPA); the Danish Veterinary

and Food Administration; the UK Department for the Environment, Food and Rural Affairs (DEFRA), the Federal Institute for Risk Assessment (BfR), the German Federal Environment Agency, Umweltbundesamt (UBA); the Health Administration of Hungary and the National Institute of Chemical Safety (Hungary); the Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH – AGES (Austria); the Environment Agency (Austria);. the Belgian Federal Public Service; the Finnish Safety and Chemicals Agency (TUKES); the Commission des affaires européennes de l'Assemblée nationale (France), the French authorities; the Regional Ministry of Agriculture of Valencia. A common response was received from the Netherlands from the Ministry of Health, Welfare and Sport, the Ministry of Infrastructure and the Environment, the Ministry of Economic Affairs, the Ministry of Social Affairs and Employment, the National Institute of Public Health and the Environment (RIVM), the Board for the Authorisation of Plant Protection Products and Biocides (Ctgb), and the Netherlands Food and Consumer Product Safety Authority (NVWA).

Six public authorities and six governments in non-EU countries sent comments: the Australian Government, the Kenya Plant Health Inspectorate Service; the Norwegian Food Safety Authority, the Ministère de l'Agriculture de Côte d'Ivoire; the Government of Canada; Health Canada; the Instituto Colombia Agropecuario (ICA); the Ministry of Agriculture, Livestock and Supply of Brazil; the Ministry for Primary Industries, Environmental Protection Authority and Ministry of Foreign Affairs and Trade of New Zealand; the República Argentina and the United States Government. No responses were received from international public health or animal health organisations.

In this group of stakeholders a consensus exists to use the WHO/IPCS definition. Authorities in non-EU countries indicated the potentially significant trade implications of setting criteria to identify endocrine disruptors, and asked for a risk-based approach to be taken. They reminded the Commission that any decision on endocrine disruptors needs to respect the principles of the WTO.

Concerning EU Member States

DVGW, the **German Technical and Scientific Association for Gas and Water** supports the WHO/IPCS definition of endocrine disruptors, insisting that the precautionary principle should be applied with regards to endocrine disruptive active substances. It recommends a hazard based approach that takes into consideration the risk of adverse impacts on water resources. The **Agriculture and Horticulture Development Board** (AHDB), from the United Kingdom, mentions a report it had commissioned to ADAS on the use and effectiveness of plant protection products used in UK agriculture and horticulture. They estimated the costs of the additional crop loss occurring as a result of withdrawal of substances as a result of possible classification as endocrine disruptor substances, providing an estimate of the overall cost to the UK industry. The impact of the loss of each substance for each crop was determined through the use of existing crop statistics and expert opinion on consequential loss. The cost to the industry was estimated to range from £905 million to over £3 billion. According to the **Swedish Chemicals Agency** (KEMI) one of the advantages of having several categories is that such an approach is less restrictive and provides a greater degree of transparency, increased awareness, and ability to further prioritise chemicals with possible endocrine properties in relation to further testing, assessment and management. The **Danish Environmental Protection Agency (EPA)** points out that 'substitutability' of plant protection products should be understood in a broader sense. Directive 2009/128/EC establishing a framework for Community action to achieve the sustainable use of plant protection products promotes Integrated Pest Management (IPM) as one of its seven main action plans. This directive sets out the principles for replacing plant protection products for pest control with alternative methods and "substitutability" of plant protection products should be understood in this context. The **UK Department for the Environment, Food and Rural Affairs (DEFRA)** stressed that it is accepted worldwide that assessment of hazard comprises two elements: hazard

identification and hazard characterisation. All aspects of hazard identification and hazard characterisation should be taken into account in identifying endocrine disruptors for regulatory purposes. Failure to take into account the elements of hazard characterisation (e.g. potency, severity and lead effect) will lead to the loss of potentially very beneficial chemicals that pose no dangers to human health or wildlife in real life. According to DEFRA, potency and other hazard characterisation factors are essential to make the regulatory consequences of ascribing endocrine disruptor status to a substance more balanced and proportionate to the potential hazardous threat that the substance might pose to human health and/or the environment. Failure to take potency into account creates inconsistencies with the way the current regulatory system considers the science, such that thyroid toxicity or adrenal toxicity will be approached and assessed differently from neurotoxicity or immunotoxicity. A joint response was received from the Netherlands from the **Ministry of Health, Welfare and Sport**, the **Ministry of Infrastructure and the Environment**, the **Ministry of Economic Affairs**, the **Ministry of Social Affairs and Employment**, the **National Institute of Public Health and the Environment** (RIVM), the **Board for the Authorisation of Plant Protection Products and Biocides** (Ctgb), and the **Netherlands Food and Consumer Product Safety Authority** (NVWA). The response notes that the WHO/IPCS definition contains all the essential elements required to designate a compound as an endocrine disrupter. According to the response, the strength of this definition lies in the fact that it is purely hazard-based and that it requires causality between the endocrine mechanism affected and the adverse health effect observed. The response also considers that risk management of endocrine disruptors should be based on risk assessment and not solely on hazard assessment. The response also advocates launching an international discussion about the appropriateness of the current regulatory testing paradigm and its underlying animal study protocols, with a view to modernising this based on state-of-the-art scientific and statistical knowledge. The **Health Administration of Hungary** and the **National Institute of Chemical Safety**, **Hungary** indicates that a large difference exists between endocrine disrupting and endocrine active effects. Endocrine disruptors always lead to harmful consequences, while endocrine-active effects are (usually) part of normal biological functions without harmful consequences. As a result, the two should not be confused. The potency of effects on humans cannot be reliably assessed from experiments carried out on animals since the potency is species specific. As the threat is global, a global restriction policy is required. Methodological developments should cover all known hormones, not only those that are currently being investigated. The **Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH** (AGES) notes that although currently adverse effects need to be proven in animal experiments, in the future it might be possible to make decisions on adverse effects with *in vitro* tests. The **German Federal Environment Agency**, Umweltbundesamt (UBA), noted in its answer that it is aware of studies conducted or commissioned by scientific, regulatory and industrial bodies to estimate the agronomical and socioeconomic consequences of banning plant protection products in accordance with the (interim) criteria set under Regulation (EC) 1107/2009/EC. In the agency's view all these studies have only limited significance for an overall impact analysis since either, (i) the procedure of identifying endocrine disrupting substances is not transparent, consistent, or all-encompassing or is only provisional and/or (ii) the agronomical / socioeconomic impact assessment lacks a robust methodological and statistical basis, i.e. qualifying the results as only very rough estimates. Furthermore, there is an obvious imbalance in the available socioeconomic studies: the vast majority only address the agronomical / societal costs of implementing the endocrine disruptor criteria, while the economic benefits generated by avoiding environmental and health costs are rarely considered. The **German Federal Institute for Risk Assessment** (BfR) referred to an exercise that conducted at the institute considering different sets of criteria for human health (Marx-Stoelting et al., 2014[16]). Three options for regulatory decision-making

[16] Marx-Stoelting P, Niemann L, Ritz V, Ulbrich B, Gall A, Hirsch-Ernst KI, Pfeil R, Solecki R (2014). Assessment of three approaches for regulatory decision making on pesticides with endocrine disrupting properties. Regul Toxicol Pharmacol. DOI 10.1016/j.yrtph.2014.09.001

were tested upon 39 plant protection products examining their applicability and to analysing their potential impact on the regulatory status of active substances that are currently approved for use in the EU. The results of this exercise demonstrate that a combination of criteria for hazard identification with additional criteria of hazard characterisation allows substances to be prioritised and differentiated with regard to their regulatory relevance. It is proposed to integrate these elements into a decision matrix to be used within a weight-o-evidence approach for the toxicological categorisation of relevant endocrine disruptors and to consider all parts of the endocrine system for regulatory decision making on endocrine disruption. The **Belgian Federal Public Service** and other relevant federal and regional authorities (coordinated Belgian position) consider that an endocrine disruptor should be identified based on the IPCS/WHO 2002 definition. This definition was originally developed in the context of considerations about human health. Nevertheless, when interpreting the term 'health effects' in a wider sense, not restricted to human health, but including all types of organisms, the definition is considered to be appropriate for the protection of both human health and wildlife. The definition implies an adverse effect related to an endocrine disruptor mode of action. Tests have already been designed to identify some endocrine disruptor mode of action as well as some endocrine disruptor adverse effects. The OECD conceptual framework on endocrine disruptors provides useful information on these aspects with the following caveats: the tests available today only cover parts of the endocrine system (EATS) and no sufficient tests are available to cover the whole life cycle for all relevant species. The **Finnish Safety and Chemicals Agency** (TUKES) considers that having categories reflecting the level of evidence will provide the authorities with a tool for a screening and final identification of endocrine disruptors. Having several categories will allow substances to be managed under different regulatory actions based on the strength of scientific evidence on endocrine disrupting effects. This approach may also trigger industry and other relevant parties to provide more information to demonstrate the safety of chemicals. The **French authorities** are in favour of a definition and of setting identical identification in all sectorial regulations. They consider that the definition must be based only on the intrinsic hazards of substances with socioeconomic elements only being taken into account at the management stage. The French authorities note that the level of exposure of the general population to certain recognized or suspected endocrine disruptors shows that it is important to act quickly to prevent adverse effects. In addition, the costs of the negative effects caused by endocrine disruptors can be extremely high and reducing these could have major economic benefits.

Responses from non-EU countries:

The **Norwegian Food Safety Authority** indicates that it is important that the criteria for endocrine disruptors are flexible and facilitate further testing in cases where there is a limited evidence for endocrine disrupting properties. Experience from assessing chemicals for potential carcinogenic or mutagenic or effects that are toxic for reproduction has shown that using categories facilitates decision-making. The **Australian Government** notes in its response that, in order to be consistent with trade obligations and international best practice, Australia uses a risk-based rather than a hazard-based approach to conduct a comprehensive assessment of health and environmental impacts before chemicals can be approved for sale. The World Trade Organization (WTO) rules in relation to sanitary and phytosanitary (SPS) measures require these measures to be based on a scientific assessment of the risks to human, animal or plant life or health. Australia's risk-based approach begins with hazard identification, but assesses these adverse effects together with the potential for human and environmental exposure arising from the proposed use pattern and a consideration of product efficacy. The Australian Government believes that hazard characterisation without risk characterisation and exposure assessment is incomplete, and is difficult to defend in terms of robustness, predictability and the wider consideration of the range of hazards which occur in the real world. Decisions based solely on the identification of a hazard would likely lead to outcomes that would be more trade restrictive than necessary to fulfil a legitimate objective. WTO rules in relation to SPS measures allow

Member countries to make a policy choice about the level of protection they consider appropriate to protect human, animal or plant life or health within their jurisdiction. However, countries must not have SPS measures that are more trade restrictive than required to achieve that level of protection. The **Government of Canada** highlights that Health Canada applies science-based, quantitative risk assessment principles when determining whether a product can be registered for use in Canada. Quantitative exposure and risk assessment informs the acceptability of product registration. The level of exposure is quantitatively determined for both dietary and non-dietary (i.e., occupational and residential/bystander) exposures. The respondent is of the opinion that hazard characterisation without exposure assessment and risk characterisation is not only scientifically incomplete, but lacks merit in terms of robustness, predictability and defensibility. Any change to the EU's scientific assessment from risk- to hazard-based criteria would likely result in the de-listing of a variety of plant protection products that are extensively and safely used in Canada, in other trading partner countries and most likely in the EU as well, resulting in maximum residue limits for delisted substances either entirely withdrawn or set at a near zero default level. The use of solely hazard-based cut-off criteria could have the potential to significantly disrupt Canadian and global exports of agriculture and agri-food products to the EU, as producers and exporters would likely be unable to meet the excessively low residue levels for substances and could face increased risk of shipment rejection/restrictions. The respondent lists the commodity groups/ products of Canadian exports to the EU (2013) which are most likely to be affected: among them are wheat: CAD549.3 Million/1.35 million tonnes and soybeans: CAD722.7 Million/1.25 million tonnes. The **United States Government** notes that implementing any hazard-based cut-off option that removes the requirement to conduct 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 plant protection products 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 EUR 4.4 billion worth of fresh and processed plant products to the EU that could be potentially impacted if the EU applies hazard-based criteria. The US government stresses that creating technical regulations on the basis of hazard-based criteria, n (i) are often more trade restrictive than necessary because risk-based mitigation measures exist, and (ii) do not fulfil a legitimate objective as they are not supported by scientific evidence. The **Ministry for Primary Industries, Environmental Protection Authority and the Ministry of Foreign Affairs and Trade of New Zealand** stress that the ability to take potency into account would enable different substances to be ranked and help prioritise substances for further research or regulatory action. Criteria for identification and characterisation of endocrine disruptors should be used to inform the health risk assessment of the substance, with subsequent regulatory decisions on approving and setting of management controls being made on the basis of this risk assessment and associated socioeconomic evaluation. The **República Argentina** indicates that any decision on endocrine disruptors must respect the multilaterally agreed principles, in particular the WTO Agreement on the Application of Sanitary and Phytosanitary Measures (the SPS Agreement) and the WTO Agreement on Technical Barriers to Trade of the WTO (the TBT Agreement). It notes that it is essential that countries use the least trade-restrictive measures possible if there are alternative ways to achieve the same level of protection. The **Kenya Plant Health Inspectorate Service** indicated in its answer that the EU is the largest consumer of Kenyan exports, receiving about 45% of the country's exports. The respondent indicates that Kenya supports subjecting chemicals to a full risk assessment guided by the international norms. Exemption should be made for substances with a negligible risk (rather than negligible exposure) and where not approving the substance would have a disproportionate negative impact on agriculture or trade.

5.3. Academic and research institutions

In total, eight responses (one of which asked to remain anonymous) were received from academic and research institutions: the Centre for Endocrine Disrupters (Center for Hormonforstyrrende Stoffer, Denmark), the Institute for Hop Research and Brewing -(Inštitut za hmeljarstvo in pivovartsvo, Slovenia), the Institute of Environmental Medicine (Karolinska Institutet, Sweden), the National Institute of Agricultural Botany (NIAB, United Kingdom), the Reproductive Toxicology Research Group of the Technical University of Denmark, the Agriculture and Food Development Authority (Teagasc, Ireland) and the Scientific Committee on Consumer Safety (an independent scientific committee providing the European Commission with scientific advice).

This group of stakeholders held a wide range of opinions.

The **Danish Centre for Endocrine Disruptors** indicated that the criteria should also consider substances where the information available is currently insufficient to evaluate the substance as an endocrine disruptor as most substances are insufficiently tested for endocrine disrupting effects. The contributor stressed that the validated test methods currently available are limited only to parts of the hormonal system (i.e. the oestrogenic, androgenic, thyroid and steroidogenesis of the endocrine system for mammals, fish and possibly amphibians) and indicated that, since endocrine related disorders in humans and wildlife are multifactorial in origin, it is very difficult to establish cause-effect relationships from epidemiological or wildlife studies. In addition, many of the effects of endocrine disruptors are only detectable a significant period (e.g. 20 years) after exposure during sensitive windows of development. The time lag from regulatory action to decrease in frequency of effects is, therefore, similarly long. **The Institute for Hop Research and Brewing in Slovenia** noted that the production of hops in Slovenia is at risk as a result of a reduction in quantity and quality of the crop of hops, depending on which criterion is chosen. The respondent suggests a risk assessment of each substance rather than prohibiting the use of active substances solely on the basis of suspicion of endocrine disruption. **The Institute of Environmental Medicine (Karolinska Institutet, Sweden)** is of the opinion that identifying and categorising of suspected endocrine disruptors is important for further research priorities, for example, and other non-legislative activities. The **National Institute of Agricultural Botany** (United Kingdom) indicated that the decision to set criteria to identify endocrine disruptors could have significant consequences on the availability of azole fungicides in Europe. Azoles are the key fungicide group which are needed to control the main wheat disease (*Septoria tritici*). Their use is a keystone of fungicide strategies and the major component of anti-resistance strategies to prevent the other major fungicide group (SDHIs) from developing resistance. The contributor argued that current plant varieties are not able to combine high yield with good disease resistance so any loss of fungicide effectiveness would inevitably lead to a reduction in yields. In addition to the drop in yield, most crop areas would be likely to decline because it would become more difficult and more expensive to grow these crops if key plant protection products are unavailable. Some crops would probably not be grown in some locations because suitable plant protection products would not be available to control pests. It is predicted that cereals and oilseed rape prices would rise by about 5% because of the drop in production. The EU produces around 20% of the world's total wheat supply. As a result, any reduction in EU production would be significant enough to raise the global price of wheat. With greater food demand from Europe, there would be increased pressure in other parts of the world to turn land over to agriculture. Thus, any environmental gains in Europe from new policies on plant protection products would likely be more than offset by environmental losses elsewhere. The **Reproductive Toxicology Research Group of the Technical University of Denmark** highlighted the risk of underestimating 'mixture toxicity' if low potency substances were to not be flagged and therefore not considered in assessing cumulative exposure of people to chemicals. The **Agriculture and Food Development Authority in Ireland** refers to a study by Jess et al. (2014). This noted that the identification of a certain

number of active substances as endocrine disruptors under the interim criteria may in fact lead to the cessation of wheat production in Ireland. The **Scientific Committee on Consumer Safety (SCCS)** is an independent committee that provides opinions on health and safety risks of non-food consumer products to the Commission. The Committee can also, at its own initiative, publish statements on specific topics. The SCCS, in accordance with EFSA and JRC, endorses the WHO/IPCS definition. Moreover, it agrees with the EFSA's conclusions that that: *'Critical effect, severity, (ir)reversibility and potency aspects are part of the hazard characterisation of endocrine disruptors. To inform on risk and level of concern for the purpose of risk management decisions, risk assessment (taking into account hazard and exposure data/predictions) makes best use of available information. endocrine disruptors 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*'. In its response, the committee also stresses that due to the ban on animal testing for cosmetic ingredients, in effect since 2013, it will be extremely difficult in the future to differentiate between a potential endocrine disruptor and an actual endocrine disruptor, if the substance is registered solely for use in cosmetic products. For substances registered under REACH and also for other (mixed) uses, information from animal tests is necessary for the time being. Replacing animal testing with alternative methods for complex toxicological endpoints remains scientifically difficult, despite the additional work to achieve this at various levels. With regard to substances with endocrine activity (potential endocrine disruptor), assessing f their impact on human health without using animal data remains a challenge.

5.4. Health institutions and hospitals

There were two web-based responses received on behalf of a health institution or hospital: Beratungsstelle für Natürliche Geburt und Elternsein e.V. (Germany) and National Institute of Public Health in Slovenia.

Beratungsstelle für Natürliche Geburt in Germany indicated that criteria which clearly identify all endocrine disruptors without including potency as an element of hazard characterisation would enable the EU to effectively address the threats of long-term health and environmental damage posed by endocrine disruptors. The respondent was of the opinion that Europe should take a leading role in regulating endocrine disruptors, as this will stimulate innovation so that all industries in the various sectors develop and use better and safer alternatives. In this way, European industry can ensure its share of the growing world market for safer products and move to more sustainable production and sustainable agriculture. The **National Institute of Public Health** in Slovenia considers that regulating based on hazard identification alone is not scientifically sound as hazard identification is too qualitative. The substances for which sufficient data are available ought to be assessed on a case-by-case basis, taking into account all the available data and the specificities and the complexity of the endocrine system. The precautionary principle ought to be used where the data are not sufficient. Regulating based purely on *in vitro* data ought to be avoided, particularly where no 'safer' substitute is available. Certain aspects, such as the existence of thresholds, the effects at low or very low doses, the non-monotonic dose-response relationship, the toxicity of mixtures, and the lack of appropriate methods for testing during periods of susceptibility are very intensely debated with regard to endocrine disruptors. However, these are also relatively common to other substances and often highlight the uncertainties in toxicity assessments in general. Challenging the degree of uncertainty may provide a further basis for categorising f endocrine disruptors in order to set the priorities for regulation.

5.5. Private companies

The Commission received 136 web-based responses from private companies. Below you find a selection of these respondents. Most of the respondents (86 responses) classified themselves as SMEs (<250 employees) and 50 classified themselves as large companies. The latter group includes large multinationals (for example BASF, Bayer, Dow Chemicals, Sony, Johnson & Johnson and Merck).

The positions of some of the companies are summarised below. Many respondents suggested following a risk-based approach.

Agrii is a UK agronomy supply and consultancy business that employs 850 people. It points out that losing key plant protection products may have on the viability and profitability of agriculture in the UK. It is predicted that total income from farming will drop by 35%. **Andrew Pennill Ltd**, an agricultural consultancy, states that two key winter oilseed rape herbicides rape would become a non-viable crop. An alternative solution may be to stop growing winter oilseed rape and start growing spring oilseed rape instead. However, the profits lost as a result from this change would be around EUR 120-160 per hectare. **Tozer Seeds** is an independent British vegetable breeding company. It emphasises that responsible use of plant protection products is key to breeding new crops, ranging from field scale trials to the final production of commercial seed. There are a number of plant protection products which are on the list of substances at risk and which are fundamental to the successful breeding and production of seeds. It is crucial for the company that all seed supplied should be free of disease and this can only be achieved through the timely application of approved plant protection products. **Alpro**, a soyfood producer, states that the effect of soyfoods on the endocrine system has received a great deal of interest due to the natural presence of isoflavones in soybeans. Studies have clearly shown that isoflavones in soy do not cause adverse effects. Due to the large amount of evidence about the potential health benefits, it is recommended that soyfoods are part of the daily diet. Alpro emphasises that EFSA endorsed the WHO/IPCS 2002 definition of an endocrine disruptor. Therefore, soyfoods, based on this definition, do not fall under the scope of the public consultation. **Henkel AG & Co**. has implemented a stringent process for assessing ingredients and products. The respondent believes that a differentiation must be made between hazard and risk as this is essential ensuring that ingredients safety assessments will reflect reality. It states that, although an endocrine-active substance can have hormone-like effects, this does not necessarily entail negative effects on human health. This is true for many food ingredients, such as soy products and beer, which show weak endocrine activity but do not produce any adverse effects. Henkel believes that a separate regulatory 'endocrine disruptor' class is scientifically inappropriate, as endocrine disruption is not a toxicological endpoint. It strongly supports the position that there is no need for additional policy changes to the EU Cosmetics Regulation. The EU Cosmetics Regulation requires a robust safety assessment of all cosmetic products and their ingredients, which already covers all possible effects including endocrine-mediated effects on human health. **Merck KGaA** points out that substitution of hazardous chemicals and other potentially dangerous materials is a major

concern for it ensuring the effective protection of human health and the environment. It underlines the point that automatic substitution of endocrine disruptors is not appropriate, as it could lead to the loss of important substances which could otherwise be safely used based on risk assessment. If these substances are lost, the benefits that they provide to society will also be lost. **Skanska** is a world leading project development and construction group. The company underlines that it is very important that their customers feel confident that the materials used during construction are safe. Skanska has for many years voluntarily worked on phasing out substances of concern from their construction materials. It wishes to see the elimination of substances that have endocrine disruptor properties. Criteria to identify endocrine disruptors would make it easier for Skanska to carry out their chemicals management and supply chain communication, since it will be much easier to restrict endocrine disruptors in the supply chain once this group of chemicals is officially identified as such. **BASF** states that it is important to recognise that generic substitution of endocrine disruptors is not appropriate as it could lead to the loss of important substances which can be safely used based on scientific risk assessment and appropriate mitigation and management. It is convinced that endocrine disruptors can be managed by risk assessment. Using cut-offs based on hazard does not take into account all relevant scientific information, and does not provide a suitable basis for regulatory decision-making. This is shown by the case of cholecalciferol (Vitamin D3) which is an essential vitamin in vertebrates and is naturally synthesised in the skin in the presence of sunlight. Cholecalciferol is supported as a new rodenticide under Regulation 528/2012. Once ingested, cholecalciferol is converted to its hormonally active form. Without a full risk assessment approach to biocides, cholecalciferol could potentially be considered an endocrine disruptor and would not be approved for rodent control despite exposure levels being well below the safe level proposed by EFSA, but would still be allowed in food supplements. **Bayer** points out that recently reports that tried to calculate health costs linked to endocrine disrupting substances are now available .The incidence or prevalence of common negative health effects is used as the starting point for these calculations. Although there have been definite increase in some diagnosed diseases, such increases can be caused by a variety of factors, as the diseases are well known to be multifactorial with lifestyle factors playing an important role. Therefore, a causal link between the diseases and endocrine disrupting substances is not substantiated. **Bayer CropScience** (BCS) and **Bayer Environmental Science** (BES) state that determination of endocrine disruptors should not be limited to the hazard characterisation element of potency alone. Additional hazard characterisation elements (severity of effect, (ir)reversibility of effect, potency and lead toxicity) are essential ensuring that all relevant scientific information on how hazardous a substance is are considered in regulatory decisions. A full risk assessment option should take into account all available information, this would also limit the need for additional, unnecessary animal testing. **Syngenta Crop Protection AGL** states that categorisation/classification schemes are an historic approach to risk management and pre-date more modern and accurate methods. These types of approaches are more appropriate to situations where there are limited data on hazards and no reliable data on exposure. The respondent underlines that endocrine disruptor modes of action are well understood (stimulation or inhibition of hormonal receptors, interference with hormonal synthetic or breakdown pathways). There is a range of tests that can be performed to highlight and understand the potential effects on the endocrine system. In addition, all plant protection products are tested in a two-generation animal study which uses up to 1 000 animals to understand the effects and dose response. The knowledge gained in these ways is sufficient to

not only identify the hazard but also to characterise them and to carry out a risk assessment to determine whether a product is safe to be used in particular circumstances. Using endocrine disruptor criteria would lead to a large amount of knowledge related to exposure and generated from regulatory mandated studies being ignored. **Dow AgroSciences Europe** and **Dow Microbial Control** support full risk assessment. **E.I. du Pont de Nemours and Company** states that it is important to note, that interim criteria may lead to the misleading identification of substances that do not show endocrine activity, and, therefore, cannot be construed as 'endocrine disruptors'. For example, the EFSA published its conclusions on the peer review of the herbicide active substance flupyrsulfuron methyl and proposed to classify the substance as carcinogenic and toxic for reproduction. However, the EFSA also recognised that the substance showed no endocrine activity. DuPont is concerned that the proposed approach for identifying and categorising endocrine disrupting substances differs substantially from the approach taken by the Environmental Protection Agency in the United States. It believes that more work should be carried out to bridge the gap between the regulatory approaches currently used in the United States and in Europe. **Quality Scientific Solutions** states that the recent emphasis on screening methodologies that aim to develop predictive tools based on *in silico* or *in vitro* models need to be validated against more traditional indicators of adverse effects manifested in living organisms. Until this happens, the resulting information can only be used for priority setting at best. **Sony Mobile Communications** states that it is very important that their customers feel confident that the products they buy are safe. It has for example already phased out brominated flame retardants and phthalates in their products due to their own and their customers' concern. The respondent regrets that no criteria to identify endocrine disruptors are yet in place since it will be much easier to restrict endocrine disruptors in the supply chain once this group of chemicals is officially identified as such. Such criteria would also enable the respondent to take a long-term perspective on developing products without endocrine disruptors. The **Thames Water Utilities** states that the regulatory approach should be relevant for the sector concerned. If a single approach is to be adopted, it should ensure consistency with, for instance, considerations on disproportionate costs under the Water Framework Directive.

5.6. Agricultural producers/farmers

In total 488 web-based and 33 email responses were received from agricultural producers/farmers. Therefore about 57% of web-based responses submitted on behalf of organisation came from agricultural producers/farmers. Companies both from within the EU and outside the EU answered to the public consultation. A high proportion of those who answered expressed concerns about the potential disappearance of key plant protection products and the high yield losses that would result from this. They also mentioned the linked resistance problem (if only a few types of similar types of plant protection products remain, the development of resistance of diseases to these products will take place easier and faster). In addition, they mentioned the fact that there might be no suitable substitutes for some of the substances that may no longer be available. Respondents referred to several reports and studies that provide quantitative information on potential impacts on the agro-food chain.

The **Agricultural and Rural Youth Association** (AGRYA) in Hungary considers that the hazard potential of new and old substances must be rated on the scientific basis of risk management that considers incident rate and hazard. The rating cannot only be based on the assumed hazard. A zero risk system is not applicable because this would mean that only the theoretical

existence of a hazard would knock out a substance. In this case, modern plant protection and crop production would not be possible. The whole plant protection products registration system should be based on the scientific assessment of risks, not on assumptions. The AGRYA states in its response that if several important plant protection products are lost, the possibility of using effective tools against pests, diseases and weeds would decrease. In the short term this would cause yield losses and a poor quality of products; in the long term it could lead to the collapse of several agricultural branches. In Hungary farmers use mainly triazol fungicides for cereal production. Without this group of plant protection products, they would not be able to protect cereals against diseases like Fusarium. Fusarium toxins are some of the most dangerous natural toxins in the food chain. Their prevention and reduction is essential for all of us. Banning triazol fungicides could cause unsolvable problems not only for farmers, but for consumers as well. The **Asociacion Valenciana de Agricultores (AVA-ASAJA), the Landwirtschaftskammer NIederösterreich** and the **Ulster Farmers' Union** stress that the WHO/IPCS (2002) definition alone is not sufficient for the purposes of regulation and regulatory decision-making on individual substances. The other elements of hazard characterisation (severity, (ir)reversibility, potency and lead toxicity) should be included in the criteria. Without these hazard characterisation elements, substances which pose little or no concern for human health or the environment could be considered to have endocrine disrupting properties and could be unnecessarily banned under Regulation (EC) 1107/2009. According to the AVA-ASAJA categorisation will inevitably lead to the creation of 'black lists' which will be highly vulnerable to misinterpretation, misuse and unwarranted additional primary or secondary regulation, in Europe and globally. Testing would involve the sacrifice of large numbers of animals to provide unnecessary data which would not add any additional understanding to the toxicological behaviour of plant protection products that already benefit from extensive data packages. **Asplins PO Ltd**, an organisation of soft and top fruit producers in the UK, is concerned that the proposed review of existing EU legislation relating to endocrine disruptors could result in the loss of significant numbers of plant protection products. If all products with the potential to cause endocrine disruption were to be withdrawn, the growers of this produce organisation would face significant crop losses, which would quickly make their businesses unviable. **Copa-Cogeca** considers that, when assessing endocrine disruptors, a plausible link between endocrine activity and adverse effect must be demonstrated, and that this assessment should be focused on field conditions. Furthermore, endocrine disruptors should be subject to risk assessment which would take into account hazard (including potency) and exposure. Based on some recent estimates, approximately 80 % of fungicide products currently used across the EU could be removed from the market, with serious impact on yields of wheat, potatoes, oilseed rape and vines. The respondent states that two thirds of relevant active substances have already been removed from the market in the last two decades, as they did not comply with the new legislative requirements. Yield losses of up to 50 % are also expected in years of high disease pressure. The respondent points out that the lack of tools to control pests and diseases is becoming a crucial factor for the cultivation of crops in the EU, including many specialty crops. This compromises not only food safety and security, but also the competitiveness of the entire agri-food chain, including its productivity and sustainability. Employment, diversity of high-quality agri-food products provided to the society and biodiversity are all under threat. Copa-Cogeca is in favour of a more risk-based decision-making process. Several organisations, including **Collectif Sauvons les fruits et légumes de France, Confederazione Nazionale Coldiretti, Cooperativas Agro-alimentarias de España** and **National Association of Agricultural Contractors (NAAC),** provided similar responses as Copa-Cogeca. The **Association Générale des producteurs de blé et autres céréales** refers to the study carried out by the ARVALIS Plant Institute, which shows that the elimination of endocrine disrupting substances will directly impact the revenue of French farms. Without these substances, and without sufficiently effective substitutes for substances, foliar fungal diseases in cereals could result in 1.5 2T / ha reduction in wheat production. Depending on the volatility of wheat prices, the direct impact could be between 150 € / ha and 600 € / ha. Eliminating these substances would mean that effective protection

of cereals against fungal diseases would no longer be ensured and this could again become dangerous for consumer health because of the occurrence of mycotoxins. The **Association Nationale Pommes Poires** states that without effective protection against scab, apples are not marketable. It also stresses that in order to ensure proper protection, it is necessary to alternate the substances used, to avoid the development of resistance. The **Association of vegetable producers of the Republic of Croatia** considers that existing plant protection products should not be prohibited if there are no alternatives. The **Central Union of Agricultural Producers and Forest Owners** (MTK) is worried about the resistance problem and the fact that some of the substances that may no longer be available might not have substitutes. For example, to control insects in cereal crops and oil seed crops there is currently no efficient substitute to pyrethroids (except neonicotinoids). **CERAFEL** (Association d'Organisations de Producteurs Légumes, Fruits et Horticulture) considers that broadening he definition of endocrine disruptors based on the precautionary principle and risking the banning of thousands of essential product, is not desirable to public health, agriculture, or the economy in general. The **International Confederation of European Beet Growers** (CIBE) considers that additional elements of risk assessment and socioeconomic considerations, including risk-benefit analysis, should be introduced into sectoral legislation. Quite a number of active substances used in sugar beet growing in different parts of the EU could apparently be withdrawn from authorisation. Several assessments suggest that the impact could be very significant. For example, in the UK alone, loss of the fungicide substance cyproconazole is expected to result in a yield loss of some 15% on 80% of the UK's beet area or, put in another way, to a reduction in revenue for farmer of 13%. In the case of the beet crop in the UK this corresponds to some GBP 28 million. The **Deutscher Bauernverband e. V.** refers in its answer to an assessment carried out by the German Ministry of Agriculture, the Federal Office of Consumer Protection and Food Safety and the British Crop Protection Administration in 2009. Various German stakeholders, including the Agricultural Industry Association (IVA), have built upon this assessment in 2013. Data were collected to examine the potential impact on the availability of cereal and potato fungicides of introducing a cut-off regulation based on an endocrine disrupting effect on people. The data shows that 24 out of the 50 most sold fungicides would be lost because of the new regulation. Nine out of the 10 mostly sold fungicides would be negatively impacted and seven azoles' substances would be affected. 11 out of the 50 currently available fungicides would likely disappear because of the regulation on endocrine disruption. Only 13 of the 50 fungicides would remain available. In concrete terms, farmers would not have the necessary tools to combat specific plant diseases such as Pseudocercosporella and would have very limited options for the control of diseases in potatoes For example, 11 out of 24 products used for the control of late blight in potatoes would disappear. **English Wines PLC** points out that it is important to have a wide range of plant production products to make it possible to carefully select and rotate products that are appropriate for the situation and to avoid resistance developing through repeated use. The other danger is that poor control of pests and disease will increase the population of pests and disease present in the vineyards, thus increasing occurrence pressure and requiring a greater level of intervention. The **Irish Teagasc Tillage Stakeholders Group** stresses that many active substances are heavily relied upon not just for disease control, but also because they are essential components of anti-resistance strategies. They refer to the study carried out by Jess et al. (2014), which outlines that the potential loss of actives, whether through the registration process or the ensuing development of fungicide resistance would have major impacts on Irish agriculture. These include the potential cessation of wheat production in Ireland due to the inability to reliably control the fungal disease *Septoria tritici* blotch and the hastening of disease control issues in both barley and potatoes due to an over-reliance on a select number of fungicides. Most of the agricultural producers/farmers from Poland who took part in the public consultation (**Polish Industry Federation of Agricultural Producers**, **Polish National Association of Growers of Black Currants, the Polish National Federation of Grain, the Polish Association of Cereal Producers Polish Hops Producers Association, the Polish National Union of Sugar Beet Growers**) favour a scientific approach and a full risk assessment. The

District Butak Sugar Growers Association (Rejonowy Związek Plantatorów Butaka Cukrowego przy Cukrowni Strzyżów), the **Provincial Sugar Beet Growers Association in Lublin** (Wojewódzki Związek Plantatorów Buraka Cukrowego w Lublinie), the **Sugar Beet Growers Association in Chelm** (Związek Plantatorów Buraka Cukrowego w Chełmie) and the **Sugar Beet Growers Association in Dobre** (Związek Plantatorów Buraka Cukrowego w Dobrem) give a similar response. The **Brassica Growers Association** points out that the horticultural brassica industry relies heavily on manual labour for most planting, harvesting and packing operations. Depending on the criteria for identification of endocrine disruptors chosen, these jobs may be at significant risk. The **Brazilian Confederation of Agriculture and Livestock** indicates that the assessment of a substance should be consistent with the SPS Agreement of the WTO. It suggests that country exporting to the EU would be informed in advance by the EU of the agrochemicals that are being considered hazardous. The **Grape Growers' Federation of India** believes that endocrine disruptors do not need special regulatory treatment, but can be dealt with like other substances of potential concern, i.e. be evaluated using a full risk assessment framework (considering both hazard and exposure). The respondent stresses that the application of the default level of 0.01 mg/kg for the setting of allowed levels of residues of substances would have a substantial impact on international trade as it would prevent the import of crops treated with these substances into the EU. The lack of a science-based approach to this regulation, and its divergence from appropriate and internationally agreed standards and guidelines is what is at the bottom of the trade issue. The adoption of this approach by the EU differs so substantially from other plant protection product regulatory programmes that it creates precisely the kind of regulatory barriers that the WTO SPS and TBT agreements are designed to address and avoid. The application of a random default level for the setting of allowed levels of residues of substances would be contrary to the EU's commitment to the WTO SPS and TBT agreements. **Mahagrapes** from India holds a similar opinion. The **Citrus Growers Association (CGA) of Southern Africa** states that, particularly for fungicides (where very few effective non-chemical alternatives are available in South Africa, the impact of implementing hazard-based criteria for endocrine disruptors that would lead to the withdrawal of EU usage authorisation would be very significant. Specifically, it would reduce the ability of the citrus industry to comply with EU plant health rules for imported citrus. The EU remains the largest market for the South African citrus industry (EUR 1 billion annually at retail level) and disruption to this market could potentially result in the collapse of the entire South African citrus industry. Currently over 100 000 people are dependent on the citrus sector. **Pulse Canada** highlights that regulating endocrine disruptors solely on the basis of hazard cut-offs can cause serious impacts on the trade of agricultural products to Europe. Canada is the world's largest exporter of pulses or grain legumes. The EU is Canada's third largest pulse market, importing an average of 300,000 tons annually (2011-2013). The Canadian pulse industry would not be in favour of the EU requiring exporters to comply with allowed levels of residues of substances that are based on defaults rather than evaluation of risk, and are contradictory to those of other importing jurisdictions whose rules are based on internationally agreed-upon approaches. The **Thai Mango Association** and the **Thai Chamber of Commerce/Board of Trade of Thailand** indicate that the export value of Thailand's trade in mangoes and mango products was about EUR 81466077 in 2014. The respondent supports a full risk assessment approach which is likely to have the least impact on trade in agricultural commodities and produce with the European Union.

5.7. Consumer/non-governmental organisation

In total 47 web-based and 9 email responses were received from consumer/non-governmental organisations. Examples of European-level associations that contributed to the consultation include the Pesticide Action Network Europe, the European Consumer Organisation (BEUC), the Eurogroup for Animals and the Health and Environment Alliance. Respondents refer to

several reports and studies that provide quantitative information on the potential impacts on the agro-food chain and on health.

The **Alliance for Cancer Prevention** (ACP), a multi-stakeholder group working towards cancer prevention, considers that there are no safe levels for endocrine disruptors. Potential cumulative, daily low-level exposures in the workplace should also be taken into account. According to the ACP, continual exposure to endocrine disruptors makes current cancer strategies unfit for purpose, inadequate, fragmented and unsustainable. This is why criteria which clearly identify all endocrine disruptors wherever they are found in the workplace, home or in the wider environment are required. The **Plant protection product Action Network Europe** (PAN Europe) considers that health impacts should be the only relevant topic: costs for farmers or the plant protection product industry cannot be a reason to allow harmful effects. The respondent emphasises the feasibility of using alternative techniques for pest control and provides the results of its research on the alternatives to endocrine disrupting plant protection products available in agriculture. It points out that the correct baseline for assessing the impact in the food chain should be Integrated Pest Management Principles as this is the legal baseline since 2014. Based on references to the UK Arable and Horticulture Development Board and the Anderson report, t**he British Crop Production Council** (BCPC) states that 39 active substances used in the UK are categorised as being at high risk of being lost, and 17 of them would be lost due to the interim endocrine disruption classification as potential endocrine disruptors. **Agrar Koordination** notes that recent bio monitoring studies from across Europe have shown that people in the general population are typically contaminated with several chemicals. Special care should be taken to reduce exposures before and during pregnancy, in early childhood, and during puberty. Many people come into contact with endocrine disruptors, on a daily basis, including from consumer products, indoor air, water, food and in the workplace. The **European Consumer Organisation** (BEUC) suggests that categories could be used to rank a chemical according to available data, as this would make it possible to focus regulatory action on chemicals in a differentiated way for the different categories. **Breast Cancer UK** notes that over the past 40 years breast cancer rates have increased dramatically throughout Europe. According to the respondent, this increase cannot be accounted for by known risk factors (e.g. lifetime exposure to natural oestrogens, longevity, genetic predisposition, obesity etc.) only and is therefore likely due to exposure to environmental pollutants. It thinks that criteria that clearly identify all endocrine disruptors and without a potency filter will enable the EU to effectively address the threats of long-term health and environmental damage posed by chemicals with ED properties. It will also stimulate research into the development of safer alternatives, providing European industry with an incentive to invest in and contribute to a more sustainable society. **The British Society for Plant Pathology** (BSPP) states that plant protection products should be assessed with potency, severity and persistence of effect included in the hazard indication. Risk criteria and socioeconomic implications must also be taken into account. Definitions and standardised assays are required for the consistent classification of endocrine disruptors into categories. The respondent states that, although precise figures cannot be provided, it is agreed that loss or restricted use of plant protection products would have a negative impact on crop management and profitability, resulting in lower yields and a downturn in the agriculture and agri-food sectors. Modelling cited in the Andersons report predicts a decrease in UK gross value added of £1.6 billion per year, and decreases in UK farming profit of £1.73 billion per year. Banning crop protection products that have passed the existing stringent safety and

efficacy thresholds would have a devastating effect on the productivity of EU agriculture. Maintaining a diverse portfolio of chemicals for disease management is essential, and the options for crop disease control should not be narrowed unless there is compelling and independently validated evidence of health or environmental harm. **CHEM Trust** states that there are many general studies that highlight the possibility of using fewer plant protection products. These studies focus on more traditional approaches to pest management, including integrated pest management. CHEM Trust points out that comparing the relative potencies of chemicals can be very misleading. Studies have shown that the substance BPA is a very weak oestrogen in some test systems, but it is reported to be equipotent with oestradiol (E2) with respect to the induction of insulin in mice. According to the respondent, this illustrates that a cut-off (or filter) at a certain potency level will always be arbitrary and may overlook harmful endocrine disruptors because of the limited range of tests that are routinely performed. **ChemSec** refers in its answer to a study carried out by the Nordic Council that points to the vast costs of inaction and highlights the importance of taking these costs into consideration in impact assessments regarding endocrine disruptors. In addition to the economic costs, human suffering and negative impact of the environment are difficult to estimate and value. Nevertheless they should weigh heavily. According to ChemSec, the impact assessment of criteria to identify endocrine disruptors must take into account the fact that that stricter regulation will spark innovation and research into new alternatives that are not commercially available today. Several NGOs, including the **Danish Consumer Council**, **DECO - Associação Portuguesa para a Defesa do Consumidor, ECOCITY, Ecologistas en Acción, France nature environnement, Kom op tegen Kanker, Mouvement Ecologique Luxemburg, Pestizid Aktions Netzwerk e.V. (PAN Germany), QuercusNational Association for Nature Conservation, R.I.S.K.Consultancy, terre de liens, the Norwegian Consumer Council, UK National Hazards Campaign** and **WECF (Women in Europe for a Common Future)** believe that categories would allow the broader inclusion of substances with endocrine disruptor properties, provide more transparency, increase awareness, and make it possible to prioritise chemicals with endocrine properties for further testing, assessment and management. Categories can play the role of an early-warning' system' for the industry giving it time to gradually replace suspect compounds without any negative economic impact. **Friends of the Earth Germany** (BUND) mentions in its answer the ToxFox-app for smartphones that it launched in the summer of 2014. The app makes it possible to identify endocrine disrupting chemicals in personal care products by scanning the product's barcode. More than 400.000 people have downloaded the app and scanned more than 10 million products. Almost 100.000 consumers have asked the producers of cosmetics to phase out endocrine disruptors from their products. The **UK Pesticides Campaign** highlights that rural residents and communities are subjected to a combination of both repeated acute exposures and chronic exposures to plant protection products. The respondent emphasises that in risk assessment real life exposure scenarios for residents and the effects of mixtures of plant protection products should be considered. The **Gezinsbond** points out that new insights into endocrine disruptors show that knowing the moment in life at which people are exposed to endocrine disruptors is crucial: exposure to endocrine disruptors at a specific time, especially when tissues are still developing, can cause lifelong adverse effects. **Eurogroup for Animals** calls for the development and use of methods that don't rely on animal testing in order to produce safety data relevant to people and replace the animal studies currently in use. Animal testing should be minimised and tests on vertebrates should be undertaken as a last resort. To lay down rules to avoid duplicate testing, risk assessment must be derived from evidence-based toxicology and state-of-the art science aimed at

replacing and reducing redundant testing on animals. The use of new available tools, such as *in silico* and *in vitro* methods must be the primary consideration. A combined approach using primarily human data to arrive at a risk assessment for endocrine active substances should be considered. **Ecobaby Foundation** states that the increase in colon cancer at a younger age might be related to the *in utero* exposure to the chemicals of PCBs and dioxins in the years 1980-1990 which resulted in an increased sensitivity to these chemicals in later life disturbing the innate immunity. **The European Environmental Bureau** (EEB) believes that the availability of alternatives and the current costs and future benefits of banning endocrine disruptors for society, human health, the environment and biodiversity should be taken into account in the impact assessment. The **European Environmental Citizens' Organisation for Standardisation** (ECOS) points out that nanoparticles can disrupt the endocrine system Therefore, introducing additional categories based on the various degrees to which the WHO/IPCS definition is fulfilled will be important for categorising nanoparticles. The **Health and Environment Alliance** (HEAL) estimated the total cost of six endocrine-related diseases (from all causes) across the EU, based on published costs of these diseases. The costs include indirect costs where these were available. Indirect economic costs include lost productivity resulting from absenteeism and premature retirement, the lost productivity or leisure time spent by family and friends in care, and the costs of rehabilitation and retraining or additional educational resources devoted to the individual, as well as subsequent losses in their own productivity (e.g. as affected children enter the workforce). EU policy change such as the phasing out of these hazardous substances and promotion of safer alternatives could save Europeans up to EUR 31 billion each year in health costs and lost productivity. The HEAL-report also found that the EUR 13-31 billion in potential savings each year could be an underestimate because future costs are likely to be even higher than today's. HEAL states that leading scientists on endocrine disruption have made clear that enough evidence now exists to justify acting to protect human health and the environment. People generally are unwittingly and involuntarily exposed to endocrine disruptors on a daily basis from consumer products, air, water, food and indoor environments. It is urgent that exposures should be immediately reduced, especially for women before and during pregnancy, for infants, young children, and people during puberty. **Health Care Without Harm (HCWH) Europe** draws attention to the issue of fallibility of animal studies in accurately identifying and characterising the endocrine disruptive potential of chemicals. The shortcomings of animal tests for endocrine disruptors have been widely discussed. Inconsistent results arising from species and strain variations are of particular concern. Extrapolation of results from animal studies to human scenarios is another area of particular difficulty. Differences in lifespan and the weakness of some endocrine effects lead to the necessity of using large 'megadoses' in animals, and these do not replicate the low-dose/long-term human exposure profiles. HCWH states that *in vivo* studies in no way represent a 'gold-standard' for the identification of endocrine disruptors. The **Humane Society International** stresses the need for a modified interpretation of the WHO definition, incorporating sufficient flexibility to allow evidence from mechanistic data and the application of adverse outcome pathways to identify the likelihood of adverse effects arising from endocrine system perturbations. Information on relative potency could play a valuable role. However, to take advantage of developing methods and assessment tools, it will once be critical to ensure that assessment of potency is not exclusively associated with *in vivo* adverse effects. Rather, a modified application of the WHO definition should allow the use of *in vitro* and *in silico* methods to determine relative potency. In the context of the screening of chemicals for further evaluation, including potency information as a means of hazard characterisation may

particularly be useful, and should aim to reduce overall testing needs through efficient prioritisation. The **Natural Resources Defense Council** (NRDC) supports an analysis based on strength of evidence (see analysis used by the US National Institute of Environmental Health Sciences, and the US National Academy of Sciences recommendation of using 'evidence integration'). The respondent believes that integrating the best available evidence from many streams (i.e. human, animal, *in vitro*, *in silico*) will result in a scientifically-based, transparent and accountable decision according to the respondent. The **PETA International Science Consortium** indicates that the WHO/IPCS definition requires evidence from experimental animal studies to support the claim that a substance has the capacity to cause endocrine-mediated adverse effects in humans or wildlife populations. The studies must show clear causal effect in the absence of other toxic effects, and the adverse effect must result in biological impairment of functional capacity. It underlines that science is moving away from apical studies and towards pathway-based approaches that do not need multi-generational animal studies to establish a strong presumption that a substance may be an endocrine disruptor. According to PETA the definition should be flexible enough to allow for the use of *in vitro* responses and application of reverse toxicokinetics instead of *in vivo* dose response when these emerging methods become accepted. Limiting the definition to rely solely on evidence of adverse effects in animals would seem to preclude the adoption of approaches that minimise or eliminate the use of animals. The respondent makes reference to the US Endocrine Disruptor Screening Program (EDSP) which incorporates 21st century toxicology (Tox21) methods to produce an EDSP21 approach that relies on knowledge of chemical properties and results of high throughput assays. . The **Swedish Society for Nature Conservation** stresses that to move away from *in vivo* testing to *in vitro* testing, there is a need to ensure that the term endocrine disrupting properties can encompass both those seen *in vivo* and *in vitro* tests, as soon as the latter are considered to be adequately predictive of effects in an animal. The **Endocrine Disruption Exchange** (TEDX) refers in its answer to the critical windows of development website tool that it launched in 2009 and that identifies primary scientific literature on physiological effects in laboratory animals exposed to low concentrations of endocrine disruptors prenatally or during early postnatal development. Study characteristics listed in the tool include: results (physiological effects), subjects (species), doses, route of administration, exposure duration and age of measurement. Full citations are provided for each study. The **Royal Society for the Protection of Birds** (RSPB) asserts that sufficient evidence exists to allow to state that endocrine disruptors are an important biodiversity conservation issue and it is plausible that they are contributing to current population declines in wildlife species, potentially in combination with other environmental stressors. RSPB argues in favour of the application of the precautionary principle in relation to impacts of endocrine disruptors.

5.8. Industrial or trade associations

In total 125 web-based and 12 email responses were received from industrial or trade associations. Examples of European-level associations that contributed to the consultation include the ECPA, CEFIC, Cosmetics Europe, the European Tyre & Rubber Manufacturers' Association, EurEau (water services), the European Diagnostic Manufacturers Association, the European Federation of Pharmaceutical Industries and FoodDrinkEurope. Many non-EU associations responded (for example the Subtropical Growers' Association of South Africa, the Grain and Feed Trade Association Bolsa de Cereales de Buenos Aires, the Japan Chemical

Industry Association, the American Petroleum Institute and the Canola Council of Canada) and in general referred to the EU's commitment to the WTO SPS and TBT agreements. Many respondents propose to have an additional option in the impact assessment: a full risk-assessment of endocrine disruptors.

The **Federació de Cooperatives Agràries de Catalunya** (FCAC) believes that the lack of effective tools is becoming a crucial factor for the cultivation of certain crops. This situation compromises not only food safety but also the competitiveness of the entire agri-food chain. Based on some recent estimates, approximately 80% of fungicide products currently used across the EU could be removed from the market. Losses of up to 50% are expected in years of high disease pressure. The respondent highlights the current critical situation in terms of resistance management at farm level for a wide range of crops. Two thirds of relevant active substances have already been removed from the market in the last two decades as they did not comply with the new legislative requirements. The respondent considers that endocrine disruptors can be treated like most other substances of concern for human health and the environment in terms of risk and exposure. The **National Farmers Union** (NFU) states that the NFU, together with the Crop Protection Association of the UK (CPA) and the Agricultural Industries Confederation of the UK (AIC,) commissioned an independent report from Andersons on the 'Effect of the Loss of Plant Protection Products on UK Agriculture and Horticulture and the Wider Economy'. Out of a total of 40 active substances at high risk of loss, 18 active substances fell into this category due to endocrine disruption classification. The Report concluded that, taking into account the whole regulatory environment, the loss or restriction of active substances identified, would result in yield decreases of 4-50%, making the UK more reliant on food imports. The gross value added of UK agriculture would fall by around £1.6 billion a year with3 500-4 000 job losses in the UK agriculture supply industries. This, in turn would impact on the food processing and manufacturing sectors, with potential losses of £2.5 billion GVA and associated job losses of 35 000 to 40 000. The NFU believes that the Commission should consider a fifth option in its impact assessment, namely a full risk assessment. The **British Leafy Salads Association** and **British Leek Growers Association** state that, depending on the scenario, yield losses to UK growers could reach 100%. The **European association representing the trade in cereals, rice, feedstuffs, oilseeds, olive oil, oils and fats** (**COCERAL**) is extremely concerned about the impacts of potentially loosing several fungicides and insecticides. Azole-based fungicides have helped increase yield by more than half. COCERAL is also concerned about a simultaneous disruption to the imports of substitute products from non-EU countries that do not comply with a default residue level of 0.01 mg /kg which could potentially jeopardise supply security of cereals and oilseed in Europe, and subsequently impair the sufficient supply of feedingstuffs for livestock production and for food production. The **Agricultural Industries Confederation** (AIC) states that the actives identified as potentially at risk are important in the production of a number of crops in the UK. The **Association of Independent Crop Consultants** (AICC) proposes a fifth option in the impact assessment namely a full risk assessment. The **Animal and Plant Health Association** (APHA) states that the total costs for the proposed changes to the agricultural industry across all sectors are estimated at £1.6 billion for Ireland. It stresses that Ireland is in a temperate climatic zone with moderate temperature and high moisture/rainfall levels that are ideal for many of the fungal diseases of food crops. Removing tools to minimise disease pressures will lead to further resistance problems and will have devastating consequences for tillage and crop agriculture in Ireland. The **British Society of Plant Breeders** stated that plant breeders and research groups are working to produce varieties with better and more durable genetic disease resistance but the breeding timescale is long and if chemical protection is withdrawn it is anticipated that the consequent yield losses will be substantial. There will be a time lag even when new genetic resistances are introduced. The **British Association of Seed Producers** points out that if endocrine disruptors are withdrawn without due cause, there is a risk that there will not be enough seed produced. In wet seasons, even after the use of plant protection products, the UK has had to import seed. This will not be possible if there is a general inability

to control pests in the EU because of a shortage of suitable plant protection product. If seed quality is reduced, the food crops grown from the seed will be adversely affected the next year. A further reason for having as wide a range of chemicals as possible is because of the development of pest resistance to plant protection products. The **Fresh Produce Consortium** states that the horticulture industry is unlikely to have new alternative products ready for use over the next ten years, given that most substances awaiting evaluation are variations on existing substances, and due to the long lead-in times and additional costs for development and approval of products for use on horticultural crops. The respondent points out the costs of production would increase significantly in some sectors, resulting in rising prices to be passed on to consumers who would find it difficult to manage any significant increase in food prices and would reduce their consumption of fresh produce. The Commission will have to consider existing residue levels and respond to any request for an import tolerance for residues which may be made by a non-EU country. The respondent believes that the Commission should allow an import tolerance if it is backed by appropriate data (even if the active substance in question is not approved in the EU). However, this would create an anomaly in that a substance could have been eliminated in the EU on 'precautionary grounds' but its residues could continue to be present in imported food. The **European Crop Protection Association** (ECPA) states that many leading fungicide products would be impacted if the identified active substances were removed from the market. For example, most market leading cereal fungicide products would be impacted (based on 2011 data: seven of the top ten products in France and all of the top ten products in Germany would be affected). The respondent refers to a study carried out by Nosema. Based on a hypothesis that azoles are no longer used, the Nosema study shows that this would result in a loss of production of 9.9 millions of tonnes in 2013 and 18.6 millions of tonnes in 2020. In turn, this decreasing production would not only mean a loss of value of EUR 2.4 billion in 2013 and EUR 4.6 billion in 2020, but it would also leave the EU to satisfy its internal demand or to maintain a 100% self-sufficiency rate. The respondent states that the review programme conducted under Directive 91/414/EEC between 1992 and 2012 led to the loss of more than 60% of active substances on the market when the review started. Additional attrition via the application of endocrine disruptor cut-off points will further decrease the substitutability of the remaining substances. Resistance management is therefore now more challenging and important than ever before. For potential impact on agricultural trade, the respondent refers to the report prepared by dtbassociates. Based on the assumptions and methods used in this report approximately EUR 65 billion of EU imports of raw and semi-processed agricultural products could be affected by this policy change. The respondent also indicates potential impacts on food safety if certain substances are removed from the market. In particular, the presence of mycotoxins in wheat has been mentioned. The ECPA supports the use of the WHO/IPCS (2002) definition as a scientific starting point and as a basis for the criteria for determining 'endocrine disrupting properties'. However, it stresses that this scientific definition alone is not sufficient for the purposes of regulation and regulatory decision making on individual active substances. The further elements of hazard characterisation (severity, (ir)reversibility, potency and lead toxicity) should be included in the criteria. The ECPA opposes the concept of categorisation for endocrine disruptors as it is not required under the Commission's legal obligations relating to endocrine disruption and will inevitably lead to the creation of 'black lists' that will be highly vulnerable to misinterpretation and misuse. Testing would involve the sacrifice of large numbers of animals to provide unnecessary data which would not add any additional understanding to the toxicological behaviour of plant protection product active substances that already benefit from extensive data packages. ECPA believes that all relevant scientific information should be considered and evaluated using a structured weight of evidence approach considering both the quality and consistency of data. It believes that endocrine disruptors can be managed by risk assessment. The following organisations gave a similar response: the **Crop Protection Association, CropLife Africa Middle East A.I.S.B.L, CropLife Canada, CropLife Cote d'Ivoire, CropLife Ghana, CropLife India, CropLife International aisbl, Croplife Kenya, Croplife Madagascar, CropLife Malawi, Croplife Mauritius, CropLife Morocco, CropLife Namibia, CropLife SA, CropLife**

Zambia, Croplife Zimbabwe, Dansk Planteværn, Belgische vereniging van de industrie van plantenbeschermingsmiddelen (Phytofar), Union de l'Industrie de la Protection des Plantes (UIPP), the Subtropical Growers' Association of South Africa (Subtrop) and Hellenic Crop Protection Association. The **Bolsa de Cereales de Buenos Aires (Buenos Aires Grain Exchange)** and **the Camara De Sanidad Agropecuaria y Fertilizantes** agree with the position presented by ECPA. It is pointed out that Argentina's exports of Argentina to EU have a value of EUR 5,000 million. The application of a random default level for the setting of import tolerances for residues would be contrary to the EU's commitment to the WTO SPS and TBT agreements. The **Finnish Crop Protection Association** supports the ECPA contribution and states that triazoles play a vital role in Finland's cereal production. Mancozeb is indispensable in growing potatoes. The **Lithuanian Crop Protection Association** concludes that reduced availability of active substances would jeopardise plant protection against *Septoria triticy* and other diseases. There is a great risk that protection of oilseed rape against major diseases will be significantly reduced. The **Dutch Crop Protection Association** (Nefyto) points out that, based on a Dutch exploratory study, the possible loss of triazoles will have great impact on some major crops such as cereals and sugar beet. Furthermore, the viability of a large number of speciality crops in the Netherlands e.g. flower bulbs, which are very important from an economic point of view, will come under serious pressure. **Jelgavas rajona lauksaimnieku apvienība** (JRLA) and the **Latvian Crop Protection Association** (LAALRUTA) state that there are 102 registered fungicides in Latvia of which 57% contain active substances from the triazole chemical group. The respondent points out that it is important that the criteria for endocrine disrupting substances should be scientific and risk-based. There is a high concern that banning azole fungicides could have a very significant effect on the Latvian agricultural sector. The **AEPLA** (trade association for plant protection products in Spain) points out that nothing in the world is totally risk free, including driving motor vehicles, but we don't ban driving even though people get killed in motor accidents every day. Instead, we assess the risks involved and set rules in order to mitigate the risk, and then we enforce control. There should be more focus on developing more effective science in the endocrine disruptor discipline to better understand potential risks. We can then develop appropriate risk mitigating strategies and regulations, before drastic and unnecessary decisions are made that compromise food security and global development. Several organisations had similar responses, including **Asociación Española de Fabricante de Productos Fitosanitarios, Agricultural Business Chamber of South Africa (Agbiz), Agro Agrargroßhandel Gmb& & Co. KG, ANIPLA, Belgische Vereniging van Verdelers van Plantenbeschermingsmiddelen, the Bulgarian Crop Protection Association, Agrofarma, The Canola Council of Canada, the Centro de Exportadores de Cereales (CEC), the Croatian Crop Protection Association, GIZ fitofarmacije (Plant Protection Industry Association of Slovenia), and Industrieverband Agrar e.V.** The respondents state that potency is a key determinant of whether a substance may induce adverse effects at environmentally relevant concentrations. However, they also believe that all elements of hazard characterisation should be included. These hazard characterisation elements are essential to ensuring that all relevant scientific information on the hazard of a substance is considered in regulatory decisions. Without them, substances which pose little or no concern for human health or the environment could be considered to have endocrine disrupting properties and could be unnecessarily banned. **FoodDrinkEurope** believes that the safety assessment and any subsequent regulatory risk management measures for chemicals present in food should continue to be based on the principles of risk assessment. In addition, the hazard classification used for industrial chemicals is based on an adverse toxicological effect e.g. carcinogenicity or mutagenicity, not on a mode of action. It is therefore inappropriate to establish a hazard classification based on endocrine disruption modes of action. Potency is a key consideration in both toxicological risk assessment and in regulatory classification and labelling of all substances. For example, for chemicals to be labelled as 'toxic' they must have a defined potency. For this reason, a highly potent toxin (e.g. cyanide) will be more strictly regulated than a less potent one (e.g. table salt). The concept of potency is especially important for endocrine disruptors since so many chemicals can interact with the endocrine system.

Thousands of natural and manmade substances have been shown to possess slight hormonal activities when tested in screening assays, without causing adverse health effects. Those endocrine-active substances should not be confused with endocrine disrupting chemicals which produce clear adverse effects *in vivo*. Since the purpose of the present regulatory scheme is the protection of people and the environment, it is critical to differentiate between those chemicals that are of a high concern and those that are not. It would therefore not serve the objectives of this scheme to put a very potent endocrine disruptor at the same level of concern as a weak endocrine-active chemical, many of which are present naturally in our food. **CEFIC ECPI** proposes the development of a single set of criteria to determine endocrine disrupting properties, using the WHO-IPCS definition as a basis, but also taking into account the relevance of the adverse effect (that is: severity of effect, (ir)reversibility of effect, potency and lead toxicity). For a substance to be considered to have endocrine disrupting properties, the adverse effect should occur as a consequence of a primary endocrine mode of action. The respondent indicates that, without these additional elements of hazard characterisation, it is likely that many natural substances, including those found in food, feed and drinks would require regulating as they could demonstrate both endocrine-active and endocrine disrupting properties. The **Association of the Austrian Chemical Industry FCIO, Arbeitsgemeinschaft PVC und UMWELT e.V. (AGPU), Bund für Lebensmittelrecht und Lebensmittelkunde (BLL) e. V., CEPE, Chemetall GmbH, Chemical Industry Federation Finland, the European Plastics Converters Trade Association (EuPC), Fachverband der Chemischen Industrie Österreichs (IndustrieGruppe Pflanzenschutz, IGP), Federchimica, IKEM - Innovation and Chemical Industries in Sweden, Industrieverband Klebstoffe e. V., PCK Raffinerie GmbH, PlasticsEurope Deutschland e.V., PlasticsEurope Services, PRODAROM, Remmers Baustofftechnik GmbH, the Technical Committee of Petroleum Additive Manufacturers in Europe, the Association of Lithuanian Chemical Industry Enterprises, Thor GmbH, the UK Chemical Industries Association (CIA), Union des Industries Chimiques, Verband der Chemischen Industrie e.V. (VCI), Verband TEGEWA e. V., Vereniging van de Nederlandse Chemische Industrie (VNCI)**, and the **Association of Chemical Industry of the Czech Republic** support the CEFIC contribution to the public consultation. **ASPA-INGRECOS** stresses that a three-category-approach raises serious concerns, especially because the cosmetics industry is faced with an animal testing ban and a marketing ban of products that contain ingredients tested on animals. The **European Paint and Printing Ink Council** believes in the safety of their products and thinks that substances that affect the safety of the population and/or of the environment should be appropriately regulated, but chemicals should not be 'guilty before proven innocent' and hence only regulations based on good science should prevail. The contribution of the **European Biocidal Products Forum** (EBPF) is similar to Cefic's position. In addition the EBPF provided the following specific information on biocidal products. The EBPF commissioned a study to investigate the number of biocidal active substances that could be potentially affected by the different proposals for endocrine disruptor criteria. According to the respondent the endocrine disruptor interim criteria, currently in the Biocidal Products Regulation (BPR), are met by 5 out of 108 active substances. If this proportion is extrapolated to the entirety of active substances in the BPR review programme (245 substances), a total of 11 active substances are expected to meet the interim endocrine disruptor criteria. The respondent highlights that a biocidal product cannot be authorised for use by the general public if it has endocrine-disrupting properties. There are no provisions for derogation or exemption under the BPR for substances used by the general public. The **Cosmetic Toiletry & Perfumery Association** (CTPA) points out that, since the criteria to identify endocrine disruptors are meant apply across various pieces of legislation, it is relevant for the Commission to take into account the specific situation of the cosmetics industry. The cosmetics industry strongly supports the idea that there is no need for additional policy changes to the Cosmetics Regulation and states that the risk-based approach is well established in the Cosmetics Regulation. It refers to documents prepared by the Scientific Committee on Consumer Safety which state that a risk based approach can be performed for any substance including those that might have some endocrine activity. **Cosmetics Europe** points out that the widely agreed

WHO/IPCS definition of endocrine disruptor states that only substances that produce adverse effects in an intact organism mediated by the endocrine system are genuine endocrine disruptors. Therefore, evidence from *in vivo* testing is required in order to identify an endocrine disruptor. However, the cosmetics industry is faced with an animal testing ban and cannot use ingredients tested on animals. The respondent emphasises that it does not make any difference to the cosmetics industry whether a categorisation will be linked to a ban, restriction or labelling as any categorisation of a substance as endocrine disruptor (regardless of category) will have a major impact and in many cases unintended effects on consumer perception even if the legal consequences are limited. The **European Organisation of Cosmetic Ingredients Industries and Services** supports using the WHO's definition to identify endocrine disruptors and the creation of only two positive lists, which will result in two categories of endocrine disruptors and suspected endocrine disruptors. The respondent proposes that the concept of risk is taken into consideration. The **German Cosmetics, Toiletry, Perfumery and Detergent Association** supports the contribution from Cosmetics Europe. The **Fédération des Entreprises de Beauté** (FEBEA) submitted a similar response to that of Cosmetics Europe. The **European Federation for Cosmetic Ingredients** (EFfCI) highlights that there is a need for an alternative concept for evaluating potential endocrine-mediated effects, one that considers both evidence of the effects and their relevance (e.g. lead toxicity, severity, potency). Changes to the existing regulation should aim to identify substances of high regulatory concern, avoid overregulation when there is no benefit for the consumer or the environment, and take into account the specificities of the cosmetics industry with respect to the animal testing ban. The **European Federation of Pharmaceutical Industries and Associations** (EFPIA) agrees with the WHO /IPCS definition while stressing the need to show a link between effects on the endocrine system and consequent adverse health effects. It is their view that regulating compounds, such as endocrine disruptors, should be based on a comprehensive assessment of all of the data. Aside from identifying hazards, this should also take into consideration, other equally important aspects such as potency, severity, reversibility and likelihood of occurrence of effects (hazard characterisation), and environmentally relevant exposure levels. The respondent states that the assumption that no safe limits can be derived for endocrine disrupting chemicals is not supported by the existing science as shown by the pharmaceutical industry's extensive experience of the in developing endocrine active medicines. The EFPIA highlights that using process chemicals in pharmaceutical manufacturing processes is highly regulated by pharmaceutical legislation and is part of a market authorisation evaluation. Substituting substances in the manufacturing processes of active pharmaceutical ingredients (API) require thorough case-by-case studies analysing alternatives to meet the ultimate objectives of patient safety and efficacy of the medicinal products legislation. Moreover, implementing any change to the API manufacturing process requires regulatory authority pre-approval before it can be implemented. This has the potential to severely affect existing market authorisation for medicinal products and availability, not only in the EU, but also around the world. An estimate of the impact on an established pharmaceutical process suggests that substitution will take 2-5 years, depending on the complexity. The estimated costs are approximately EUR 1.3-2.6 million per substance that is substituted. This includes the cost of updating the medical product around the world can take up to approximately 6 months to get approved. It can be concluded that any substitution is therefore highly time consuming and thus could therefore endanger the supply of and patient access to important pharmaceutical products. The **Association of the European Self-Medication Industry** (AESGP) states that the process of identifying substances with endocrine disrupting properties under REACH is progressing (even without criteria). One of the substances identified to be of concern for endocrine disruptors is 4-tert-OpnEO (Triton X100) which is a very important process chemical for biotechnological processes used in pharmaceutical production. It is underlined that the use of process chemicals in pharmaceutical manufacturing processes is highly regulated by pharmaceutical legislation and is a part of the market authorisation. The respondent agrees with the WHO/IPCS definition while stressing the need to show between effects on the endocrine system and consequent adverse health effects. It considers that the

assumption that no safe limits can be derived for endocrine disrupting chemicals is not supported by the existing science. The **European Diagnostic Manufacturers Association** (EDMA) represents the voice of *in vitr*o diagnostic (IVD) manufacturers in Europe. The respondent stresses that, given that both IVD reagents and positive controls will contain endocrine active substances in order for the IVD test to perform as intended, it is important that EU adopts an approach which will not limit or restrict the use of endocrine disrupting or active chemicals in the IVD sector. The use of endocrine active substances is an often essential requirement for certain IVD, particularly if such substances are present as positive control or in biologically active reagents. If endocrine substances be defined in a broad enough way so as to allow their use in in IVD, the European Commission should note that all IVD kits include a positive control to ensure that the test is performing as intended. The positive control contains the same marker or 'analyte' which is being tested for in the patient's sample (e.g. blood sample). In many cases the positive control will therefore need to contain an endocrine active substance. It is impossible in many cases to substitute these substances for 'less hazardous' substances. The **European Federation for Cookware, Cutlery and Housewares industries** (FEC) identifies the need to have harmonised tests to show the release of an endocrine disruptor from a manufactured or imported object. These should be relatively simple to carry out and should be accessible for SMEs. Risk assessment of the (possiblel) release of endocrine disruptors from food contact materials should be carried out under realistic conditions of exposure. **UNITAM**, the French organisation for the Cookware, Cutlery and Housewares industries, points out the necessity of having an harmonised definition of an endocrine disruptor for legal purposes, as well as harmonised science-based criteria and test methods that makes it possible to correctly decide whether a substance is an endocrine disruptor or not. The **European Tyre & Rubber Manufacturers' Association** (ETRMA) recommends that clear and unambiguous criteria for identifying endocrine disrupting chemicals are adopted and that the scope of the upcoming impact assessment is broadened to include the impact on industrial chemicals subject to REACH (not just those which are under the scope of the biocides and plant protection products regulations). The ETRMA also suggests using industry associations and to involve downstream users in the early stages of the decision-making processes. It believes that an undifferentiated, no-threshold approach to endocrine disrupting substances, would not be proportionate. It would create enormous legal uncertainty for downstream users if there are impurities, which can be found at residual concentration in substances or in mixtures. **Concawe** (Environmental Science for the European Refining Industry) believes that regulation of endocrine disruptors should be based on use, exposure and risk. **EurEau** (the voice of the water services in Europe) considers that an EU-wide definition of endocrine disruptors will have a positive impact on water resource protection. EurEau supports the WHO/IPCS definition of endocrine disruptors and insists that the precautionary principle should be applied to endocrine active substances. It believes that a ban on substances should be decided based on a hazard based approach which takes into consideration the risk of adverse impacts on water resources (groundwater and surface water). The **Swedish Water&Wastewater Association** provided a similar response. According to **Eurometaux** substances should only be considered as endocrine disruptors of regulatory concern if there are clear adverse effects unambiguously caused by a well identified and empirically described mode of action. These adverse effects must be relevant to humans and wildlife populations. The **American Petroleum Institute** (API), a national trade association representing over 600 member companies involved in all aspects of the oil and natural gas industry, considers that using the WHO definition of endocrine disrupting chemicals could provide a platform for regulatory consistency beyond the EU. The respondent advocates the use of a single set of identification criteria based upon a comprehensive weight-of-evidence framework incorporating species relevance, biologically plausible causality, the characterisation of the dose-response/potency, exposure assessment and adverse health consequences. The **US Personal Care Products Council** considers that endocrine disruptors can 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. **CropLife America** (CLA)

supports a scientific, risk-based approach to regulating plant protection products. The proposed hazard-based approach places Regulation (EC) 1107/2009 in breach of the WTO SPS Agreement. Furthermore, none of the four options can be considered as correct application of the EU precautionary principle, which is meant to enable precautionary decisions if data are insufficient for conducting a full risk assessment. Hazard-based endocrine disruptor criteria may impact EUR 65 billion worth of imports into the EU, many of them commodities that cannot be grown in the EU but that are essential to its food processing industry. The EU approach to regulating plant protection products using hazard based cut-off points for endocrine disruptors, coupled with a default residue level of 0.01mg/kg could block over EUR 4 billion in US agricultural trade. The respondent points out that food safety, including the control of fungal aflatoxins in grain should be a consideration. The European Commissions' rapid alert system for food and feed (RASFF) has reported 10 notifications of aflatoxin B1 in maize of European origin since the last maize harvest in autumn 2012. In 2013 several European countries, including Romania, Serbia and Croatia reported the nation-wide contamination of milk for human consumption with aflatoxins. **Ghana Agri-Input Dealers Association** (GAIDA) referred in its response to CroplifeAmerica. The **Brazilian Crop Protection Association,** ANDEF, highlights that regulating endocrine disruptors purely based on hazard cut-off points is likely to have a serious impact on the trade in agri-commodities and produce. It states that such a restrictive interpretation would have a substantial impact on trade between the EU and non-EU countries. For Brazil this could result in a trading loss of about EUR 10,3 billion. The **Canola Council of Canada** states that applying a random default level when setting import tolerances for endocrine disruptor substances would be contrary to the EU's commitment to the WTO SPS and TBT agreements. This would limit the benefits of the Canada-Europe Comprehensive Economic and Trade Agreement (CETA). The **Camara de la Industria Aceitera de la República Argentina** (CIARA) considers that risk assessment is the best scientific practice, as it is congruent with the approach followed by other organisations. A risk-based approach also complies with international and binding WTO-agreements. The **American Chamber of Commerce** points out that the chemical industry and downstream users throughout the supply chain continuously assess the socioeconomic impact of substitution. They continuously assess trade-offs between performance, health, safety, environmental impact and economic consequences for manufacturers, suppliers and customers. The whole process relies on thorough risk assessments. Because the resulting product represents the best balance between all requirements, substances often cannot be easily substituted, and this is particularly the case for high volume commodity chemicals which take decades and major capital investment to develop the products and bring them to full commercialisation. While the US and EU may adopt different legislative approaches for regulating endocrine-active substances, the ACC believes that it would be possible to minimise unwarranted negative trade impacts and improve EU regulatory cooperation by using a definition of endocrine disruptor that includes demonstrating adverse effects and by more fully characterising hazards when identifying endocrine disruptors. The **Cranberry Institute** furthers the success of cranberry growers and the industry in the Americas. With over 30% of the US cranberry crop exported and the EU being the single largest export market, meeting EU plant protection product residue standards is important to US cranberry growers and handlers. The respondent urges the EU to include science-based risk assessments for endocrine disruptors and encourage the EU and US to seek harmonization by taking similar risk-based approaches in the regulatory decision-making process for endocrine disruptors. The **Fundación Instituto para las Negociaciones Agrícolas Internacionales** links the defining of criteria for endocrine disruptors to WTO agreements and cites several conclusions of WTO Panels and the Appelate Body that may be of importance for setting a definition. The respondent emphasises that any policy option chosen must take into account these international standards. If the measures are adopted without a well-founded scientific basis, they will probably turn into a non-tariff barrier to trade. The **Japan Chemical Industry Association** considers that an alteration in the endocrine system in itself is not an adverse effect; it is just a biological process that may or may not lead to adverse effects. Endocrine 'disruption' and 'modulation (or modulatory

activity)' must be strictly distinguished because the endocrine system has a homeostasis capacity with a specific compensatory feed-back mechanism. The **Grain and Feed Trade Association** (Gafta) represents the international trade in agricultural commodities. Gafta was established in 1878, and represents over 1500 companies around the world. It suggests that a full risk assessment approach should be considered as an additional and preferred policy option.

5.9. Other

In the 'other' category, a total of 26 web-based responses were received from farmers, trade organisations, industry, NGOs, a trade union, and medical doctors. The **AHDB's Potato Council division** commissioned a report on the potential impact on British potatoes of the loss of plant protection products that may be identified as endocrine disruptor's. It estimated that the loss of endocrine disruptor's could cost the UK growers £341 millions - £502 millions in yield losses a drop of 35-56% in current farmgate value. **Asociatia Industriei de Protectia Plantelor din Romania** supports the use of the WHO / IPC (2002) definition as a starting point and as a basis for scientific criteria for determining 'endocrine disrupting properties'. Further elements of risk characterisation (severity (ir) reversibility, potency and toxicity lead) should be included in the criteria. **CropLife Tanzania** believes that endocrine disruptors do not need special regulatory treatment, but can be dealt with like other substances of potential concern, i.e. be evaluated using a full risk assessment framework. **Direct produce supplies plc**, is a fresh produce importer. It states that fresh produce are living organisms, and subject to diseases, not only in the fields, but also after harvest, during transport, distribution and in the consumer's fruit bowl too. Fruits such as mangoes and citrus have been traditionally exported by sea-freight, and the use of prochloraz or thiabendazole have proven to be extremely effective in providing protection against post-harvest diseases. The increased occurrence of diseases post-harvest adds further costs to the product. This has consequences on the diet of the consumers (disregarding fresh produce as it costs more). This will also lead to lower returns to the suppliers. The **Endocrine Society** states that the term "adverse effects" must include effects not only during and after exposure throughout an individual's lifetime, but also possible effects on future generations (i.e. transgenerational effects). For evidence of relevance the default assumption should be that an effect seen in mammalian animals should always be considered as relevant for humans. The respondent believes that the implications of the following characteristics of endocrine disruptors should be considered. A single hormone will have changing effects at different times and places in the body during development and with different sensitivity. Therefore sensitive endpoints with predictive ability must be prioritized to identify endocrine disruptors. Hormones act at very low concentrations so the effects of very small amounts of endocrine disruptors need to be taken into account systematically. Chemical interference with hormone actions during early development can have long-lasting consequences that might manifest years later. Multiple chemicals can affect a single hormone pathway, and humans and wildlife are exposed to mixtures of chemicals throughout their life cycles. Therefore, assessment of endocrine disruption should include examination of the effects of mixtures of chemicals and not only one chemical at a time. The **European Trade Union Confederation**, ETUC, believes there is a need to identify not only confirmed endocrine disruptor but also suspected and potential endocrine disruptor. Confirmed and suspected endocrine disruptor need to be regulated while potential endocrine disruptors need to be investigated further. The **Fungicide Resistance Action Group**, UK, highlights an increased risk of resistance development in key diseases if a diversity of plant protection products is not available to growers. Hrvatsko društvo biljne zaštite, the **Croatian Plant Protection Society**,

highlights that endocrine disruptor criteria will affect the availability of crop protection products and will impact agriculture. The **Policy Research Centre of Environment and Health** (Dutch: Steunpunt Milieu & Gezondheid) is a consortium consisting of all Flemish Universities and two partners, VITO (Flemish Institute for Technological Research) and PIH (Provincial Institute of Hygiene). Since 2002 a human biomonitoring network has been set-up in Flanders (Belgium). One of the major focuses is the question of whether combinations of pollutants in the general population are associated with biological effects. The reported associations were statistically significant. Negative associations with sex hormones in boys, genital stage (boys) and breast development (girls) for the sum of the urine metabolites were found. The **Resorcinol Task Force** points out that resorcinol has been on the EU market for many decades and it is used in the tyre and rubber industries. Resorcinol has been the subject of several regulatory reviews over time, most recently REACH, and so an extensive technical database has been developed. The independent assessment of the CEHOS/Danish EPA report concluded that, based on human data and i*n vivo* studies, there is insufficient direct evidence of endocrine disruption (specifically thyroid function) to place resorcinol into the Danish EPA Category 1. The **Società Italiana di Tossicologia**, SITOX, states that substances should only be considered as endocrine disruptors when they produce clear adverse effects *in vivo* in intact animals, unambiguously caused by an endocrine mode of action, and at exposure levels of relevance to the potential human and population exposure. The respondent believes that endocrine disruptors can be treated like most other substances of potential concern, and be subject to risk assessment, where both hazard and exposure are considered in regulatory decision making. The **Society for Endocrinology** points out that there is a growing body of evidence that shows the health effects of endocrine disrupting chemicals on wildlife, laboratory animals and humans. It can be concluded that like hormones, endocrine disrupting chemicals are active at even low doses, and can induce a range of adverse health outcomes. Many of these adverse effects are not examined by traditional toxicology assays. As a result, there is a need for a policy change taking into consideration this evidence. The respondent indicates that using a hazard-based mode of assessment may mean ignoring much data that already exists on exposure and effects. Substances should be assessed on the weight of evidence that exists already. Potency is considered a fundamentally important aspect of the activity of any compound and this applies also to endocrine-active/disruptive activity. The respondent considers that the main problem in assessing whether a chemical is an endocrine disruptor for humans is the fact that the classic toxicology experiments one would undertake are not doable in humans for obvious reasons and particularly in the most vulnerable groups: the foetus, developing infant and child. So, investigators concerned about the effects of endocrine disruptors have to resort to epidemiological human studies. When these are conducted appropriately, the results can be helpful. The **Society of Irish Plant Pathologists** states that the potential loss of fungicides is of particular concern to both cereal and potato growers. The potential categorisation of particular azoles as endocrine disruptors and hence their possible removal from the European market will lead to restrictions on the production of cereals in Ireland, through the potential cessation of wheat production due to the inability to control *septoria tritici* blotch, and also increased difficulties with disease control in barley crops. Furthermore, any restrictions which reduce the number of effective actives for the control of late blight in potatoes will have a devastating impact on potato production in Ireland (without effective control of late blight, potato production in Ireland is not economic). It is stressed that certain regions of Ireland are largely unsuited to other forms of crop production. The **Ulster Arable Society** states that the 'azole' group of plant protection products are a vital tool to help producers protect their crops. The loss of these products would be a major blow to the arable industry and future food production. It would undoubtedly lead to significant yield reductions and an increase of mycotoxins especially in grain. It is noted that yields of many cereals over the last few years have 'flatlined' and that climate change in other major food producing areas in the world is becoming a major concern. Removal of these products can only have one effect and that is to reduce agriculture production within Europe. The

Wirtschaftskammer Österreich supports the proposal for the criteria for the identification that has been elaborated by the German Association of the Chemical Industry.

6. THE POTENTIAL IMPACTS OF THE OPTIONS AS SPECIFIED BY RESPONDENTS TO THE PUBLIC CONSULTATION

6.1. Health

- Plant protection products serve an important public health objective by controlling pests and diseases. Notably, the products 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. 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'.
- Plant protection products help control invasive pests that can damage the environment and undermine ecological diversity.
- Health damage to people by residues of plant protection products in food, including the daily mix of plant protection products consumed and the cumulative effects with other chemicals.
- Effects on residents, for example by air pollution of plant protection products for residents.
- Contamination of surface water, ground water and drinking water by plant protection products.
- Health costs of diseases developed due to plant protection product exposure.
- Rising production prices will be passed on to consumers who would find it difficult to manage any significant increase in food prices and will reduce their consumption of fresh produce.
- The diet of the consumers (disregarding fresh produce as it costs more).
- Presence of mycotoxins in agricultural products with the loss of plant protection products.
- Los of plant protection products that fight disease in stored grains and other post-harvest treated commodities and eliminate noxious weeds such as *Ambrosia artemisiifolia,* and *Heracleum mantegazzianum* which are harmful to humans or animals.

6.2. Environment/sustainability

- Plant protection products make farming more efficient, and reduce 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.
- Loss of eco-services (soil biodiversity due to monocultures, beneficial organisms, nesting for birds and other organisms, feed for bees, birds, etc.).

- Damage of plant protection products to the environment & biodiversity (decrease of bird populations, bees, mammals, aquatic organisms, plants, ecosystems, etc.).
- Loss of soil fertility.
- Effects on future generations. Several plant protection products, including endocrine disrupting plant protection products, have shown to be capable of affecting DNA and the mutations pass onto the next generations manifesting in diseases and disorders.
- Sustainable agricultural production demands efficient use of a scarce resource, land, in order to limit land being drawn into agricultural production at the expense of natural habitat. Efficiency is achieved through the use of a variety of agricultural technologies, one of the oldest being that of the use of plant protection products.

6.3. Agriculture

- Loss of individual active substances incorporated in plant protection products.
- Blacklisting of categorised chemicals as suspected endocrine disruptors.
- Disease control in crops and the knock on impact on yields, profitability, production and trade in agricultural products.
- Crop losses/ yield reduction; increase of cultivation costs; reduced quality and unreliable supplies.
- Farm income will be less stable if key fungicides are no longer available.
- Less disease management tools.
- Less tools for integrated plant protection management.
- Threatening crop diversity in Europe.
- If endocrine disruptors are withdrawn without due cause there is a risk that there will not be enough seed produced
- Costs of producing stronger plant protection products due to the gradual increase of resistance of pests and the costs of disposal of the non-effective plant protection products.
- The loss of soil fertility.
- The loss of many plant protection products could lead to a few products monopolizing the market and thereby drastically increasing the cost of production.
- Crop viability. Decisions on which crop to grow will depend on a range of factors including market prices, costs of production and expected yields, as well as alternative options. The point at which a crop becomes unviable will vary for different crops and production systems.

- Business viability. For some, the loss of marketable yield could be a threat to business viability, particularly on smaller holdings with fewer alternative options. This is particularly the case where businesses have very specialised infrastructure, or capital investment, targeted at particular crops or groups of crops.

- Adaptation. Farmers and growers will take mitigating actions to minimise any potential yield loss, such as using alternative active substances where available, modifying their

production systems or using new technology.

- Resistance. A range of active substances, with different modes of actions, are required to prevent resistance developing in target organisms. The loss of one or more active substances active against the target organism will impact on the ability to implement resistance management strategies.

- Outbreak of fungi resistance to other substances.
- Sector variations

    - The largest impacts are expected in the sectors where there are limited plant protection product active substances available, and therefore fewer potential alternatives available in the event of losing and active substance.

    - The horticultural sectors (edible and ornamental) are severely affected, with the added challenge of high quality specifications for produce.

    - Where profitability is sufficiently high the horticultural sector is highly innovative and has the potential to adapt. The parts of the sector with lower profitability or highly specialised growing systems will find it more difficult to adapt.

    - The impacts in the other edible crops are mixed, with crops such as potatoes, sugar beet and hops more severely affected than the cereals.
- Lack of effective treatments at the appropriate time will lead to further wastage along the supply chain. Wastage doesn't only mean rotting fruit at the consumer, but more work has to be put in by the importer.
- Some agricultural production has particular economic significance in certain regions which are largely unsuited to other forms of crop production and are severely affected by rural decline.

- Supply businesses to farmers.
- The Commission has to consider existing residue limits and has to respond to any request for an import tolerance which may be made by a third country.
- Prices of agricultural products; increased costs for consumers.
- Production of baby-food (must be mycotoxins free).
- Certain type of agricultural production has strong cultural and historical significance.

6.4. Trade

- Imports into the EU, many of which are commodities that cannot be grown in the EU but which are essential to its food processing industry.
- Exports.

- Increase Europe's dependence on importing food, feed and bioenergy feed-stocks, making Europe an even greater drain on global resources.
- Because the EU is moving to an entirely different regulatory framework based on a hazard only paradigm for assessing endocrine disruptors, it will make regulatory coherence very difficult, particularly between trading partners and their regulatory authorities which use a risk based paradigm for evaluating chemicals.
- Developed nations having preferential trading agreements with the EU.
- Potential confusion in the market place, enforced through private retailer standards.
- Upward pressure on global prices for agricultural products.
- Alternatives must be looked at in a broad sense.
  Permitting a derogation for agricultural produce, such as canola, which may be produced using certain plant protection products and have residue limits above the permitted levels but as they are destined for biofuels there would be minimal human health risk

6.5. Chemical industry

- Downstream users of chemicals.
- On the cosmetic sector via the use of ingredients falling under regulations other than the European legislative framework for cosmetic products (Cosmetic Products Regulation (EC) No 1223/2009).

6.6. Food security

- Possibility of EU to satisfy internal demand to plant products (self-sufficiency rate).
- Global food security.

6.7. Innovation

- Criteria for endocrine disruptors may create another barrier for innovation.
- Commercial R&D on plant protection products is moving away from the EU to other countries where regulatory systems are more objective and predictable.
- R&D for new plant protection products needed by European farmers will further decline.
- Denying access to useful products and technologies.

6.8. Animal testing

- Additional animal testing.

6.9. Social inequality

- To reinforce existing patterns of economic and social inequality.

7. ARGUMENTS PROVIDED IN RESPONSES SUPPORTING OR REJECTING THE OPTIONS FOR DEFINING ENDOCRINE DISRUPTORS AS SET OUT IN THE ROADMAP

This chapter list the arguments made by respondents in favour or against the various options.

7.1. Option 1 No policy change

7.1.1. In favour

-None of the respondents favoured option 1.

7.1.2. Against

Objectives of the roadmap

-This option does not meet objectives 2 ('scientific criteria and regulatory operability') and 3 ('horizontal application to all legislation') as set out in the roadmap. .

Intention of EU rules

-The legislators' intention was clearly for these criteria to be temporary, and not permanent, as they specifically used the term interim. Option 1 therefore goes against the spirit and letter of the Plant Protection Products Regulation (EC) 1107/2009 and the Biocides Product Regulation (EU) 528/2012.

- The option of 'no policy change' is not in line with the Plant Protection Products Regulation (EC) 1107/2009 which states that criteria for identifying endocrine disrupting chemicals must be drawn up by the European Commission.

Application of ED criteria across all sectors

-We need endocrine disruptor criteria which apply across all sectors. The current interim criteria set out only apply to plant protection products and biocides.

-De facto the interim criteria differ between Plant Protection Products Regulation (EC) 1107/2009 and Biocidal Products Regulation (528/2012). The Biocidal Products Regulation assumes that substances which are identified in accordance with Articles 57(f) and 59(1) of REACH as having endocrine disrupting properties as fulfilling the criteria for endocrine disruptor.

-If option 1 is applied, different approaches would be used under PPPR, BPR and REACH. This would create a lack of consistency across similar regulations, which might be inappropriate for regulating endocrine disrupting substances which are used both in

plant protection products or in biocides and for industrial or consumer uses. There is no provision for these interim criteria to be applied to industrial chemicals under REACH.

-A proposed EU rule taken in line with Option 1 would discriminate among end uses of the same chemical product, by differentiating among the following uses: cosmetic, industrial, biocide, and plant protection product. Agriculture use falls under plant protection products, and this is the class with most draconian restrictions proposed: no exposure assessment, no socio-economic assessment, and no registration.

-Option 1 ignores consumer protection as scientific criteria for identifying endocrine disruptors are needed also for other legislation too, especially in relation to provisions regulating endocrine disruptors in consumer products such as toys, products for children and toiletries.

-Option 1 would not improve the current situation which is marked by the under-regulation of endocrine disruptors in consumer products. Science-based criteria for identifying hormone disrupting chemicals in other products with which consumers come in contact every day such as toys, cosmetics, food contact material etc. are urgently needed.

-The plant protection product regulation (PPPR) and biocidal products regulation (BPR) are the only laws that identify if a substance is a hormone disrupting chemical (or endocrine disrupting chemical) and so cannot be used within the EU. However, all endocrine disruptors need to be identified, regardless of whether they are used as plant protection products or biocides, in cosmetics, food packaging, children's toys or elsewhere.

-To protect public health, and reduce the exposure of all EU residents to endocrine disruptors, we need criteria that identify these across all sectors, in line with the EU's 7th EAP which says in Art 54 (d) 'by 2020: […] the combination effects of chemicals and safety concerns related to endocrine disruptors are effectively addressed in all relevant Union legislation, and risks for the environment and health, in particular in relation to children, associated with the use of hazardous substances, including chemicals in products, are assessed and minimised'. Therefore, cross-cutting criteria to scientifically identify endocrine disruptors in all sectors are needed, to tackle the ubiquitous public and environmental exposure.

<u>Covering all endocrine routes</u>

- The identification of endocrine disruptors using Option 1 would be scientifically and factually incorrect, being based solely on decisions on cancer and reproductive toxicity classification decisions rather than scientific evidence indicating that a particular substance causes an adverse endocrine effect.

-The current interim criteria could overlook chemicals which do not cause cancer or harm reproduction, but which do affect the brain or metabolism, and thus can contribute to other endocrine associated illnesses.

-The interim criteria do not sufficiently cover endocrine disruptors interfering with axes other than the estrogenic or androgenic axes are not sufficiently covered by the interim criteria (e.g. the thyroid axis).

-The interim criteria are not science-based and simply rely on an unreliable association of endocrine disrupting properties with Category 2 carcinogens and Category 2 reproductive toxicants. It cannot be assumed that substances with these properties will automatically be endocrine disruptors.

Occurrence of false positives and negatives

- There will be active substances that have or are to be classified as carcinogenic (category 2, C2) and toxic for reproduction (category 2, R2), but where it is clear that this classification is based on an adverse effect which is not mediated via an endocrine mode of action.

- This option is prone to identifying both false positives and false negatives due to its limitation on substances classified for reproductive toxicity

Hazard versus risk

-This option only determines whether a certain chemical might have an effect on an endocrine system in an animal—irrespective of whether in the real world there is a situation where this would actually happen.

-Option 1 does not follow the accepted science-based risk assessment process found in international standards and guidelines would not be followed. Instead, 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.

Causal link

-Option 1 is inconsistent with the WHO/IPCS (2002) definition which requires a causal link between observed effects and endocrine activity.

-Option 1 fails to provide the information necessary to apply the WHO/IPCS 2002 definition of an endocrine disruptor.

Uncertainty

-The part of the interim criteria stating that substances have to be classified as endocrine disruptors which are toxic for reproduction category 2 and which have toxic effects on endocrine organs, creates considerable uncertainty, as there is no specification or definition of “toxic effects on the endocrine organs” in this context.

-This option will have a limited reproducibility if different regulators interpret the ‘‘may be’’ criteria differently.

Environmental effects

- With this human-centred definition compounds which may cause adverse effects in populations of non-target organisms with an endocrine mode of action, cannot be identified.

-Option 1 will lead to a lower level of protection for the environment than intended when f the BPR and PPPR were developed. It was the intention that the final criteria

should protect both human health and the environment, but the interim criteria focus on human health hazard classification (the environment is indirectly covered by the interim criteria in the BPR, since Article 5.1(d) specifies that substances identified as endocrine disruptors under Article 57(f) and 59 in REACH must also not be approved).

Other

-Option 1 may discourage the development of new data to better understand the adverse effect. Failure to incorporate this scientific knowledge will cause regulators to implement actions which do not give additional protection to human health or the environment.

- The vast array of data required by the EU regulatory authorities is not utilised.

- The interim criteria should only be meant to flag possible endocrine mechanisms, not to classify or apply these endpoints as final cut-offs, without further investigation. If the latter was meant to be the purpose, the duty on the EC to establish endocrine disruptor criteria would have been unnecessary.

7.2. Option 2 WHO/IPCS definition to identify endocrine disruptors

7.2.1. In favour

Causal link

- A definition of endocrine disruptors that requires a finding of adverse effects recognises that, while substances may have the potential to interact with the endocrine system, such interactions will not necessarily lead to any adverse health or environmental effects. Within endocrine systems, natural variations in hormone levels and reversible or transient changes that are not considered adverse have been well documented. The endocrine system is complex and seeks to maintain homeostasis in a continually variable and fluctuating natural environment. Substances can interact with the endocrine system by a variety of mechanisms, including direct effects on hormone dependent or producing tissues, on enzymes involved in the excretion of a hormone, on enzymes for hormone synthesis and through agonistic or antagonistic hormone receptor binding. Evidence that a substance interacts with a component of the endocrine system through one of those mechanisms, however, does not provide any information on whether that substance causes other biological changes, which may, in turn, cause adverse health effects.

WHO/IPSC definition widely recognised

-The scientific definition of endocrine disruptors proposed by WHO/IPCS is a well-established and widely recognised definition produced by a global, authoritative organisation through a world-wide initiative of highly scientific rigour (WHO/IPCS, 2002). In addition, it is supported by a number of organisations and regulatory bodies around the world, including the US Environmental Protection agency, the Canadian Centre for Occupational Health and Safety (CCHOS) and the International Union of Pure and Applied Chemistry (IUPAC).

Other

-The 'Community strategy for endocrine disrupters (COM(1999) 706 final, p.5-6)' specifically refers to a 'working' definition developed by the WHO/IPCS.

- The current legal texts in which endocrine disruptors are mentioned do not need to be changed with Option 2, which would presumably be the case when categories as in Option 3 are included.

7.2.2. Against

Animal testing

-Option 2 will not facilitate cross-cutting criteria for identifying endocrine disruptors, because adverse effects must be observed in intact organisms, and Option 2 does not allow for identification based on in vitro testing. As a result, this option will not provide an incentive to develop better in vitro testing strategies for identifying endocrine disruptors. This is not in line with the PPP Regulation's aim to reduce the use of animal testing.

-Directive 2010/63 requires scientifically satisfactory non-animal methods/testing strategies be used in preference to animal tests wherever possible. Linking the EU definition of endocrine disruptors to *in vivo* data will contradict this.

Precautionary principle

-As it is currently not possible to explicitly proof a causal relationship between hormonal changes, and adverse health effects, and current test methods are limited, a precautionary approach is required.

- Option 2 would contradict the precautionary principle by leading to action only when the risk had been fully evaluated. In reality, the evidence required to do this might never become available due to insurmountable problems in designing suitable experiments, or simply because the necessary research is never attempted. It would certainly not be in the commercial interests of a company producing a potential endocrine disruptor to fund research to explore suspected impacts on wildlife, for example.

Differentiation between levels of evidence for classification as ED

- No differentiation can be made between the levels of certainty regarding the endocrine disrupting properties is possible. However, this differentiation can be made for the classification of carcinogenicity or reproductive toxicity.

-Given the different kinds and amounts of data available, Option 2 lacks the ability to differentiate between different levels of evidence which is very much needed when dealing with potential or suspected endocrine disruptors.

-The option lacks the ability to identify/classify compounds that not (yet) meet all the criteria. Identification and categorisation of suspected endocrine disruptors is important for, for example, identifying further research priorities and other non-legislative activities.

-Option 2 would result in many chemicals not being identified as endocrine disruptors that would therefore go unregulated when in fact the research has not been carried out in relation to endocrine endpoints and adequately understanding their endocrine disrupting properties. This would allow the continued use of these chemicals with resulting damage to human, environmental and wildlife health.

-This option uses the first part of the WHO/IPCS definition on endocrine disruptors: 'Endocrine disruptor is 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'. However, it neglects the second part of the WHO/IPCS definition: 'a potential endocrine disruptor is an exogenous substance or mixture that possesses properties that might be expected to lead to endocrine disruption in an intact organism, or its progeny, or (sub) populations'. The PPP and BP Regulations state that 'substances having endocrine disrupting properties which may cause adverse effects will not be approved for the respective use', adding this extra element of precaution ("may cause") in the legislation. Focusing only on the first part of the WHO definition and having one category where only 'clear evidence of endocrine-mediated adverse effects' are considered means that substances that alter the hormone levels but for which the adverse effects are not yet fully understood, or where the mechanism of action is still being investigated, will not be identified as endocrine disruptors.

-In Option 2 the full WHO definition is shortened and 'potential endocrine disrupter' is omitted. If 'potential endocrine disrupters' is omitted and only confirmed endocrine disruptors are considered, this will block the full and effective consideration of scientific knowledge and its translation into an EU regulatory classification.

-This option leaves out the matching WHO definition for "potential endocrine disruptors". Using only the definition for confirmed endocrine disruptors is a 'black or white' approach.

-Option 2 is incomplete as it leaves out potential hormone disrupting chemicals. To better protect consumers from endocrine disruptors, it will be insufficient to only regulate confirmed endocrine disruptors. Suspected chemicals need to be further investigated with regard to their potential endocrine disrupting effects and so chemicals which 'may' cause adverse effects - as is the case in the plant protection product and biocide legislation – also need to be covered by the definition and criteria.

-Option 2 will lead to practical difficulties, as it is impossible with regard to most substances to unequivocally prove a causal relationship between hormonal changes and adverse health effects in an experimental study. As a consequence, the 'yes-no' option is considered to be too restrictive and rigid a system, relying only on identifying clear positive endocrine disruptors. Such an approach could possibly work if the available validated test methods were not limited only to parts of the hormonal system (i.e. the estrogenic, androgenic, thyroid and parts of the steroidogenesis of the endocrine system (EATS) for mammals, fish and possibly amphibians). At present, we do not have the scientific tools to categorically assess, with an appropriate level of certainty, chemicals regarding their endocrine properties for all relevant endpoints.

-Option 2 will lead to practical difficulties since, despite the studies carried out in recent years, current knowledge of endocrine disruptive chemicals, is still limited and most research into this issue has concentrated on a few groups of chemical substances such as plant protection products or persistent organic pollutants (POPs). Data on a number of other xenobiotics, which may act as endocrine disruptors, is still insufficient and

incomplete. Therefore, to adequately address the issue of endocrine disruptive chemicals, the first step should be to identify all the possible compounds that may interfere with and disrupt the homeostasis and the regulatory mechanisms of the endocrine system. This is particularly urgent for those chemicals that have recently been used in workplaces and consumer products and whose toxicological profile has not yet been clearly and unequivocally defined.

Validated test methods

-The available validated test methods are limited only to parts of the hormonal system (i.e. the estrogenic, androgenic, thyroid and steroidogenesis of the endocrine system for mammals, fish and possibly amphibians).

-The availability of validated test methods currently used to identify endocrine disruptors are extremely limited, only able to cover parts of hormone systems that are best understood (e.g. oestrogen, androgen and thyroid) with no broad set of validated testing methods for non-mammals.

-The lack of government-approved scientific tools to carry out Option 2 further restricts its effectiveness, meaning that endocrine disruptors cannot be addressed in human and wildlife exposure scenarios with strong certainty.

Causal link

-The legislative wording in EU rules on plant protection products and biocides requires a lower degree of causality than the WHO/IPCS definition. The WHO/IPCS definition uses 'consequently causes adverse effects', while PPPR and BPR use "may cause adverse effect" and REACH uses 'probable serious effects'. The scientific committee of EFSA (as the EU Commission Endocrine Disrupters Expert Advisory Group) recommends identifying endocrine disruptors by three criteria 1) presence of an adverse effect in an intact organism or a (sub)population, ii) the presence of an endocrine activity, and (iii) a plausible causal relationship between the endocrine activity and the adverse effect (EFSA 2013).

- The proposed approach requires established evidence of harm, whereas the burden of proof should fall upon those seeking to demonstrate the safety of a potential endocrine disruptor. Action must not be dependent on companies voluntarily carrying out research to explore potential impacts of their products on wildlife.

- The proposal to use the WHO/IPCS definition of endocrine disruptors makes sense insofar as it requires an alteration of the endocrine system causing an adverse effect makes sense, but using this definition implies an assessment of environmental exposures, which Option 2 does not include.

Hazard versus risk

-Option 2 does not make a distinction between substances of high and low concern. Identifying a hazard does not, in and of itself, lead to a concern because harm requires sufficient exposure to the hazard.

-An endocrine disruptor is 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. Thus, for a substance to be defined as an endocrine disruptor, there should be demonstration of an adverse effect and an endocrine disruption mode of action must exist. The definition implies a causal link

between the observed adverse effect and the endocrine disruption mode of action. This is a hazard identification approach (which considers adversity, mode of action and plausibility) but does not take into account the additional element of hazard characterisation i.e. consideration of potency and other criteria such as specificity, severity and irreversibility in an overall weight-of-evidence approach.

-While Option 2 does have some potential consistency with a risk-based approach to regulating, it does not explicitly mention potency, exposure or risk in direct terms.

-The problem with the WHO/IPCS (2002) definition is that it does not include dose applied and exposure levels, and so is incapable of differentiating substances of high regulatory concern from substances of little or no concern. It would include substances with negligible or no actual endocrine disruption effect, as a result of the dose applied, absorption, distribution, metabolism and excretion, and so target organ exposure levels, would be included.

-The criteria defined for Option 2 preclude consideration of exposure, despite the fact that Part (d) of Option 2 states that 'where there is (e.g. mechanistic) information demonstrating that the effects are clearly not relevant for humans and not relevant at population level to animal species living in the environment, then the substance should not be considered an endocrine disruptor'. Because 'real life' exposure (level, duration, timing) must be sufficient to trigger a molecular initiating event sufficiently strong to override the cells' adaptive responses and cause a consequential adverse effect, it is not possible to identify a compound using the definition in Part (d) without considering exposure, or to determine whether or not the effects are "relevant" to humans or at the population levels to animal species living in the environment.

-Regulation (EC) 1107/2009 states 'An active substance, safener or synergist shall only be approved if, on the basis of the assessment of Community or internationally agreed test guidelines or other available data and information, including a review of the scientific literature, reviewed by the Authority, it is not considered to have endocrine disrupting properties that may cause adverse effect in humans, unless the exposure of humans to that active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible'. However, with only hazard identification and with no consideration of exposure or any risk assessment, it is entirely unclear how 'negligible exposure' can be determined. As 'negligible' depends on the nature of the compound and the adverse effect to which it is regulated – which may not be an endocrine disruptor related effect - legislation must allow for a risk based decision making process to define "negligible".

-For data rich compounds such as PPPs, Option 2 fails to utilize the full extent of scientific data available for characterising a hazard. There have been considerable advances in knowledge generated through the ongoing development of internationally accepted, validated test methodologies, advanced mathematical modelling techniques, exposure assessment methodologies and exploratory science. These provide insights into the impact of chemicals from receptor binding, cellular responses, through to the impact on live animals. Considering the extent of scientific knowledge now available, the rationale for taking a limited, hazard based approach is unclear, other than it serves to remove compounds from the market.

<u>Other</u>

-The language of Regulation (EC) 1107/2009 requires the Commission to present 'specific scientific criteria for the determination of endocrine disrupting properties'. Neither Regulation (EC) 1107/2009 nor the Council or the European Parliament (EP)

requires the Commission to classify PPP as endocrine disruptor but rather to set out a single set of criteria to determine whether or not a substance has endocrine disrupting properties.

- The definition provided in Option 2 (a)-(d) would also capture substances such as coffee, wine, ibuprofen and many other compounds which, depending on the dose or exposure can either be wholly beneficial or lethal.

7.3. Option 3 Using the WHO/IPCS definition to identify endocrine disruptors and introducing additional categories based on the different strength of evidence for fulfilling the WHO/IPCS definition

7.3.1. In favour

Differentiation between levels of evidence for classification as ED

-There will be always a list of candidate substances which are suspected of being endocrine disruptors or for which no final conclusion on whether the WHO/IPCS definition applies can – in view of the available information – be answered. Therefore, the Commission should use categories based on a clearly described set of (sub-)criteria, in combination with a mechanism for a an acknowledged regulatory authority to review the listed substances. This mechanism should trigger the generation of data for substances falling in these categories and should enable regulators to either include the substances of concern on the list of endocrine disruptors according to the WHO/IPCS definition, or to reject the concern and to remove the chemicals from the list. Criteria to prioritise further action (data generation, regular review e.g.) on substances in these categories also need to be set.

-The first two categories (confirmed; suspected) should be used for regulation. The third category (potential) is important to steer industry to gather more information on potentially harmful properties. This additional information will help to either remove doubts about the chemicals or to move them into one of the other categories.

-When placing chemicals in the different categories, the burden of proof must not be set too high. Waiting for complete knowledge means risking taking action too late to prevent illness and save lives.

-The set of three categories is very transparent about the different levels of scientific evidence available which should be used to categorise the substances. This option can be used to properly rank a given chemical according to the data held about it.

-This option allows assessors to make a fair assessment of data, and ensures assessors are not forced, simply because there is only one category, to ‘bump up’ or ‘push back’ a given substance from the Option 2 confirmed endocrine disruptors or [nothing] category.

-Option 3 will allow potential endocrine disruptors to be identified by screening/in vitro/QSAR methods. This means chemicals can be 'flagged' as potential endocrine disruptors which require further investigation.

- Data gaps should be filled within a reasonable time frame and regulators should draw up and publish the process for 'promoting' or 'demoting' chemicals between the three categories based on newly available data. The latter is particularly important as some regulated chemicals are subjected to periodic re-evaluations while others are not.

Priority setting for further research

-This option provides several advantages through its use of categories: Category 1 (substances with sufficient information to identify them as endocrine disruptors), Category 2 (substances with some but not enough information to clearly identify them and which may be prioritised/selected for further work and testing), Category 3 (substances that may have endocrine disrupting properties, but where data are lacking or inadequate to properly evaluate them and allocate them to category 2). This set of categories will be a signal to researchers and product developers to consider substances appropriately.

-For the majority of chemical substances - even for active substances with extensive documentation - data are not available to assess whether a substance should be identified as an endocrine disruptor. Although the standard information requirements may provide some information about endocrine disruption effects, endocrine disruptor relevant effects are not included in most standard test methods, or not investigated after exposure during the most critical window(s) of exposure. Therefore, for most substances, only (Q)SAR/read across/chemicals category, in vitro, and/or limited in vivo data are available to assess possible endocrine disruptive effects. It is important to create a system that facilitates prioritisation for further investigation. More categories should be created to allow more data to be requested systematically and transparently under the different pieces of legislation.

-Creating categories is the best option as it will capture a wider range of substances with ED properties and will allow space for regulative decision-making based on human and environmental exposure to endocrine disruptors. It will also detect the gaps of knowledge for specific substances that could be endocrine disruptors, which can act as an “early-warning” for the manufactures and industry to disregard or gradually replace such chemicals.

-Introducing more categories allows integrated testing strategies to be developed and systematically used. These allow a suspicion about endocrine disruptive to be confirmed or rejected. This can guide both authorities and industry to focus their resources on investigating and if necessary testing the most problematic substances.

Approach in line with CMR-substances

-This option is in line with current classifications (CMR categories 1A, 1B and 2) set out in EU legislation which have shown their usefulness in practice. These three endocrine disruptor categories could be used as the basis for rules, in the same way as it is done for CMRs (e.g. to eliminate one, two or all categories of endocrine disruptors from products depending on the user group and exposure patterns). The categorisation system including the corresponding criteria will need to be used in all relevant legislation (REACH, CLP, product legislation for example for biocides and plant production products).

-Since substances classified as carcinogenic, mutagenic, or toxic for reproduction (CMR substances), are categorised based on the level of evidence, it would be most logical and consistent to also categorise endocrine disruptors based on the available level of evidence.

Animal testing

- In the roadmap it is discussed whether Option 3 will be a problem because of the ban on animal tests for substances exclusively used in cosmetic products, thus resulting in a permanent listing under Category 3 for those substances. However, category 2 in Option 3 is described as follows: 'Substances where there is some evidence for endocrine-mediated adverse effects from humans, animal species living in the environment or from experimental studies'. The term 'experimental studies' can also include *in vitro* studies. Thus, *in vitro* studies could be used to place chemicals either in Category 3 or Category 2, provided that a significant number of *in vitro* studies is available.

-This option meets the requirement in the PPP Regulation of reducing the number of animal studies, because of the inclusion of *in vitro* studies.

Other

- With Option 3 there is a risk of 'under classification' where risk assessors may hesitate to classify a chemical in Category 1 or 2 and instead will use Category 3 for most chemicals. This concern has also been raised regarding the assessment of chemicals for carcinogenicity and reproductive toxicity.

- It allows for an effective and efficient use of resources by focusing regulatory action in the right places in differentiated ways according to the categories.

7.3.2. Against

Causal link

-Category 3 is too broad. A very large number of substances would be likely to be classified purely on the basis of an in vitro finding that may not be relevant for human health or the environment. Given the large number of substances that may be affected it is considered unlikely that further assessment of many of these substances will be possible. Therefore they may be subject to some form of restriction or concern for a very long time without an appropriate scientific justification, and, in many cases unnecessarily.

-The endocrine system is highly complex, and thus results obtained in the laboratory may not be the same as those occurring when the chemical is used in non-laboratory environments. The transfer of laboratory results to real life situations is a cause for uncertainty associated with EDCs is the transfer of laboratory results to real life situations.

-Substances should only be considered as endocrine disruptors of regulatory concern when there are clear adverse effects unambiguously caused by a well identified and empirically described mode of action. These adverse effects must affect humans and wildlife populations, not to be secondary to other toxic effects, and must occur at exposure levels that indicate f significant potency.

Uncertainty

-There is currently insufficient clarity about the distinction between Categories 1 and 2I, as proposed.

-Weight of evidence requires detailed knowledge and experience and therefore may be prone to generate different outcomes if performed by different regulators.

-Based on the current definitions it is anticipated that decisions on classification of assessors/authorities may vary considerably.

- It is unclear how the weight of evidence assessment is to be conducted, within different chemicals schemes that have different processes carried by different co-ordinating bodies. This could lead to inconsistent decision-making.

-Weight of evidence plans have not been set out in detail and need further elaboration before they can be implemented in a regulatory context.

-It is unclear what will be the regulatory consequence of a chemical being placed in a particular category.

-It is not clear how compounds will transition in and out of the categories without further testing, neither is there an option for 'not an endocrine disruptor.

Confusion of the public

- This option would place many chemicals for which there is only weak evidence of endocrine disruption into a kind of limbo in which they would be tainted by association. Businesses might feel forced by public opinion to withdraw them on the basis of vague and uncertain assertions.

-Creating such categories is likely to confuse the public, who will likely assume any listed substance, under any of the three categories, are 'endocrine disruptors' that pose a real risk to human health and the environment.

-Categorisation will inevitably lead to the creation of 'black lists' that will be highly vulnerable to misinterpretation, misuse and unwarranted additional primary or secondary regulation, in Europe and globally. Substances not considered to be endocrine disruptors under the proposed scheme will still be labelled as 'suspected endocrine disruptors', despite the fact that they will have been fully tested for their effects on human health and environmental safety.

-Classification using additional categories would also lead to unnecessary concern amongst stakeholders in the agricultural food chain and consumers about substances which were not endocrine disruptors per se but were classified as potential endocrine disruptors or endocrine active substances. This in turn could lead to products which are approved under Regulation (EC) 1107/2009 as presenting no risk to human health (or the environment) being blacklisted as consumers sought to reduce their exposure to them. These substances could then potentially be withdrawn as their use would be avoided and, as a result, their commercial viability would be affected.

-The proposed criteria for categorising endocrine disruptors are not precise enough for their purpose and require extensive interpretation by experts, resulting in differing categorisation of the same substances. This would create major unpredictability and lack of consistency for industry and lead to more fragmented chemical regulatory schemes that could cause the unnecessary stigmatisation of many substances in the marketplace.

Adverse effects

-Categorisation of endocrine disruptors has no scientific basis. Effects that are carcinogenic, mutagenic or toxic for reproduction are well-defined toxicological outcomes which are suitable to categorisation. 'Endocrine disruption' is not an adverse effect in itself. Instead it rather artificially groups together multiple modes of action leading to adverse effects of variable nature, severity and concern (i.e. effect that manifest as carcinogenic, reproductive, developmental or other effects which are already considered in regulatory decision -making). Adverse effects themselves are and should be regulated, not the underlying modes of action that cause them.

Animal testing

-It should be noted that to be able to clarify the status of active substances placed in the second and third categories ('suspected endocrine disruptor', 'endocrine active substance' respectively), additional animal testing would be required.

-According to the WHO/IPCS definition, only substances which cause adverse effects in an intact organism by altering the function of the endocrine system are classified as endocrine disruptors. To identify an endocrine disruptor according to this definition, *in vivo* testing will be required. Due to the animal testing and marketing bans, it will not be possible for the cosmetics industry to generate additional animal data to defend substances which are classified as Category 3 as a result of positive *in vitro/in silico* data or substances indicated as having hormone-like activity by artificial test design or structure-activity relationships.

Hazard versus risk

-This option does not include dose applied and exposure levels of relevant organisms and their physiological systems.

-Categorization is a process developed through the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). It is an optional and voluntary system which countries can use according to their needs. Endocrine disruption is not a hazard class within this system because endocrine disruption per se is not an adverse effect, but a mode of action, which may or may not lead to an adverse effect.

-The globally harmonised system of classification an labelling of chemicals is meant to provide a uniform and scientific approach to labelling used to protect workers and handlers. Using a system like this to categorise compounds and then using those categories to remove them from the market is an entirely inappropriate use of the GHS system.

Other

-If adopted, Categories 1 and 2 should be used to inform the health risk assessment of the substance, with subsequent regulatory decisions on approval and setting of management controls being made on the basis of the risk assessment and associated socioeconomic evaluation. They should not be used as a 'cut-off' to preclude further consideration of a substance for approval.

-There is no agreed test for assessing the endocrine disruption potential of active ingredients and therefore no way to directly compare active ingredients, which could be an effective way of categorising compounds.

-The list of endocrine disruptors could become very long as more and more screening data will become available in the EU and from outside the EU. Given the wide scope of the definition of this category, a large number of chemicals might be listed and so the category would be of no relevance to different stakeholders including regulators.

-Companies will hesitate to invest in development of a product that may be considered to fall into these categories.

- Under Regulation (EC) 1107/2009, the Commission is required to present …specific scientific criteria for the determination of endocrine disrupting properties''. Therefore Regulation (EC) 1107/2009 requires a single set of criteria to determine whether or not a substance has endocrine disrupting properties, and it is not necessary to establish e a set of categories for endocrine disruptors.

7.4. Option 4 Using the WHO/IPCS definition to identify endocrine disruptors and including potency as element of hazard characterisation (hazard identification and characterisation)

7.4.1. Favouring

Hazard versus risk

-It is accepted worldwide that hazard assessment of hazard comprises two elements, hazard identification and hazard characterisation. All aspects of hazard identification and hazard characterisation should be taken into account in identifying endocrine disruptors for regulatory purposes.

- Failure to take into account the elements of hazard characterisation (e.g. potency, severity and lead effect) will lead to the loss of potentially very beneficial chemicals that pose no dangers to human health or wildlife in real life.

-Potency and other hazard characterisation factors are essential to making the regulatory consequences of ascribing endocrine disruptor to a substance more balanced and proportionate to the potential hazardous threat that the substance might pose to human health and/or the environment.

-Potency is a key determinant of whether a substance may induce adverse effects at environmentally relevant concentrations. A substance with toxic properties with high potency, e.g. cyanide, will be regulated more strictly than a substance with toxic properties with low potency, e.g. table salt.

-This option has the benefit of being properly scientifically based, as it recognises the importance of dosage applied and exposure levels for organisms and their physiological systems in determining whether a substance may cause adverse effects. It enables an assessment of whether the substance is likely to be administered at concentrations which will be toxicologically relevant.

- This option would apply a threshold approach. There are two reasons supporting this kind of approach. The need for this approach is based on two ways of reasoning: 1) A theoretical consideration of the possible modes of action on the endocrine system indicates that such interaction is generally based on an interference with the physiological (including hormonal) regulation of the target organism (e.g. an oestrogenic compound introduced into an organism will compete with the available

natural oestrogens for receptor sites). As a result, a substance can only disturb the physiological regulation if it is present at levels high enough to make an impact. 2) There is comprehensive experimental experience with characterising the hormonal activity of compounds in developing f pharmaceuticals. Experts in this field have no seen evidence that compounds with these effects would follow a non-threshold dose-effect relationship.

-Failure to take potency into account creates inconsistencies with the way the current regulatory system considers scientific data, so that, for example, such that thyroid toxicity or adrenal toxicity will be approached and assessed differently from neurotoxicity or immunotoxicity.

-Failure to take potency into account conflicts with the approach adopted under the CLP Regulation. One example is the assessment of aquatic toxicity, which uses chronic NOECs to distinguish between different degrees of long-term hazard. If the CLP Regulation sees value in distinguishing between different levels of potency towards the aquatic environment, then such discrimination is surely relevant for the threat of endocrine disruption in the aquatic environment. Similar arguments can be made for human health hazard considerations.

-Potency and effect on in the environment are essential to provide information on the appropriate level of concern, regardless of whether on exposure is available. If one substance is readily degradable and of very low potency and another is persistent and of high potency, it is clear which is of most concern.

-In the report on State-of–the-Art-Assessment of Endocrine Disrupters from 2011 is stated: 'Defining endocrine disrupters for regulatory purposes will have to rely on criteria for adversity and endocrine-related modes of action. Based on earlier proposals by various Member States and other organisations, including ECETOC, a decision tree approach is developed that proceeds in a step-wise manner by excluding substances that neither produce adverse effects, nor show endocrine-related modes of action. […] The final regulatory decision rests on a consideration of the toxicological profile of the substances in a weight-of-evidence approach. This weight-of-evidence approach will have to consider potency together with other factors such as severity and specificity of effect and irreversibility. Rigid potency-based cut-off values as decisive decision criteria are not recommended. Procedures that incentivise the provision of data in the case of data gaps are suggested…' (Kortenkamp et al., 2011).

-Under artificial experimental conditions, many substances could interact with physiological processes controlled by the endocrine system. In addition, many commonly used safe substances, such as caffeine, have been show to mimic hormonal effects or possess slight hormonal activities in tests. If potency is not taken into account, these substances would be included in the same category as a potent endocrine disruptor such as diethylstilboestrol.

7.4.2. Against

Hazard versus risk

- Potency does not take into account different mechanisms of action, critical windows of susceptibility, non-linear dose response curves, low-dose-response curves, additive effects by mixtures of low doses of endocrine disruptors, non-threshold mechanisms, effects on the population and vulnerable sub-groups.

-The potency of a chemical has nothing to do with whether the chemical can be identified as an endocrine disrupting compound or not. A chemical with low potency may still be of concern, if exposure is high, or if exposure occurs simultaneously with exposure to other endocrine disrupting chemicals. Conversely, an endocrine disrupting chemical with high potency may be of limited concern, if exposure is minimal.

-Endocrine disruptor evaluation should be purely hazard-based.

-Potency is a risk assessment element used in characterising rather identifying a hazard.

-A Report by the Endocrine Disrupters Expert Advisory Group (Key scientific issues relevant to the identification and characterization of endocrine disrupting substances)(2013), noted:

> 'In the human health sub-group, it was agreed that (…) an appropriate potency cut-off value between higher concern and lower concern endocrine disruptors could not be scientifically determined and it would be primarily a policy decision on where to place the cut off'. 'In the environment sub-group (…) In line with the human health sub-group, it was agreed that an appropriate potency-based cut-off between higher concern and lower concern endocrine disruptors could not be scientifically determined'.

-Option 4 fails to include a consideration of exposure, or to conduct a risk assessment. It remains a hazard-based approach to regulating compounds.

-Without consideration of exposure, Option 4 is still insufficient to identify a compound as an endocrine disruptor with adverse effects.

-The option is not in line with the recommendations from the report 'State of the Art Assessment of Endocrine Disrupters', in which the following is stated: 'Defining endocrine disrupters for regulatory purposes will have to rely on criteria for adversity and endocrine-related modes of action. Based on earlier proposals by various Member States and other organisations, including ECETOC, a decision tree approach is developed that proceeds in a step-wise manner by excluding substances that neither produce adverse effects, nor show endocrine-related modes of action. […] The final regulatory decision rests on a consideration of the toxicological profile of the substances in a weight-of-evidence approach. This weight-of-evidence approach will have to consider potency together with other factors such as severity and specificity of effect and irreversibility. Rigid potency-based cut-off values as decisive decision criteria are not recommended. Procedures that incentivise the provision of data in the case of data gaps are suggested…' (Kortenkamp et al., 2011). According to the Endocrine Disruptors Expert Advisory Group, potency considerations should not be part of the identification of a substance as an endocrine disruptor but it could play a role in the hazard characterization (JRC 2013). The EFSA scientific committee considers potency considerations as a part of the hazard characterization, not as part of the (hazard) identification of endocrine disruptors (EFSA 2013).

-The selection of a threshold for potency for endocrine disruptors is not in line with the current scientific knowledge, which suggests that such thresholds may be impossible to define in the case of exposure during the early developmental stages of life. Thresholds and safe limits therefore cannot be assumed for endocrine disruptors.

-Endocrine disruption is not a specific endpoint (effect) but a network of mechanisms that lead to deferential endocrine-related diseases. Strong and weak triggers on specific sites may equally result in the development of disease and therefore potency cannot be

used as an indicator to characterise the severity of the adverse effect. For example, a chemical that weakly imitates the function of the female hormones may strongly inhibit the neuronal signals in the brain leading to mental disorders. Further, potency will vary not only in different sites of the endocrine system but also among old and young individuals and across different species.

-Timing is more critical than dose. As a result, legislation based on a dose related premise is outdated. Endocrine disruptors can alter gene behaviour at extremely low doses and exposures pre-birth can result in adult disease in later life. Experiments using high doses don't predict low dose responses.

- Effects are not appropriately examined over a range of low doses and the effects being looked for may not represent the most sensitive effects. As a result, even quite potent chemicals are likely to be missed. Therefore, a potency cut-off should not be applied to the criteria.

-Endocrine disruptors exert their effects through a range of mechanisms and so vary in how they affect different parts of the body and different hormone systems. Therefore, relying on selective tests for potency may wrongly leave some chemicals unregulated. For example, an endocrine disruptor may be weakly potent in disrupting female hormonal signalling but significantly disrupt brain development. In addition, many animals in ecosystems are exposed to endocrine disruptors and potency varies across different species.

-Potency is not a simple thing to measure as it is depends on a) the type of test system and which effect is being monitored, b) the organism/species used in the test system; and c) the observed life-stage (e.g. pregnancy). That means the timing of exposure may have more effect, rather than the substance's potency.

-Potency may be impossible to calculate for many chemicals because data on their dose responses may be incomplete and test would probably not have included doses at which hormones and known endocrine disruptors are active.

-Another variable that complicates the issue of potency is that hormones function in a dynamic environment where hormone activity varies tremendously depending on things like receptor occupancy and the presence of other synthetic hormones (which are ever-present in our environment). These variables can have a big influence on the impact of an individual endocrine disruptor at a given point in time, regardless of its stated 'potency' in one particular experiment.

- The measured 'potency' of an endocrine disruptor will depend greatly on the type of test that is used; the species and developmental stage of the test subjects; what other stressors (including other endocrine disruptors) the subjects have been exposed to; what effects are being looked for (e.g. which of the organisms' biological systems are examined) and over what time period the test is taking place.

- This option would introduce an inconsistency in the EU legal system as there is no consideration of potency in the hazard classification of substances as carcinogenic, mutagenic or toxic to reproduction.

-There is a strong risk that a lack of evidence for sufficiently 'strong' impacts (which may be due to inadequacies in the research carried out) would be used as justification

for authorising endocrine disruptors.

-There is no potency element in the WHO/IPCS definition of endocrine disruptors.

-This option would be inconsistent with the Globally Harmonised System of Classification and Labelling (GHS) which the EU follows, because hazard characterisation does not normally include potency, and because it is not separate from exposure assessment.

Environment

-Option 4 is unworkable for criteria relating to effects on the environment because of the differences in sensitivities among species.

-This option would present the difficulty of selecting which animal species in which tests the potency threshold should be based on.

Combination effects

-Humans and the environment may be exposed to high levels of weakly potent endocrine disruptors, or exposed to several weak endocrine disruptors which may act together.

-Option 4 will potentially lead to underestimation of mixture toxicity if substances of low potency would not be flagged and therefore not be considered in assessing cumulative exposure.

-People and wildlife are exposed to many endocrine disruptors from different sources at the same time and over time, and science has shown that endocrine disruptors can act together, leading to harmful cocktail effects. Not identifying 'low potency' endocrine disruptors would hamper any attempts to address health risks arising from cumulative exposure to these chemicals.

Other

-The 7th Environment Action Programme outlines that: 'In particular, the Union will develop harmonised hazard-based criteria for the identification of endocrine disruptors' (EU 2013).

7.5. Option A: No change to the existing provisions in the BPR and the PPPR

7.5.1. In favour

Emergency situations

-The provisions in Regulation (EC) 1107/2009 allow for PPPs to be used in emergency situations when a serious threat to plant health occurs (Article 53) and this allows for socioeconomic considerations to be taken into account. The problem in implementing

the Regulation in this area is that the Commission has not fulfilled its obligations in regard to proposing scientific criteria for identifying endocrine disruptors.

Other

-Options B and C would undermine democratically agreed legislation in the EU.

7.5.2. Against

Comparative analysis

-After a substance has been identified as an endocrine disruptor according to WHO/IPCS definition, a subsequent assessment should take place. This assessment should focus on the overall environmental burden. This burden must not increase through replacing an endocrine disruptor with an environmental even more harmful non-endocrine-disrupting substance.

Hazard versus risk

-The only scientifically sound way to identify an endocrine disruptor with an adverse effect is to consider both hazard and exposure, and the most appropriate way to regulate compounds is to use a risk assessment. This is a far more time consuming, resource intense, complex and multidisciplinary task than conducting a simple hazard assessment, and it remains the most robust approach to protecting human health and the environment, including vulnerable sub populations and sensitive species. A risk-based approach also complies with international binding agreements from the WTO.

-A risk assessment allows flexibility in regulatory decision making as new data become available and as product uses or application technologies change.

-Limiting regulatory approaches to hazard identification based on a mechanistic definition alone allows for no consideration of exposure and overall risk.

-In terms of time and resources from regulators and potential socioeconomic impacts, elements of risk assessment should be considered when determining the level at which an identified endocrine disruptor should be regulated. The new and developing methods promise not only to speed up the process of identifying endocrine disruptors and protecting human health and the environment, but also will avoid the use of animal tests as much as possible.

International standards

-This option entails moving away from internationally agreed standards and guidelines.

7.6. Option B: introducing further elements of risk assessment

7.6.1. In favour

Hazard versus risk

-Regulating substances based on hazard identification alone is not scientifically sound, as hazard identification is too qualitative. The substances for which sufficient data are available ought to be assessed on a case-by-case basis, taking into account all the available data and the specificities and the complexity of the endocrine system.

-The current hazard-based cut-off criteria under Regulation (EC) 1107/2009 would be improved by adding risk assessment elements and socio-economic considerations.

-A full risk assessment approach is the most protective and scientifically robust approach.

Precautionary principle

-Caution should be taken if the data are not sufficient.

7.6.2. Against

Hazard versus risk

-Option B should be amended to ensure that risk assessment is a fundamental component of regulatory evaluation.

-Option B is the return to traditional risk assessment and safe thresholds; this option will lead to no bans of endocrine disruptors and will have no impact on health and environment.

Comparative analysis

-After a substance is identified as an endocrine disruptor according to the WHO/IPCS, a subsequent assessment should take place. This assessment should focus on the overall environmental burden, which should not be increased by replacing an endocrine disruptor, with an environmental even more harmful, non-endocrine disrupting substance.

-Option B does not meets the criteria needed for this assessment as it is hampered by the fact that the methodological basis for conducting an appropriate socioeconomic analyses, is still at an early stage, especially with regard to environmental impacts and in particular costs. Carrying out these assessments would require methodological developments to bring about scientifically robust and widely agreed approaches.

-For endocrine disruptors which have been shown to have effects at very low concentrations, it may be impossible to identify a safe exposure level for the effect that is most sensitive to disruption. A more effective approach from a health standpoint would be to conduct assessments of safer alternatives to endocrine disruptors. Safer alternative assessments have many benefits over risk assessment, including that they avoid the pitfalls of trying to identify safe exposure levels, they allow for quicker

decision-making and they encourage efforts to design safer chemicals.

Uncertainty

-Exemptions are provided through a derogation process, which is an inherently subjective and therefore unpredictable and inconsistent approach to regulating.

Combination effects

-Changing the legal text to move from negligible exposure to negligible risk is not acceptable because a single substance risk assessment would not prevent effects that result from exposure to mixtures to combination of substances, including endocrine disruptors used in products other than plant protection products.

-The criteria for endocrine disrupting properties should not be developed based on an assumption that changes to regulatory decision-making will occur simultaneously, as such changes would require legislative amendments to Regulation (EC) 1107/2009 via a formal co-decision procedure.

7.7. Option C: introducing further socioeconomic considerations

7.7.1. In favour

Application of ED criteria across all sectors

-Option C would increase the regulatory consistency between the PPP and BPR Regulations and REACH. In the case of REACH an endocrine disrupting substance can be placed on the candidate list for authorisation if there is scientific evidence of probable serious effects on human health or the environment which give rise to an equivalent level of concern to those of other substances (substances which are carcinogenic, mutagenic, toxic for reproduction, persistent, bio accumulative and toxic or very persistent and very bio accumulative] and which have been identified on a case-by-case basis; this is analogous to consideration of potency. Subsequently, authorisation can be granted where use of the substance is appropriately controlled, or where the socioeconomic benefits of use outweigh the risk(s) to human health or the environment and where there are no alternative substances or technologies that can be used instead. Alternatively REACH provides for substances to be restricted. For this to take place, an unacceptable risk needs to be demonstrated, and the decision must take into account the socioeconomic impact of the restriction, including the availability of alternatives

Hazard versus risk

-Adding risk assessment elements and socioeconomic considerations as options for regulatory decision-making would be an improvement over the current hazard- based cut-off criteria under Regulation (EC) 1107/2009.

-The EU Plant Protection Product Regulation (PPPR) stipulates that substances with endocrine disrupting properties (that may cause adverse effects in humans) cannot be approved for use unless human exposure (under realistic conditions of use) is negligible. The Biocidal Product Regulation (BPR) stipulates that substances considered as having endocrine disrupting properties (that may cause adverse effects in humans) should not be approved unless the risk to humans is negligible. Therefore, it would appear that any

assessment under either Regulation would require not just a hazard assessment but a risk assessment, not only to establish whether a substance shown/suggested to have 'endocrine-disrupting' properties in toxicology studies conducted *in vitro* or in test organisms *in vivo* may be likely to cause adverse effects in humans (or other organisms in the environment) but also to assess the likely exposure humans would face to the substance.

7.7.2. Against

Uncertainty

-Option C, proposes introducing additional socioeconomic 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, however, define what a disproportionate negative effect would be or what socioeconomic costs would be considered.

-After a substance has been identified as endocrine disruptor ED according to the WHO/IPCS definition, a subsequent assessment should take place. This assessment should focus on the overall environmental burden, which should not be increased by replacing an endocrine disruptor with an even more harmful non-endocrine substance. Option C does not meet the criteria required to carry out this assessment, as this option is hampered by the fact that the methodological basis for conducting an appropriate socioeconomic analysis is still at an early stage, especially with regard to environmental impacts and, in particular, costs. Carrying out these assessments would require methodological developments to bring about scientifically robust and widely agreed approaches.

--The criteria for endocrine disrupting properties should not be developed based on an assumption that changes to regulatory decision making will actually occur simultaneously, as such changes would require legislative amendments to Regulation (EC) 1107/2009 via formal co-decision procedure.

- Exemptions are provided through a derogation process, which is an inherently subjective - and therefore unpredictable and inconsistent - approach to regulating.

Hazard versus risk

-Risk assessments identify tolerable doses. It is impossible to identify safe doses for endocrine disruptors, and current risk assessment methodologies do not consider the potentially most sensitive individuals (e.g. foetuses, young children, and individuals going through puberty), when defining safe doses.

-A full risk assessment approach is the most protective and scientifically robust approach. Managing endocrine disruptors through a combination of hazard- based cut-offs and derogations is not an appropriate substitute for risk-based regulation.

- Legislation must allow for a risk-based decision-making process. The option should therefore be added to amend Regulation (EC) 1107/2009 to allow a step-wise decision-making process relating to substances that meet the criteria for being endocrine disruptors. This process should comprise full hazard characterization, assessment of human and environmental exposure levels, assessment of human and environmental

risk, if necessary, and consideration of risk mitigation measures. It should then proceed to consider additional socioeconomic issues, including a risk/benefit analysis.

Emergency situations

-There may be instances where a known endocrine disrupting plant protection product is really needed to protect a crop. However, there is already provision for this, because under the existing regulation, as it can be granted a derogation and used for another five years (according to Article 4.7).

Other

-Risk assessment approaches usually do not assess toxicity during the development process, which covers the most sensitive periods for endocrine disrupting effects. In addition, they do not always follow test organisms for their entire lifetime, which is required to assess any resulting diseases for which there is a considerable time lag between exposure and development of symptoms

-It will not be possible to calculate the financial benefits to society of banning endocrine disrupting plant protection products, due to inherent and practical problems. Implementation of Option C will mean arbitrary political decisions and the abandoning of Regulation (EC) 1107/2009.

8. CONCLUSION

The Commission received over 27,000 responses to the public consultation which illustrates the public's great interest in the EU's policy on endocrine disruptors. The public consultation report presents the outcome of the consultation focusing on qualitative rather than quantitative terms.

The respondents came from various parts of society and included doctors, farmers, NGOs, representatives of the chemical, electronic, food and medical devices industries, water companies and scientists. This shows how widely these chemicals are used. Individual contributions accounted for more than 90% of the responses. 863 web-based responses were received on behalf of an organisation and 64% of these came from one Member State (United Kingdom). Many respondents raised issues related to food safety, the threat that endocrine substances might pose to human health and/or the environment and the impact of the different options proposed in the roadmap on agriculture, industry, health and the environment. In particular farmers and agri-business highlighted the potential serious implications of setting scientific criteria to identify substances with endocrine disrupting properties on agriculture. Authorities of non-EU countries stressed the potential impact on trade.

The objective of this consultation was to gather information for the impact assessment. This objective was reached as there were many respondents that provided information. The public consultation generated a great deal of data consisting of scientific articles, studies, reports, views and legal opinions. The overall message from respondents is that there is a need for the EU to identify criteria for endocrine disruptors. Therefore, Option 1, with no specific criteria for endocrine disruptors is not supported. Respondents expressed divergent views and provided arguments supporting or rejecting the options on how to define the criteria and how endocrine disruptors should be regulated. Many respondents supported the use of the WHO/IPC 2002 definition as a starting point for defining an endocrine disruptor. As regards the regulatory approach, many respondents that identified themselves as farmers, private

companies, industrial or trade organisations, or authorities in non-EU countries, proposed to have a risk-based approach.

The public consultation provided useful input to the on-going impact assessment process that addresses the economic, environmental and health impacts of different policy options. The opinions and information received in reply to the consultation will be considered within the Impact Assessment.

9. ANNEXES

9.1. Indicated studies, reports and articles by respondents to the public consultation

9.1.1. General

Adler S. et al. (2011).
Alternative (non-animal) methods for cosmetics testing: current status and future prospects-2010. NCBI Archives of Toxicology 85(5), 367-485.
http://www.ncbi.nlm.nih.gov/pubmed/21533817

ANSES. French Agency for Food, Environment and Occupational Health & Safety.
The French Agency ANSES evaluated a range of chemicals and the resulting categories according to different proposals (see table 3, page 22 and 23 of the following document):
https://www.anses.fr/sites/default/files/documents/DPR2011sa0237EN.pdf

ANSES. French Agency for Food, Environment and Occupational Health & Safety.
Opinion of the French Agency for Food, Environment and Occupational Health & Safety on a request for scientific and technical support regarding the European strategy for endocrine disruptors (Request no. 2011-SA-0237).
https://www.anses.fr/sites/default/files/documents/DPR2011sa0237EN.pdf

Benzyl butyl phthalate Annex XV – Identification of SVHC format
Proposal for identification of a substance as a cmr cat 1 or 2, pbt, vpvb or a substance of an equivalent level of concern
http://echa.europa.eu/documents/10162/1c5023db-5a6c-464b-bfb6-b5881f0c5c72

ChemSec- International chemical secretariat
SIN List
http://chemsec.org/what-we-do/sin-list

CHEM Trust (2010)
CHEM Trust and WWF-EPO proposals for the regulation of chemicals with endocrine disrupting properties under REACH (EC 1907/2006) and under the Plant Protection Products Regulation (EC No 1107/2009)
http://www.chemtrust.org.uk/wp-content/uploads/CHEM-Trust-WWF-EDC-Classification-Paper-Dec-2010.pdf

CHEM Trust (2011)
CHEM Trust's Contribution to the Ongoing Debate on Criteria for EDCs
http://www.chemtrust.org.uk/wp-content/uploads/CHEM-Trust-Position-on-EDC-Criteria-Sept11.pdf

CHEM Trust (2012)
A CHEM Trust and HEAL Briefing: Challenges and solutions in the regulation of chemicals with endocrine disrupting properties.
http://www.chemtrust.org.uk/wp-content/uploads/Criteria-Briefing-CTHEAL-FINAL.pdf

Committee on the Design and Evaluation of Safer Chemical Substitutions (2014)
A Framework to Guide Selection of Chemical Alternatives
http://www.nap.edu/catalog/18872/a-framework-to-guide-selection-of-chemical-alternatives

Concawe (2014)
Hazard classification and labelling of petroleum substances in the European Economic Area
Report no.10/14
https://www.concawe.eu/publications/3/40/Report-No-10-14

COPHES- European Biomonitoring project
Human Biomonitoring in Europe
http://www.eu-hbm.info/

COWI (2009) for ECHA

Data on manufacture, import, export, uses and releases of bis(2-ethylhexyl)phthalate (dehp) as well as information on potential alternatives to its use
http://echa.europa.eu/documents/10162/13640/tech_rep_dehp_en.pdf

Data on manufacture, import, export, uses and releases of dibutyl phthalate as well as information on potential alternatives to its use
http://echa.europa.eu/documents/10162/6ce77be0-6c61-4e95-9241-0c262817555a

Data on manufacture, import, export, uses and releases of benzyl butyl phthalate as well as information on potential alternatives to its use
http://echa.europa.eu/documents/10162/8065581d-1abf-4077-97f0-ab00e1c0e2b2

DG SANCO database on approved substances in the EU
https://ec.europa.eu/food/plants/pesticides/eu-pesticides-database_en

DK EPA (Danish Ministry of Environment-Environmental protection agency) (2011).
Establishment of Criteria for Endocrine Disruptors and Options for Regulation.
http://mst.dk/media/mst/9106718/danskeforslag.pdf

Defra- Department for Environment Food and Rural Affairs(2012)
Extended impact assessment study of the human health and environment criteria for endocrine disrupting substances proposed by HSE , CRD. - PS2812
http://sciencesearch.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&Completed=0&ProjectID=18083

Downs, Georgina (2014)
Negligent and unlawful: EFSA's latest guidance on pesticide use and exposure

http://www.theecologist.org/News/news_analysis/2661835/negligent_and_unlawful_efsas_latest_guidance_on_pesticide_use_and_exposure.html

ECHA
Proposal to identify substances of very high concern previous consultations
http://echa.europa.eu/proposals-to-identify-substances-of-very-high-concern-previous-consultations/

Databases on chemicals
http://echa.europa.eu/information-on-chemicals

EC/DG ENV

Priority list
http://ec.europa.eu/environment/chemicals/endocrine/strategy/substances_en.htm

Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption (2000)
BKH Consulting Engineers, Delft, The Netherlands in association with TNO Nutrition and Food Research, Zeist, The Netherlands
http://ec.europa.eu/environment/archives/docum/pdf/bkh_main.pdf

Study on gathering information on 435 substances with insufficient data(2002)
http://ec.europa.eu/environment/chemicals/endocrine/pdf/bkh_report.pdf

European Parliament (2008)
The Consequences of the"cut off" Criteria for Pesticides: Agronomic and Financial Aspects
http://www.europarl.europa.eu/RegData/etudes/note/join/2008/408963/IPOL-AGRI_NT(2008)408963_EN.pdf

European Parliament (2008)
Benefits of strict criteria "cut-off" on human health in relation to the proposal for a regulation on plant protection products
http://www.europarl.europa.eu/RegData/etudes/etudes/join/2008/408559/ IPO L-JOIN_ET (2008) 408559_EN.pdf

Endocrine Disruptor Screening Program

January 29-31, 2013: Prioritizing the Universe of Endocrine Disruptor Screening Program (EDSP) Chemicals Using Computational Toxicology Tools
http://www.epa.gov/scipoly/sap/meetings/2013/012913meeting.html

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

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

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

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

Environmental Protection Agency (2014)
*Integrated Bioactivity and Exposure Ranking: A Computational Approach for the Prioritization and Screening of Chemicals in the Endocrine Disruptor Screening Program*http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2014-0614-0003

EPA (2010)
Identification and assessment of alternatives to selected phthalates
http://www2.mst.dk/udgiv/publications/2010/978-87-92708-00-7/pdf/978-87-92708-01-4.pdf

Germany (2013)
DE Position Paper on Endocrine Disruptors
http://www.reach-info.de/dokumente/DE-Positionspapier_ED.pdf

Michael K. Grimmer, Frank van den Bosch, Stephen J. Powers and Neil D. Paveley.
Evaluation of the predictive value of fungicide resistance risk assessment.
Pest Management Science. In press

Hans-Olov Adami et al. (2011)
Toxicology and Epidemiology: Improving the Science with a Framework for Combining Toxicological and Epidemiological Evidence to Establish Causal Inference.
Oxford journals, Toxicological sciences 122(2), 223–234 (2011).
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3155086/

Hobbelen, P., Paveley, N. & van den Bosch, F. (2011)
Delaying Evolution of Fungicide Insensitivity by Mixing Fungicides at a Low and High Risk of Resistance Development.
Phytopathology, 101:1224-1233.
Philips McDougall (2013)
R&D trends for chemical crop protection products and the position of the European Market.
http://www.ecpa.eu/files/attachments/R_and_D_study_2013_v1.8_webVersion_Final.pdf

P. H. F. Hobbelen, N. D. Paveley, R. P. Oliver and F. van den Bosch. (2013)
The Value of Alternation or Mixtures of Fungicides for Delaying the Selection of Resistance Against Two Modes of Action in Populations of Mycosphaerella graminicola on Winter Wheat. Phytopathology, 101:690-707.

KEMI- Swedish Chemical Agency(2008)
Interpretation in Sweden of the impact of the "cut-off" criteria adopted in the common position of the Council concerning the Regulation of placing plant protection products on the market (document 11119/08)
http://www.kemi.se/Documents/Bekampningsmedel/Docs_eng/SE_positionpapper_annenII_sep08.pdf

Institute for Environment and Health (2005)

Chemicals purported to be endocrine disrupters. A compilation of published lists
Leicester, UK: MRC Institute for Environment and Health
http://www.cranfield.ac.uk/about/people-and-resources/schools-institutes-research-centres/school-of-applied-sciences/groups-institutes-and-centres/ieh-reports-/endocrine-disruptors/w20.pdf

International Programme on Chemical Safety (2002)
Global assessment of the state-of-the-science of endocrine disruptors.
Damstra, Terri; Barlow, Sue; Bergman, Aake; Kavlock, Robert; Van der Kraak, Glen. 2002, WHO/PCS/EDC/02.2, WHO.
http://www.who.int/ipcs/publications/en/toc.pdf

JRC(2013):

Key scientific issues relevant to the identification and characterisation of endocrine disrupting substances.
Report of the Endocrine Disruptors Expert Advisory Group (Munn S & Goumeneau M, Eds.) EUR 25919 EN.
https://ec.europa.eu/jrc/en/publication/key-scientific-issues-relevant-identification-and-characterisation-endocrine-disrupting?search

Thresholds for endocrine disruptors and related uncertainties. Report of the Endocrine Disruptors Expert Advisory Group (Munn S & Goumeneau M, Eds.). EUR 26068 EN
https://ec.europa.eu/jrc/sites/default/files/lb-na-26-068-en-n.pdf

JRC (2014):

Alternative methods for regulatory toxicology – a state-of-the-art review.
A. Worth et al. EUR 26797 EN
http://echa.europa.eu/documents/10162/13634/echa_jrc_sla_report_en.pdf

List of Restricted Substances under RoHS 2
http://www.umweltbundesamt.at/rohs2

Lowell Center for Sustainability - University of Massachusetts (2011)
Phthalates and their alternatives: Health and Environment concerns
http://www.sustainableproduction.org/downloads/PhthalateAlternatives-January2011.pdf

OECD
Series on Testing and Assessment for endocrine disruptors.
http://www.oecd.org/chemicalsafety/testing/seriesontestingandassessmenttestingforendocrinedisrupters.htm

OECD Conceptual Framework for Testing and Assessment of Endocrine Disrupters
http://www.oecd.org/env/ehs/testing/OECD%20Conceptual%20Framework%20for%20Testing%20and%20Assessment%20of%20Endocrine%20Disrupters%20for%20the%20public%20website.pdf

Kortenkamp (2007)
Environmental Health Perspectives 115(7): 98-105; Orton et al. (2014) Toxicology and Applied Pharmacology 278: 201–208).
http://www.brunel.ac.uk/people/andreas-kortenkamp

Kwack, S., Kim, K., Kim, H., & Lee, B. (2009).
Comparative Toxicological Evaluation of Phthalate Diesters and Metabolites in Sprague-Dawley Male Rats for Risk Assessment. Journal of Toxicology and

Environmental Health, Part A, 1446-1454.
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0050465

Philips McDougall (2013)
R&D trends for chemical crop protection products and the position of the European Market.
http://www.ecpa.eu/files/attachments/R_and_D_study_2013_v1.8_webVersion_Final.pdf

PAN Europe
Impact assessment on endocrine disrupting pesticides
http://pan-europe.info/Resources/Other/impact_assessment_ed/

PAN Europe (2012)
Disrupting food
http://www.disruptingfood.info/en/

PAN Germany (2013)
Endokrine Wirkung von Pestiziden auf Landarbeiter, insbesondere auf Beschäftigte in Gewächshauskulturen und Gärtnereien
http://www.pan-germany.org/download/pan_studie_endokrine_pestizide_1303.pdf

James W. Simpkins et al. (2011)
Atrazine and Breast Cancer: A Framework Assessment of the Toxicological and Epidemiological Evidence. Oxford journals, Toxicological sciences 123(2), 441–459
http://toxsci.oxfordjournals.org/content/123/2/441.full.pdf

SCCNPF opinions:

- SCCNFP/0483/01

Opinion on the Evaluation of Potentially Estrogenic Effects of UV-filters
adopted by the SCCNFP during the 17th Plenary meeting of 12 June 2001
http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/sccnfp_opinions_97_04/sccp_out145_en.htm

- SCCP/1017/06

Opinion on Parabens (Colipa n° P82), adopted by the SCCP during the 9th plenary meeting of 10 October 2006.
http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_074.pdf

- SCCP/1086/07

Opinion on Homosalate (Colipa n° S12), adopted by the SCCP during the 11th plenary meeting of 21 March 2007.
http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_097.pdf

- SCCP/1183/08

Opinion on 4-Methylbenzylidene camphor, 4-MBC (Colipa n° P82),adopted by the SCCP during the 16th plenary of 24 June 2008.

- SCCP/1184/08

Opinion on Parabens (Colipa n° S60), adopted by the SCCP during the 16th plenary of 24 June 2008.

- SCCP/1192/08

Opinion on Triclosan (Colipa n° P32), adopted by the SCCP during the 19th plenary meeting of 21 January 2009.

- SCCS/1501/12

The SCCS's notes of guidance for the testing of cosmetic substances and their safety evaluation 8th revision. The SCCS adopted this opinion at its 17th plenary meeting of 11 December 2012.
http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_006.pdf

- SCCS/1241/10

Opinion on Cyclomethicone – Octamethylcyclotetrasiloxane (Cyclotetrasiloxane, D4) and Decamethylcyclopentasiloxane (Cyclopentasiloxane, D5),adopted by the SCCS during the 7th plenary meeting of 22 June 2010.

- SCCS/1294/10

Memorandum on alternative test methods in human health safety assessment of cosmetic ingredients in the European Union, adopted by the SCCS during the 5th plenary meeting of 8 December 2009.

- SCCS/1348/10

Opinion on Parabens (Colipa n° P82), adopted by the SCCS during the 9th plenary meeting of 14 December 2010.

- SCCS/1414/11

Opinion on Triclosan (Colipa n° P32) – Addendum to the SCCP opinion on Triclosan (SCCP/1192/08) from January 2008; adopted by the SCCS during the 10th plenary meeting of 22 March 2011.

- SCCS/1446/11

Clarification on Opinion SCCS/1348/10 in the light of the Danish clause of safeguard banning the use of parabens in cosmetic products intended for children under three years of age, adopted by the SCCS by written procedure on 10 October 2011.

- SCCS/1513/13

Opinion on 3-Benzylidene camphor (Colipa n° S61), adopted by the SCCS during the 2nd plenary meeting of 18 June 2010.

- SCCS/1514/13

Opinion on Parabens - Updated request for a scientific opinion on propyland butylparaben (Colipa n° P82), adopted by written procedure on 3 May 2013.

- SCCS Memorandum on Endocrine Disruptors

http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_009.pdf

Stockholm Convention-Persistent Organic Pollutants Review Committee (POPRC) *Documents*
http://chm.pops.int/Convention/POPsReviewCommittee/POPRCMeetings/POPRC8/POPRC7WorkingDocuments/tabid/2801/Default.aspx

TEDX-The Endocrine Disruption Exchange
TEDX List of Potential Endocrine Disruptors
http://www.endocrinedisruption.org/endocrine-disruption/tedx-list-of-potential-endocrine-disruptors/overview

Kendall, R., & Dickerson, R. (n.d.).
Principles and processes for evaluating endocrine disruption in wildlife.
Environ Toxicol Chem Environmental Toxicology and Chemistry, 1253-1254.

Egmond, Roger van (2000)
Ecological Risk Assessment of Endocrine Disruptors.
Environmental Health Perspectives.
http://www.thefreelibrary.com/Ecological+Risk+Assessment+of+Endocrine+Disruptors.-a077277033

Rooney AA, Boyles AL, Wolfe MS, Bucher JR, Thayer KA (2014)
Systematic review and evidence integration for literature-based environmental health science assessments.
Environ Health Perspect 122: 711-718.
http://ehp.niehs.nih.gov/1307972/

Rehm S, White TE, Zahalka EA, Stanislaus DJ, Boyce RW, Wier PJ. (2008)
Effects of food restriction on testis and accessory sex glands in maturing rats.
Toxicol Pathol. 2008 Jul;36(5):687-94.
Reif et al. (2010)
Endocrine Profiling and Prioritization of Environmental Chemicals Using ToxCast Data
Environmental Health Perspectives 118(12) 1714-1720)
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3002190/

UBA
http://www.umweltbundesamt.de/sites/default/files/medien/1/dokumente/tabelle-ref-werte-biozide_2009_0.pdf

WRc-NSF (2002)
Study on the scientific evaluation of 12 substances in the context of endocrine disrupter priority list of actions.
http://ec.europa.eu/environment/chemicals/endocrine/pdf/wrc_report.pdf

Yamasaki, K. (2004).
*Comparative study of the uterotrophic potency of 14 chemicals in a uterotrophic assay and their receptor-binding affinity.*Toxicology Letters, 111-120.
http://www.researchgate.net/publication/271603668_Comparative_study_of_the_uterotrophic_potency_of_14_chemicals_in_a_uterotrophic_assay_and_their_receptor-

Zoeller et al, (2014)
A path forward in the debate over health impacts of endocrine disrupting chemicals
Environmental Health 2014, 13:118 doi:10.1186/1476-069X-13-118
http://www.ehjournal.net/content/pdf/1476-069X-13-118.pdf

Zoeller RT, Brown TR, Doan LL, Gore AC, Skakkebaek NE, Soto AM, Woodruff TJ, Vom Saal FS (2012)
Endocrine-disrupting chemicals and public health protection: a statement of principles from the endocrine society.
Endocrinology 2012, 153:4097–4110.
http://www.ncbi.nlm.nih.gov/pubmed/22733974leino

9.1.2. Agricultural impacts

ADAS UK (2011)
Evaluation of the benefits provided by the azole class of compounds in wheat, and effect of losing all azoles in wheat and potato production in Denmark, France and U.K.

http://www.ecpa.eu/files/attachments/Microsoft%20Word%20-%20ADAS-ECPA%20report%201%20-%20Azoles%20-%2030%20Sep%2011.pdf

ADAS UK (2012)
Evaluation of the agronomic impact of losing azole fungicides in the production of oilseed rape
http://www.ecpa.eu/files/attachments/22205_Azoles%20in%20OSR%20ADAS-JKI%20.pdf

AHDB - Agriculture&Horticulture Development Board (2014)
Endocrine disruptors – collation impacts across all sectors to give clear messages on impacts of changing availability on farmers and production
http://www.ahdb.org.uk/downloads/304064/304001/Endocrine%20Disruptors%20Report%20-%20Final%20181114.pdf

Aepla
http://www.aepla.es/files/Estudios%20e%20Informes/ESTUDIO_DE_IMPACTO_AEPLA_ALTERADORES_ENDOCRINOS_AGRICULTURA_ESPAOLA.pdf

Bianchi F.J.J.A et al (2006)
Sustainable pest regulation in agricultural landscapes: A review on landscapes composition biodiversity and natural pest control
Proceedings of the Royal Society B: Biological Sciences, 2006, DOI: 10.1098/rspb.2006.3530
https://www.agroparistech.fr/IMG/pdf/Bianchi-etal-ProcRSoc-2006.pdf

Cook S.K., Wynn S.C. & Clarke J.H. (2010)
How valuable is glyphosate to UK agriculture and the environment?
Outlooks in Pest Management. 21(6) 280-284.
http://www.researchgate.net/publication/233602600_How_Valuable_is_Glyphosate_to_UK_Agriculture_and_the_Environment

Danish centre on endocrine disrupters (2012)
Evaluation of tebuconazole, triclosan, methylparaben and ethylparaben according to the Danish proposal for criteria for endocrine disrupters
http://mst.dk/media/mst/9106715/chemicalsreportandannex.pdf

Evaluation of 22 SIN List 2.0 substances according to the Danish proposal on criteria for endocrine disrupters
http://mst.dk/media/mst/67169/SIN%20report%20and%20Annex.pdf

Daniels, Robert W. (2012)
The Potential Impact of Recent EU Legislation on the Future of Home Garden Pesticides

http://www.pesticides.gov.uk/Resources/CRD/MigratedResources/Documents/O/Outcomes_paper_-summary_impact_assessment_(Jan_09).pdf

ECPA (2014)
ECPA response to public consultation
http://www.ecpa.eu/files/attachments/24405_ECPA_response_to_Public_Consultation_on_Defining_criteria_for_identifying_endocrine_disruptors_6_November_2014.pd

ECPA (2014)

ECPA's position on the criteria for the determination of endocrine disrupting properties under Regulation 1107/2009
http://www.ecpa.eu/files/attachments/23734_ECPA%20position%20paper%20on%20endocrine%20disruptors%20-%2010%20March%202014.pdf

EFSA

Conclusions on pesticides
http://www.efsa.europa.eu/en/pesticides/pesticidesscdocs.htm?text=conclusion+on+pesticides
Key scientific issues and characterisation of endocrine disrupting substances
http://www.efsa.europa.eu/en/events/documents/130320a-p07.pdf

European Parliament-Policy Department Economic and Scientific Policy (2008)
The benefits of strict cut-off criteria on human health in relation to the proposal for a Regulation concerning plant protection products
http://www.europarl.europa.eu/RegData/etudes/etudes/join/2008/408559/IPOL-JOIN_ET%282008%29408559_EN.pdf

European and Mediterranean Plant Protection Organization
EPPO Workshop on Azole fungicides and Septoria leaf blotch control.
Harpenden (GB), 2010-12-07/09
http://archives.eppo.int/MEETINGS/2010_conferences/septoria/Triazole_Workshop_Conclusions.pdf

Fera (2013)
Agronomic and economic impact assessment for possible human health and ecotoxicology criteria for endocrine disrupting substances
http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=18746&FromSearch=Y&Publisher=1&SearchText=ps2818&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description

ForumPhyto (2001)
Étude d'impact économique des usages orphelins
http://www.forumphyto.fr/2014/02/11/etude-dimpact-economique-des-usages-orphelins/

HGCA Research Review (2009)
Pesticide availability for cereals and oilseeds following revisions of Directive 91/414/EEC effects of losses and new research priorities
http://www.lib.k-state.edu/gracroplands/cite.php?CiteID=3683

HSE (2008)
Revised assessment of the impact on crop protection in the UK of the 'cut-off criteria' and substitution provisions in the proposed Regulation of the European Parliament and of the Council concerning the placing of plant protection products on the market
http://www.pesticides.gov.uk/Resources/CRD/Migrated-Resources/Documents/R/Revised_Impact_Report_1_Dec_2008(final).pdf

Humboldt Forum for Food and Agriculture (2013)
The social, economic and environmental value of agricultural productivity in the EU
http://hffa.info/index.php/resources/download-publications/publications/working-paper-5.html

Institute for Agribusiness (2011)
Restricted availability of azole-based fungicides: impacts on EU farmers and crop agriculture
http://www.agribusiness.de/images/stories/pdf/iab_nr_27_triazole.pdf

F. Jacquet et al (2011)
An economic analysis of the possibility of reducing pesticides in French field crops
doi:10.1016/j.ecolecon.2011.04.003
http://www.sciencedirect.com/science/article/pii/S0921800911001510

Stephen Jess et al. (2014)
European Union policy on pesticides: implications for agriculture in Ireland
DOI: 10.1002/ps.3801. Pest Management Science Volume 70, Issue 11, pages 1646–1654, November 2014
http://onlinelibrary.wiley.com/doi/10.1002/ps.3801/abstract

Liu Y. et al (2014)
Current agricultural practices threaten future global food production
Journal of Agriculture and Environmental Ethics DOI: 10.1007/s10806-014-9527-6
http://www.researchgate.net/publication/269932666_Current_Agricultural_Practices_Threaten_Future_Global_Food_Production

Noémi Nemes (2009)
Comparative analysis of organic and non-organic farming systems: a critical assessment of farm profitability.
Food and Agriculture Organization of the United Nations, Rome.
http://www.fao.org/3/a-ak355e.pdf

Nomisma (2012)
The assessment of the economic importance of azoles in European agriculture: Wheat case study
http://www.phytofar.be/Files/Upload/Docs/Nomisma%20-%20Economic%20importance%20of%20azoles%20in%20Europe%2006.2012.pdf

PAN EU (2013)
Reducing pesticide use across the EU
http://www.pan-europe.info/Resources/Reports/PANE%20-%202013%20-%20Reducing%20pesticide%20use%20across%20the%20EU.pdf

PAN Europe
NAP Best Practice: Meeting the challenge, protecting health, environment & biodiversity. Sustainable use of pesticides: Implementing a National Action Plan
http://www.pan-europe.info/Resources/Reports/NAP_best_practice.pdf

Ponisio LC, M'Gonigle LK, Mace KC, Palomino J, de Valpine P, Kremen C (2014)
Diversification practices reduce organic to conventional yield gap
Royal Society Proceedings B, DOI: 10.1098/rspb.2014.1396
http://rspb.royalsocietypublishing.org/content/282/1799/20141396

Teagasc (2013)
Overview of the potential impact the withdrawal of azoles
http://www.asktheeu.org/en/request/795/response/2817/attach/6/4th%20Annex.pdf

The Andersons Centre (2014)
The Effect of the Loss of Plant Protection Products on UK Agriculture and

Horticulture and the Wider Economy
http://www.cropprotection.org.uk/media/89364/andersons_final_report.pdf

Universitá Cattolica del Sacro Cuore (2012)
Evaluation of the benefits provided by and of the effect of losing the azole class of compounds on durum and common wheat production in Italy (Horta Scl Report)
http://www.ecpa.eu/files/attachments/azoles_wheat_italy_report_2012.pdf

9.1.3. Health impact

American Public Health Association (2014)
Breast Cancer and Occupation: The Need for Action
http://www.apha.org/policies-and-advocacy/public-health-policy-statements/policy-database/2015/01/07/14/55/breast-cancer-and-occupation

Ankley and Gray (2013)
Cross-species conservation of endocrine pathways: a critical analysis of tier 1 fish and rat screening assays with 12 model chemicals
Environ Toxicol Chem. 2013 Apr;32(5):1084-7.
http://www.ncbi.nlm.nih.gov/pubmed/23401061

J.C. Axelrad, C.V. Howard, W.G. McLean (2002)
Interactions between pesticides and components of pesticide formulations in an in vitro neurotoxicity test
Toxicology 173:259–268
http://www.sciencedirect.com/science/article/pii/S0300483X02000367

Bansal R, Tighe D, Danai A, Rawn DF, Gaertner DW, Arnold DL, Gilbert ME, Zoeller RT (2014).
Polybrominated Diphenyl Ether (DE-71) Interferes With Thyroid Hormone Action Independent of Effects on Circulating Levels of Thyroid Hormone in Male Rats.
Endocrinology 2014, 155(10):4104-4112.

Berlaymont (2013)
The 2013 Berlaymont Declaration on Endocrine Disruptors
http://www.brunel.ac.uk/__data/assets/pdf_file/0005/300200/The_Berlaymont_Declaration_on_Endocrine_Disrupters.pdf

Boobis AR, et al. (2006)
IPCS framework for analyzing the relevance of a cancer mode of action for humans.
Crit. Rev. Toxicol. 36: 781–792.

Boobis AR, et al. (2008)
IPCS Framework for Analyzing the Relevance of a Non-cancer Mode of Action for Humans. Crit Rev Toxicol, 38, 87–96

Boobis, AR, et al. (2009)
Application of Key Events, Analysis to Chemical Carcinogens and Noncarcinogens.
Critical Reviews in Food Science and Nutrition, 49(8), 690-707

Bradford Hill Criteria: Hill, Austin Bradford (1965)
The Environment and Disease: Association or Causation?
Proceedings of the Royal Society of Medicine 58 (5): 295-300 and OECD CF level IV & V

Cefic-ECPA (2014)
Proposal for criteria for identification of endocrine disruptors

http://www.ecpa.eu/files/attachments/Proposal_and_explanatory_note_on_the_criteria_for_identification_of_ED_final_version_October_2014.pdf

CEHOS (2013)
Information/Testing Strategy for identification of substances with endocrine disrupting properties
Danish Centre on Endocrine Disruption
http://www.cend.dk/rapporter/EDtestingstrategy.pdf

Chamorro-Garcia R, Sahu M, Abbey RJ, Laude J, Pham N, Blumberg B (2013)
Transgenerational inheritance of increased fat depot size, stem cell reprogramming, and hepatic steatosis elicited by prenatal exposure to the obesogen tributyltin in mice. Environ Health Perspect 2013, 121(3):359-366.

Cao J, Joyner L, Mickens JA, Leyrer SM, Patisaul H (2013)
Sex Specific Estrogen Receptor beta (ERbeta) mRNA Expression in the Rat Hypothalamus and Amygdala is Altered by Neonatal Bisphenol A (BPA) Exposure.
Reproduction 2013

M. Casas et al (2013)
Exposure to brominated flame retardants, perfluorinated compounds, phthalates and phenols in European birth cohorts
International Journal of Hygiene and Environmental Health 216 (2013) 230-242.
http://www.ncbi.nlm.nih.gov/pubmed/22795704

Charlton SJ (2009)
Agonist efficacy and receptor desensitization: from partial truths to a fuller picture.
British journal of pharmacology 2009, 158(1):165-168.

Richard Clapp. Et al. (2008)
Environmental and Occupational causes of Cancer New Evidence, 2005-2007
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2791455/

Chen J, Wu S, Wen S, Shen L, Peng J, Yan C, Cao X, Zhou Y, Long C, Lin T, He D, Hua Y, Wei G(2015)
The Mechanism of Environmental Endocrine Disruptors (DEHP) Induces Epigenetic Transgenerational Inheritance of Cryptorchidism.
http://www.ncbi.nlm.nih.gov/pubmed/26035430

CMS-French health insurance (2015)
To improve the quality of the health system and to master the spending, the proposal of the health insurance for 2015
http://www.cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2015-Fact-sheets-items/2015-01-26.html

S Costello, M Cockburn, J Bronstein, X Zhang, B Ritz (2009)
Parkinson's disease and residential exposure to maneb and paraquat from agricultural applications in the central valley of California
J. Epidemiol. (2009) 169 (8): 919-926.
http://aje.oxfordjournals.org/content/169/8/919.short

COT. 2003. Committee on Toxicity of Chemicals in Food, Consumer products and the Environment
Report Phytoestrogens and health 2003.

http://cot.food.gov.uk/cotreports/cotwgreports/phytoestrogensandhealthcot

K. Croes & E. Den Hond & L. Bruckers & E. Govarts & G. Schoeters & A. Covaci & I. Loots & B. Morrens & V. Nelen & I. Sioen & N. Van Larebeke & W. Baeyens (2014)
Endocrine actions of pesticides measured in the Flemish environment and health studies (FLEHS I and II)
Received: 10 May 2014 /Accepted: 10 August 2014 Environ Sci Pollut Res

Kim Croes, Elly Den Hond, Liesbeth Bruckers, Ilse Loots, Bert Morrens, Vera Nelen, Ann Colles, Greet Schoeters, Isabelle Sioen, AdrianCovaci, Tara Vandermarken, Nicolas Van Larebeke,Willy Baeyens (2014)
Monitoring chlorinated persistent organic pollutants in adolescents in Flanders (Belgium): Concentrations, trends and dose–effect relationships (FLEHS II)
Environment International 71 (2014) 20-28

Danish Environmental Protection Agency (2014)

- *Proposal for Identification of a Substance of Very High Concern on the Basis of the Criteria Set out in REACH Article 57. Benzyl Butyl Phthalate (BBP)*
http://echa.europa.eu/documents/10162/09b7985b-bdbd-4594-874a-ab73ee1a8d70

- *Proposal for Identification of a Substance of Very High Concern on the Basis of the Criteria Set out in REACH Article 57. Dibutyl phthalate (DBP)*
http://echa.europa.eu/documents/10162/d3796777-6d15-4d7a-8ee8-e8eda0aff18f

- *Proposal for Identification of a Substance of Very High Concern on the Basis of the Criteria Set out in REACH Article 57. Bis (2-ethylhexyl) phthalate(DEHP)*
http://echa.europa.eu/documents/10162/04233311-4be2-4a41-8c1b-8e6d0c6fe260

- *Proposal for Identification of a Substance of Very High Concern on the Basis of the Criteria Set out in REACH Article 57. Diisobutyl phthalate (DIBP)*
http://echa.europa.eu/addressing-chemicals-of-concern/authorisation/substances-of-very-high-concern-identification/-/substance/6717/search/+/term

DeMatteo R, Keith MM, Brophy JT, et al. (2012)
Chemical exposures of women workers in the plastics industry with particular reference to breast cancer and reproductive hazards
New Solut. 2012;22:427–448
http://www.ncbi.nlm.nih.gov/pubmed/23207955

Democophes
Human biomonitoring on a European scale
eu-hbm.info/democophes

Wilem Dhogge, Elly Den Hond, Gudrun Koppen, Liesbeth Bruckers, Vera Nelen, Els van de Mieroop, Maaike Bilau, Kim Croes, Willy Baeyens, Greet Schoeters, Nicolas van Larebeke (2009)
Internal exposure to pollutants and sex hormone levels in Flemish male adolescents in a cross-sectional study: associations and dose–response relationships
Journal of Exposure Science and Environmental Epidemiology (2009), 1–8

Elly Den Hond, Harry A. Roels, Karel Hoppenbrouwers, Tim Nawrot,Lutgarde Thijs, Corinne Vandermeulen,Gerhard Winneke, Dirk Vanderschueren, and Jan A. Staessen (2002)

Sexual Maturation in Relation to Polychlorinated Aromatic Hydrocarbons: Sharpe and Skakkebaek's Hypothesis Revisited
Environmental Health Perspectives 110 (8), 2002

Willem Dhooge, Elly Den Hond, Gudrun Koppen, Liesbeth Bruckers, Vera Nelen (2010)
Internal exposure to pollutants and body size in Flemish adolescents and adults: Associations and dose–response relationships
Environment International 36 (2010) 330–337

EU (2013)
Decision No 1386/2013/EU of the European Parliament and of the council of 20 November 2013 on a General Union Environment Action Programme to 2020 'Living well, within the limits of our planet'
http://data.europa.eu/eli/dec/2013/1386/oj

EU Commission (2013)
Minutes of the expert meeting on endocrine disruptors
http://ec.europa.eu/archives/commission_2010-2014/president/chief-scientific-adviser/documents/minutes_endocrine_disruptors_meeting_241013_final.pdf

EU Parliament (2013)
Report on the protection of public health from endocrine disrupters
http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+REPORT+A7-2013-0027+0+DOC+XML+V0//EN

Eva Govarts, Mark Nieuwenhuijsen, Greet Schoeters, Ferran Ballester, Karolien Bloemen, Michiel de Boer, Cécile Chevrier, Merete Eggesbø, Mònica Guxens, Ursula Krämer, Juliette Legler, David Martínez, Lubica Palkovicova, Evridiki Patelarou, Ulrich Ranft, Arja Rautio, Maria Skaalum Petersen, Rémy Slama, Hein Stigum, Gunnar Toft, Tomas Trnovec, Stéphanie Vandentorren, Pál Weihe, Nynke Weisglas Kuperus, Michael Wilhelm, Jürgen Wittsiepe, and Jens Peter Bonde (2012)
Birth Weight and Prenatal Exposure to Polychlorinated Biphenyls (PCBs) and Dichlorodiphenyldichloroethylene (DDE): A Meta-analysis within 12 European Birth Cohorts
Environmental Health Perspectives 120 (2), 2012

EFSA Scientific Committee (2013)
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. http://www.efsa.europa.eu/en/efsajournal/doc/3132.pdf

European Environment Agency (2002)
The impacts of endocrine disrupters on wildlife, people and their environments
Technical Report No. 2/2012
http://www.eea.europa.eu/publications/the-impacts-of-endocrine-disrupters

Greenberg E.R., Barnes A.B., Resseguie L., et al. (1984)
Breast Cancer in Mothers Given Diethylstilbestrol in Pregnancy
N Engl J Med 1984; 311:1393-1398
http://www.nejm.org/search?q=311%3A+1393-1398

Gee D (2006)
Late lessons from early warnings: Toward realism and precaution with endocrine-

disrupting substances.
Environ Health Perspect 2006, 114 Suppl 1:152-160.
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1874173/

Health Canada (2000)
A Decision Framework for Risk Assessment and Risk Management at the Pest Management Regulatory Agency
http://www.hc-sc.gc.ca/cps-spc/pubs/pest/_pol-guide/spn2000-01/index-eng.php

Health and Environment Alliance (HEAL) (2014)
Health costs in the EU - How much is related to EDCs
http://www.env-health.org/IMG/pdf/18062014_final_health_costs_in_the_european_union_how_much_is_realted_to_edcs.pdf

ISPOR (2011)
Value in Health
http://www.ispor.org/publications/value/JVAL_14-3_final%204-26-2011.pdf

Iavicoli, I., Fontana L., Leso V., Bergamasch A. (2013)
The effects of nanomaterials as endocrine disruptors
Int. J. Mom. Sci. 14, 16732-16801

Janesick A, Blumberg B. (2011)
Endocrine disrupting chemicals and the developmental programming of adipogenesis and obesity. Birth Defects Research, Part C: Embryo Today—Reviews.

Joint German-UK Position (2011)
Report: "Regulatory Definition of an Endocrine Disrupter in Relation to Potential Threat to Human Health"
http://www.bfr.bund.de/cm/343/regulatory_definition_of_an_endocrine_disrupter_in_relation_to_potential_threat_to_human_health.pdf

Lamb et al. (2012)
Critical comments on the WHO-UNEP State of the Science of Endocrine Disrupting Chemicals
http://www.sciencedirect.com/science/article/pii/S0273230014000269

Langer P, Kocan A, Tajtakova M, Koska J, Radikova Z, Ksinantova L, Imrich R, Huckova M, Drobna B, Gasperikova D et al (2008)
Increased thyroid volume, prevalence of thyroid antibodies and impaired fasting glucose in young adults from organochlorine cocktail polluted area: outcome of transgenerational transmission?
Chemosphere 2008, 73(7):1145-1150.

S Lee, R McLaughlin, M Harnly, R Gunier and Kreutzer, R (2002)
Community Exposures to Airborne Agricultural Pesticides in California: Ranking of Inhalation Risks
Environmental Health Perspectives110: 1175-1184
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1241103/

O. Leino et al. (2013)
Pollutant concentrations in placenta
Food and Chemical Toxicology 54 (2013), 59-69
http://orbit.dtu.dk/en/publications/pollutant-concentrations-in-placenta(7991cfc4-db02-4cbb-9374-8715c66dbbc8).html

Marike M. Leijs, Janna G. Koppe , Kees Olie, Wim M.C. van Aalderen, Pim de Voogt, Gavin W. ten Tusscher (2010)
*Effects of dioxins, PCBs and PBDEs on immunology and haematology in adolescents*https://www.amc.nl/web/Het-AMC/Agenda/Overzicht/Evenementen-overzicht/Marike-Leijs-Toxic-effects-of-dioxins-PCBs-and-PBDEs-in-adolescents..htm

Maruvada P, Baumann CT, Hager GL, Yen PM (2003)
Dynamic shuttling and intranuclear mobility of nuclear hormone receptors.
J Biol Chem 2003, 278(14):12425-12432.
http://www.jbc.org/content/278/14/12425.full

Manikkam M, Tracey R, Guerrero-Bosagna C, Skinner MK (2013)
Plastics derived endocrine disruptors (BPA, DEHP and DBP) induce epigenetic transgenerational inheritance of obesity, reproductive disease and sperm epimutations. PLoS One 2013, 8(1):e55387.
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0055387

Marx-Stoelting et al. (2014)
Assessment of three approaches for regulatory decision making on pesticides with endocrine disrupting properties
Regulatory Toxicology and Pharmacology. Volume 70, Issue 3, December 2014, Pages 590–604
http://www.sciencedirect.com/science/article/pii/S0273230014002050

Maastricht University (2014)
Time trends in the incidences of human health disorders hypothesized to be associated with exposure to endocrine disrupting chemicals
http://gcb.mumc.nl/sites/genetics/files/time_trends_in_the_incidences_of_human_health_disorders_0.pdf

Johan Maervoet, Griet Vermeir, Adrian Covaci, Nicolas Van Larebeke, Gudrun Koppen, Greet Schoeters, Vera Nelen, Willy Baeyens, Paul Schepens, and Maria K. Viaene (2007) *Association of Thyroid Hormone Concentrations with Levels of Organochlorine Compounds in Cord Blood of Neonates*
Environmental Health Perspectives 115 (12), 2007
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2137114/

Mahoney MM, Padmanabhan V. (2010)
Developmental programming: impact of fetal exposure to endocrine-disrupting chemicals on gonadotropin-releasing hormone and estrogen receptor mRNA in sheep hypothalamus.
Toxicology and Applied Pharmacology.
http://www.ncbi.nlm.nih.gov/pubmed/20621667

Meek ME, et al. (2014a)
New developments in the evolution and application of the WHO/IPCS framework on mode of action/species concordance analysis.
J. Appl. Toxicol. 34: 1–18
http://www.ncbi.nlm.nih.gov/pubmed/24166207

Meek et al. (2014b)
Mode of action human relevance (species concordance) framework: Evolution of the Bradford Hill considerations and comparative analysis of weight of evidence.
J. Appl. Toxicol. 34:595-606

http://ntp.niehs.nih.gov/iccvam/meetings/aop-wksp-2014/presentations/meek-508.pdf

Sara Mostafalou and Mohammad Abdollahi (2013)
Pesticides and Human Chronic Diseases: Evidences, Mechanisms, and Perspectives
Toxicology and Applied Pharmacology 268:157–177
http://www.sciencedirect.com/science/article/pii/S0041008X13000549

Ntzani et al. EFSA External Scientific Report (2013)
Literature review on epidemiological studies linking exposure to pesticides and health effects
http://www.efsa.europa.eu/en/supporting/doc/497e.pdf

Nordic Council of Ministers (2014) (Olsson, IM)
The cost of inaction – A socioeconomic analysis of costs linked to effects of endocrine disrupting substances on male reproductive health
http://norden.diva-portal.org/smash/get/diva2:763442/FULLTEXT04.pdf

Nagaich AK, Rayasam GV, Martinez ED, Becker M, Qiu Y, Johnson TA, Elbi C, Fletcher TM, John S, Hager GL (2004)
Subnuclear trafficking and gene targeting by steroid receptors.
Annals of the New York Academy of Sciences 2004, 1024:213-220.

Ong KM, Blackford JA, Kagan BL, Simons SS, Chow CC (2010)
A theoretical framework for gene induction and experimental comparisons.
Proc Natl Acad Sci U S A 2010, 107(15):7107-7112.

Paloma Alonso-Magdalena, Sumiko Morimoto, Cristina Ripoll, Esther Fuentes, and Angel Nadal (2006)
The Estrogenic Effect of Bisphenol A Disrupts Pancreatic β-Cell Function In Vivo and Induces Insulin Resistance
Environ Health Perspect 114:106–112 (2006). doi:10.1289/ehp.8451
http://www.ncbi.nlm.nih.gov/pubmed/16393666

Pest Management Regulatory Agency (2003)
Assessing Exposure from Pesticides in Food - A Users Guide
Science Policy Notice SPN2003-03
http://www.hc-sc.gc.ca/cps-spc/pubs/pest/_pol-guide/spn2003-03/index-eng.php

Greet Schoeters, Elly Den Hond, Willem Dhooge, Nik van Larebeke and Marike Leijs
Endocrine Disruptors and Abnormalities of Pubertal Development (2008)
Nordic Pharmacological Society. Basic & Clinical Pharmacology & Toxicology 102, 168–175 (2008)
http://www.ncbi.nlm.nih.gov/pubmed/18226071

Skinner MK, Manikkam M, Tracey R, Guerrero-Bosagna C, Haque M, Nilsson EE (2013) *Ancestral dichlorodiphenyltrichloroethane (DDT) exposure promotes epigenetic transgenerational inheritance of obesity.*
BMC medicine 2013, 11:228.
http://www.biomedcentral.com/1741-7015/11/228

Skinner MK, Haque CG, Nilsson E, Bhandari R, McCarrey JR: Environmentally induced transgenerational epigenetic reprogramming of primordial germ cells and the subsequent germ line. PLoS One 2013, 8(7):e66318
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0066318

RTI Health Solutions (2015)
Targeted Literature Review of Factors Associated With Time Trends in the Risk for Prostate Cancer, Breast Cancer, Excess Weight, Diabetes, and Autism
Summary Report

Rozman KK, Bhatia J, Calafat AM, Chambers C, Culty M, Etzel RA, Flaws JA, Hansen, DK, Hoyer PB, Jeffery EH, Kesner JS, Marty S, Thomas JA, Umbach D. (2006).
NTP-CERHR expert panel report on the reproductive and developmental toxicity of genistein. Birth Defects Res B Dev Reprod Toxicol 77(6):485-638
http://www.ncbi.nlm.nih.gov/pubmed/17186522

Schug, T.T., Janesick, A., Blumberg, B., Heindel J.J.
Endocrine disrupting chemicals and disease susceptibility
J Steroid Biochem Mol Biol (2011) 127:204-215
http://www.ncbi.nlm.nih.gov/pubmed/21899826

Berrin Serdar, William G LeBlanc, Jill M Norris and Miriam Dickinson (2014)
Potential effects of polychlorinated biphenyls (PCBs) and selected organochlorine pesticides (OCPs) on immune cells and blood biochemistry measures: a cross-sectional assessment of the NHANES 2003-2004 data.
Environmental Health 2014, 13:114
http://www.ehjournal.net/content/13/1/114

Jan A Staessen, Tim Nawrot, Elly Den Hond, Lutgarde Thijs, Robert Fagard, Karel Hoppenbrouwers, Gudrun Koppen, Vera Nelen, Greet Schoeters, Dirk Vanderschueren, Etienne Van Hecke, Luc Verschaeve, Robert Vlietinck, Harry A Roels (2001)
Renal function, cytogenetic measurements, and sexual development in adolescents in relation to environmental pollutants: a feasibility study of biomarkers
The Lancet Vol 357, 2001
http://www.greenpeace.org.uk/media/reports/how-environmental-pollutants-affect-sexual-development-in-adolescents

Testai E, Galli CL, Dekant W, Marinovich M, Piersma AH, Sharpe RM (2013).
A plea for risk assessment of endocrine disrupting chemicals.
Toxicology 2013 Dec 6;314(1):51-9.
http://www.research.ed.ac.uk/portal/en/publications/a-plea-for-risk-assessment-of-endocrine-disrupting-chemicals(23a9652b-8ba2-45d8-87e0-53f3ff5a92db)/export.html

Tinwell et al (2013)
The screening of chemicals in everyday life Validated Assays targeting the pituitary-gonadal axis
Regul Toxicol Pharmacol. 2013 Jul;66(2):184-96. doi: 10.1016/j.yrtph.2013.04.002. Epub 2013 Apr 13.
http://www.ncbi.nlm.nih.gov/pubmed/23590819

Tracey R, Manikkam M, Guerrero-Bosagna C, Skinner MK (2013)
Hydrocarbons (jet fuel JP-8) induce epigenetic transgenerational inheritance of obesity, reproductive disease and sperm epimutations.
Reprod Toxicol 2013, 36:104-116.

L. Trasande (2014)
Further Limiting Bisphenol A in Food Uses Could Provide Health and Economic Benefits, Health Affairs, January 2014
http://content.healthaffairs.org/content/early/2014/01/16/hlthaff.2013.0686.abstract

Troisi et al. (2007)
Cancer risk in women prenatally exposed to diethylstilbestrol
International Journal of Cancer 121: 356-360
http://onlinelibrary.wiley.com/doi/10.1002/ijc.22631/epdf

Stijn L. Verhulst, Vera Nelen, Elly Den Hond, Gudrun Koppen, Caroline Beunckens, Carl Vael, Greet Schoeters, and Kristine Desager (2009)
Intrauterine Exposure to Environmental Pollutants and Body Mass Index during the First 3 Years of Life
Environmental Health Perspectives 117: 122-6
http://www.ncbi.nlm.nih.gov/pubmed/19165398

Waddell, G., Burton, K. (2006)
Is work good for your health and well-being?
The Stationary Office, London.
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/214326/hwwb-is-work-good-for-you.pdf

Walker DM, Gore AC (2011)
Transgenerational neuroendocrine disruption of reproduction.
Nat Rev Endocrinol 2011, 7(4):197-207
http://www.ncbi.nlm.nih.gov/pubmed/21263448

Zoeller RT, Bansal R, Parris C (2005)
Bisphenol-A, an environmental contaminant that acts as a thyroid hormone receptor antagonist in vitro, increases serum thyroxine, and alters RC3/neurogranin expression in the developing rat brain.
Endocrinology 2005, 146(2):607-612.
http://www.bio.umass.edu/biology/zoeller/pdf/ZoellerBPA.pdf

Zoeller et al.(2014)
A path forward in the debate over health impacts of endocrine disrupting chemicals.
Environmental Health 2014 13:118.
http://www.ehjournal.net/content/13/1/118

9.1.4. Environmental impact

Allner B, von der Gönna S, Griebeler EM, Nikutowski N, Weltin A, Stahlschmidt-Allner P. (2010)
Reproductive functions of wild fish as bioindicators of reproductive toxicants in the aquatic environment
Environ Sci Pollut Res Int. 2010 Feb;17(2):505-18.
http://www.ncbi.nlm.nih.gov/pubmed/?term=allner+wild+fish

Baroiller JF, D'Cotta H. (2001)
Environment and sex determination in farmed fish.
Comp Biochem Physiol C Toxicol Pharmacol. 2001 Dec;130(4):399-409. Review.
http://www.ncbi.nlm.nih.gov/pubmed/11738628

Danish Ministry of the Environment, Environmental Protection Agency (2013)

- *Survey of parabens, part of the LOUS-review*

Environmental Project no.1474, 2013.
http://www2.mst.dk/Udgiv/publications/2013/04/978-87-93026-02-5.pdf

- *Survey of alkylphenols and alkylphenolethoxylates, part of the LOUS-review*

Environmental Project no.1470, 2013.
http://www2.mst.dk/Udgiv/publications/2013/04/978-87-92903-99-0.pdf

Danish Ministry of the Environment, Environmental Protection Agency (2014)

- *Survey of selected phthalates, part of the LOUS-review*

Environmental Project no.1541, 2014.
http://www2.mst.dk/Udgiv/publications/2014/01/978-87-93026-95-7.pdf

- *Survey of MTBE, part of the LOUS-review*

Environmental Project no.1540, 2014.
http://www2.mst.dk/Udgiv/publications/2014/01/978-87-93026-94-0.pdf

European Environment Agency (2011)
Hazardous substances in Europe's fresh and marine waters: An overview.
EEA Technical report No 8/2011
http://www.eea.europa.eu/publications/hazardous-substances-in-europes-fresh

European Environment Agency (2012)
The impacts of endocrine disrupters on wildlife, people and their environments – The Weybridge (1996–2011) report
http://www.eea.europa.eu/publications/the-impacts-of-endocrine-disrupters

Frische, T., Bachmann, J, Frein, D., Juffernholz, T., Kehrer, A., Klein, A., Maack, G., Stock, F., Stolzenberg, H.-C., Thierbach, C., Walter-Rohde, S. (2013).
Identification, assessment and management of "endocrine disruptors" in wildlife in the EU substance legislation - Discussion paper from the German Federal Environment Agency (UBA).
Toxicology Letters. Online 15 March 2013
http://authors.elsevier.com/sd/article/S0378427413001021

Frische, T., Kotschik, P. (2011)
Where to cut-off? Endocrine hazard profiles of EBI fungicides.
SETAC Europe 21st Annual Meeting, Milano/Italy, 15-19.05.2011

Jobling S, Tyler CR. (2003)
Endocrine disruption, parasites and pollutants in wild freshwater fish.
Parasitology. 2003;126 Suppl:S103-8.
http://www.ncbi.nlm.nih.gov/pubmed/14667177

Ministers of the Environment (2014)
Letter to Commissioner Mr. Karmenu Vella and Commissioner Elzbieta Bienkowska
http://mim.dk/media/129353/courrier-aux-commissaires-vella-et-bienkowska-12-11-2014.pdf

Schabuss M, Gemeiner M, Gleiss A, Lewis JW, Miller I, Möstl E, Schober U, Tschulenk W, Walter I, Grillitsch B. (2005)
Ligula intestinalis infection as a potential source of bias in the bioindication of endocrine disruption in the European chub Leuciscus cephalus.
J Helminthol. 2005 Mar;79(1):91-4
http://www.ncbi.nlm.nih.gov/pubmed/?term=schabuss+ligula

Stolzenberg, H.C., Frische, T., Dellario, V., Timm, G., Gourmelon, A., Iguchi, T., Ingerslev, F., Roberts, M. (2013).

The regulatory need for tests to detect EDCs and assess their hazards to wildlife.
In: Matthiessen, P. (Ed.): Endocrine Disrupters – Hazard Testing and Assessment Methods.
http://onlinelibrary.wiley.com/doi/10.1002/9781118355961.ch3/summary

Thomas P, Rahman MS, Khan IA, Kummer JA. (2007)
Widespread endocrine disruption and reproductive impairment in an estuarine fish population exposed to seasonal hypoxia.
Proc Biol Sci. 2007 Nov 7;274(1626):2693-701.
http://www.ncbi.nlm.nih.gov/pubmed/17725976

The Weybridge (1996–2011) report
http://www.eea.europa.eu/publications/the-impacts-of-endocrine-disrupters

Wu RS, Zhou BS, Randall DJ, Woo NY, Lam PK. (2003)
Aquatic hypoxia is an disrupter and impairs fish reproduction.
Environ Sci Technol. 2003 Mar 15;37(6):1137-41.

9.1.5. Trade impact

Kyd D. Brenner LLC (2014)
Potential Trade Effects on World Agricultural Exporters of European Union Regulations on Endocrine Disruptors
http://www.dtbassociates.com/docs/EUregsEndocrineDisruptorsTradeEffects2-2014.pdf

Brief on India's agricultural trade relations with European Union
http://agricoop.nic.in/imagedefault/trade/European%20Union%20brief.pdf

Kortenkamp A, Martin O, Faust M, Evans R, McKinlay R, Orton F, Rosivatz E (2011)
State of the Art Assessment of Endocrine Disruptors, Final Report.
http://ec.europa.eu/environment/chemicals/endocrine/pdf/sota_edc_final_report.pdf

WHO/UNEP (2012)
State of the science of endocrine disrupting chemicals 2012.
Edited by Åke Bergman, Jerrold J. Heindel, Susan Jobling, Karen A. Kidd and R. Thomas Zoeller.
http://www.unep.org/hazardoussubstances/Portals/9/EDC/StateOfEDCScience.pdf.

9.2. Web-based platforms run by EDC-Free Europe to encourage participation in the consultation process

9.2.1. Web-based platform run by EDC-Free Europe to encourage email responses in the consultation process

The content of the responses of the emails originating from EDC-Free Europe is as follows:

> "Je crois que cette consultation publique n'est pas vraiment faite pour le public mais je tiens à combattre le lobbying de l'industrie qui pourrait autrement affaiblir l'action publique sur les produits chimiques perturbateurs hormonaux au détriment de la santé des personnes, de l'environnement et de la faune !
>
> La feuille de route sur les perturbateurs hormonaux, aussi connus sous le nom de perturbateurs endocriniens (PE), définit quatre options différentes pour les critères permettant d'identifier quelles substances chimiques ont des propriétés de perturbation endocrinienne. L'option 4 est à proscrire, et l'option 3 (Utilisation de la définition de l'OMS/PISSC pour identifier les perturbateurs endocriniens et les catégories en fonction de la solidité des preuves) m'apparait comme la meilleure option pour protéger la santé publique.
>
> Pour les approches à la prise de décision réglementaire, si le format de consultation l'avait permis, j'aurais souhaité montrer mon soutien à l'option A - pas de changements réglementaires."

(translation)

I believe that this public consultation is not really made for the public but I want to fight the lobbying industry that might otherwise weaken public action on hormone-disrupting chemicals at the expense of health, the environment and wildlife!

The roadmap on hormone disruptors, also known as endocrine disruptors (PE), sets out four different options for criteria to identify which chemicals have endocrine disrupting properties. Option 4 is to be avoided, and Option 3 (using the definition of WHO / IPCS to identify endocrine disruptors and categories according to the strength of evidence) appears to me as the best option to protect the public health.

For approaches to regulatory decision-making, if the consultation format had allowed, I wish to show my support for Option A - no regulatory changes.

9.2.2. Web-based platform run by EDC-Free Europe to encourage web-based responses in the consultation process available in English, Spanish, German, French, Swedish, Dutch and Danish

EN - ES - DE - FR - SV - NL - DA

stop hormone disrupting chemicals

SAY "NO" TO... HORMONE DISRUPTING CHEMICALS

EDC Free Europe

THEIR QUESTIONS, OUR ANSWERS

Options for determining hormone disrupting properties

The roadmap on hormone disrupting chemicals, also known as endocrine disrupting chemicals (EDCs) defines **four different options** for the criteria to identify which chemicals have endocrine disrupting properties. Below is a response to each option.

OPTION 1: The interim criteria remain in place.

This option will mean some hormone disrupting chemicals will be overlooked

I do not agree with option 1.

In option 1, the interim criteria set in the plant protection product (PPPR) and biocidal products regulation (BPR) continue to apply. These are the only laws in the EU that say if a substance is a hormone disrupting chemical (or endocrine disrupting chemical or EDC for short) it will not get permission to be used in the EU.

But all EDCs need to be identified, no matter if they are used as pesticides, biocides, in cosmetics or food packaging, children's toys or elsewhere.

Therefore, criteria for a scientific identification of EDCs are needed for other EU laws, and any other uses as well; which option 1 will not deliver.

Moreover, option 1 will not protect people because the current interim criteria can overlook EDCs which do not cause cancer or harm reproduction, but affect the brain or metabolism, and thus can contribute to mental disorders, diabetes or obesity.

This corresponds to Question 2.1.4 in the EU public consultation

This corresponds to Questions 2.1.1, 2.1.2 and 2.1.3 in the EU public consultation

There are three technical questions for option 1, to which we advise the answer 'no'. If you exceptionally want to answer yes, please use the European Commission website to directly submit your answers to the consultation.

- **No,** I have not conducted nor am I aware of an assessment of substances which would be identified as hormone disrupting chemicals according to option 1.
- **No,** I am not aware of any assessment(s) of substitutability of the identified substances.
- **No,** I am not aware of any assessment(s) of the socio-economic impact if the identified substances were regulated without further risk assessment.

OPTION 2: Using the World Health Organization International Programme on Chemical Safety (WHO/IPCS) definition to identify hormone disrupting chemicals (hazard identification)

This corresponds to Questions 2.2.1, 2.2.2 and 2.2.3 in the EU public consultation

There are three technical questions for option 2, to which we advise the answer 'no'. If you exceptionally want to answer yes, please use the European Commission website to directly submit your answers to the consultation.

- **No,** I have not conducted nor am I aware of an assessment of substances which would be identified as hormone disrupting chemicals according to option 2.
- **No,** I am not aware of any assessment(s) of substitutability of the identified substances.

This option will leave out "potential hormone disrupting chemicals (EDCs)"

I do not agree with option 2.

In option 2, the World Health Organization International Programme on Chemical Safety (WHO/IPCS) definition to identify confirmed EDCs will apply. But option 2 leaves out the twin WHO definition for "potential EDCs". Using only the definition for confirmed EDCs is a 'black or white' only approach which blocks full and effective consideration of the state of the science. This truncated definition would also exclude all chemicals that need to be further investigated to determine whether they are EDCs or not.

The EU pesticide and biocide laws aim to ban both confirmed and suspected EDCs as the legal texts say 'may cause adverse effects'. So we need a definition that is not only for "confirmed EDCs".

The world's leading scientific report on the "State of the science of EDCs 2012" from the WHO and United Nations Environment Programme (UNEP) highlights that endocrine disrupting chemicals are a global threat to human health and ecosystems. Therefore, we

stop hormone disrupting chemicals

SAY "NO" TO... HORMONE DISRUPTING CHEMICALS

EDC Free Europe

THEIR QUESTIONS, OUR ANSWERS

Options for determining hormone disrupting properties

The roadmap on hormone disrupting chemicals, also known as endocrine disrupting chemicals (EDCs) defines **four different options** for the criteria to identify which chemicals have endocrine disrupting properties. Below is a response to each option.

OPTION 1: The interim criteria remain in place.

This option will mean some hormone disrupting chemicals will be overlooked

I do not agree with option 1.

In option 1, the interim criteria set in the plant protection product (PPPR) and biocidal products regulation (BPR) continue to apply. These are the only laws in the EU that say if a substance is a hormone disrupting chemical (or endocrine disrupting chemical or EDC for short) it will not get permission to be used in the EU.

But all EDCs need to be identified, no matter if they are used as pesticides, biocides, in cosmetics or food packaging, children's toys or elsewhere.

Therefore, criteria for a scientific identification of EDCs are needed for other EU laws and any other uses as well, which option 1 will not deliver.

Moreover, option 1 will not protect people because the current interim criteria can overlook EDCs which do not cause cancer or harm reproduction, but affect the brain or metabolism and thus can contribute to mental disorders, diabetes or obesity.

This corresponds to Question 2.1.4 in the EU public consultation

This corresponds to Questions 2.1.1, 2.1.2 and 2.1.3 in the EU public consultation

There are three technical questions for option 1, to which we advise the answer 'no'. If you exceptionally want to answer yes, please use the European Commission website to directly submit your answers to the consultation.

- **No**, I have not conducted nor am I aware of an assessment of substances which would be identified as hormone disrupting chemicals according to option 1.
- **No**, I am not aware of any assessment(s) of substitutability of the identified substances.
- **No**, I am not aware of any assessment(s) of the socio-economic impact if the identified substances were regulated without further risk assessment.

OPTION 2: Using the World Health Organization International Programme on Chemical Safety (WHO/IPCS) definition to identify hormone disrupting chemicals (hazard identification)

This corresponds to Questions 2.2.1, 2.2.2 and 2.2.3 in the EU public consultation

There are three technical questions for option 2, to which we advise the answer 'no'. If you exceptionally want to answer yes, please use the European Commission website to directly submit your answers to the consultation.

- **No**, I have not conducted nor am I aware of an assessment of substances which would be identified as hormone disrupting chemicals according to option 2.
- **No**, I am not aware of any assessment(s) of substitutability of the identified substances.

This option will leave out "potential hormone disrupting chemicals (EDCs)"

I do not agree with option 2.

In option 2, the World Health Organization International Programme on Chemical Safety (WHO/IPCS) definition to identify confirmed EDCs will apply. But option 2 leaves out the twin WHO definition for "potential EDCs". Using only the definition for confirmed EDCs is a 'black or white' only approach which blocks full and effective consideration of the state of the science. This truncated definition would also exclude all chemicals that need to be further investigated to determine whether they are EDCs or not.

The EU pesticide and biocide laws aim to ban both confirmed and suspected EDCs as the legal texts say 'may cause adverse effects'. So we need a definition that is not only for "confirmed EDCs".

The world's leading scientific report on the "State of the science of EDCs 2012" from the WHO and United Nations Environment Programme (UNEP) highlights that endocrine disrupting chemicals are a global threat to human health and ecosystems. Therefore, we

- **No**, I am not aware of any assessment(s) of the socio-economic impact if the identified substances were regulated without further risk assessment.

must be able to distinguish between definite and potential disruptors and track potential ones until more evidence can confirm or eliminate their 'potential' status.

This corresponds to Question 2.2.4 in the EU public consultation

OPTION 3: Using WHO/IPCS definition to identify hormone disrupting chemicals and categories based on strength of evidence

Best option to protect public health.

Option 3 would provide a good way forward.

In option 3, the WHO/IPCS definition to identify EDCs will apply, with the addition of three categories (confirmed; suspected; potential EDC). This set of categories is very transparent and portrays the different levels of scientific evidence available. This option can be used to properly rank a given chemical according to the data situation. It allows for an effective and efficient use of resources by focusing regulatory action in the right places – in differentiated ways according to the categories. It must be pointed out, however, that the WHO definition is a scientific working definition and not a regulatory definition. The legal text such as Regulation 1107/2009 talks of pesticides with endocrine disrupting properties that 'may cause adverse effects'.

This option is coherent with current approaches to rank other chemicals, e.g. how cancer causing chemicals are classified. It also facilitates regulating these chemicals according to the different laws governing their various uses (food contact materials, pesticides, cosmetics, etc.).

The first two categories (confirmed; suspected) should be used for regulation. The third category (potential) is important to steer industry to gather more information on the potentially harmful properties. This additional information will help to either remove chemicals from this category or upgrade them.

When placing chemicals in the different categories, it will be crucial not to raise the bar of proof too high. Waiting for complete knowledge means risking taking action too late to prevent illness and save lives (as happened with asbestos). EU law has recognised that we can't afford to delay for absolute proof of harm, because it seeks to ban pesticides and biocides that "may cause adverse effects", instead of only banning definite hormone disruptors.

This corresponds to Questions 2.3.1, 2.3.2 and 2.3.3 in the EU public consultation

There are 3 technical questions for option 3, to which we advise the answer 'no'. If you exceptionally want to answer yes, please use the Commission website to directly submit your answers to the consultation.

- **No**, I have not conducted nor am I aware of an assessment of substances which, in addition to those identified according to option 2, would be identified as suspected endocrine disruptors or endocrine active substances according to option 3.
- **No**, I am not aware of any assessment(s) of substitutability of the identified substances.
- **No**, I am not aware of any assessment(s) of the socio-economic impact if the identified substances were regulated without further risk assessment.

This process of categorising chemicals can only be successful if the criteria for assessing endocrine effects are applied in a strictly scientific way. There are too many cases in current regulatory assessments where a concern relating to a substance is downplayed because of doubts about "human relevance" without a valid scientific justification.

Humanity faces rising levels of hormone related illnesses, so what the European Commission must do is to establish a system that leads to reducing our exposures to hormone disruptors, to help prevent these illnesses. Using categories is a sophisticated but powerful and necessary part of such a system.

This corresponds to Question 2.3.4 in the EU public consultation

OPTION 4: Using WHO/IPCS definition to identify endocrine disruptors and include potency.

This corresponds to Questions 2.4.1, 2.4.2 and 2.4.3 in the EU public consultation

There are 3 technical questions for option 4, to which we advise the answer 'no'. If you exceptionally want to answer yes, please use the Commission website to directly submit your answers to the consultation.

- **No**, I have not conducted nor am I aware of an assessment of substances which would be identified as endocrine disruptors according to option 4.
- **No**, I am not aware of any assessment(s) of substitutability of the identified substances.
- **No**, I am not aware of any assessment(s) of the socio-economic impact if the identified substances were regulated without further risk assessment.

No way. Worst option.

I do not agree with option 4.

In option 4, the WHO/IPCS definition to identify EDCs will apply, with the addition of potency as a cut-off. This proposal is scientifically flawed and is contrary to the policy advice the European Commission received in reports by the Joint Research Centre (JRC) and the European Food Safety Agency (EFSA). This option is preferred by pesticides and chemical companies who want to effectively minimise the number of chemicals barred from the market. However, the identification of EDCs needs to identify all hormone disrupting chemicals which harm our health, not just some, which is what the potency factor would result in.

Potency is not used to identify chemicals which cause cancer or are toxic for the reproduction, and it makes no scientific sense for identifying whether a chemical is a hormone disruptor or not.

EDCs vary in how strongly they affect different parts of the body and different hormone systems, so relying on selective tests for potency may wrongly leave some chemicals unidentified. For example, an EDC may be weak in disrupting female hormonal signalling but strong in disrupting some aspect of brain development. Furthermore, many animals in our ecosystems are also exposed, but potency may vary dramatically between different species – so using potency cannot reliably protect people and wildlife.

Furthermore, industry protocol studies often dose test animals with very high, unrealistic amounts of the chemical under examination and do not include many low doses. However, the effects occurring at the high doses will be qualified as irrelevant using the potency criterion. In addition, because effects are not adequately examined over a range of low doses and the effects looked for may not represent the most sensitive ones, even quite potent chemicals are likely to be missed. Therefore, a potency cut-off should not be applied to the criteria.

In addition, during the most vulnerable periods, such as development in the womb, even extremely small amounts of weak EDCs may contribute to ill health, particularly later in life.

Moreover, people and wildlife are exposed to many EDCs from different sources at the same time and over time, and science has shown that EDCs can act together, leading to harmful cocktail effects. Not identifying 'low potency' EDCs would hamper any attempts to address health risks arising from cumulative exposure to these EDCs.

Therefore, option 4 is absolutely inadequate as identification criteria because it would lead to EDCs which can severely affect human health not being identified or restricted.

This corresponds to Question 2.4.4 in the EU public consultation

Options for approaches to regulatory decision making

Should we change democratically agreed laws?

The EDC roadmap defines three different options for approaches to regulatory decision making: Option A (no changes of the existing provisions in BPR and PPPR); Option B (introduction of further elements of risk assessment) where necessary and desirable to reduce potential socio-economic impacts; and Option C (introduction of further socio-economic considerations) where necessary and desirable to prevent adverse socio-economic impacts.

This corresponds to Questions 3.1 and 3.2 in the EU public consultation

There are 2 technical questions for this Section, to which we advise the answer 'no'. If you exceptionally want to answer 'yes', please use the Commission website to directly submit your answers to the consultation.

- **No**, I have not conducted nor am I aware of an assessment applying any of the 3 different options for regulatory approaches to decision making (option A-C) to substances identified as endocrine disruptors by any of the options for defining criteria (option 1-4)?
- **No**, I have not conducted nor am I aware of an assessment of the socio-economic impact of the 3 different options for regulatory approaches to decision making (option A-C) for substances identified as endocrine disruptors by any of the options for defining criteria (option 1-4)?

If the consultation format would have allowed it, I would have shown my support for Option A, no regulatory changes.

What else needs to be done?

The solution in a nutshell

The only practical solution is committed regulatory action, by putting EU laws into practice, and improving and making new laws, to reduce all our exposures. Criteria which clearly identify all EDCs without a potency filter will enable the European Union (EU) to effectively address the threats of long-term health and environmental damage posed by EDCs.

EDCs are a threat to our society's current and future public health and prosperity. Europe should take a leading role in regulating EDCs, as this will stimulate innovation so that all industries in the various sectors develop and use better and safer alternatives. In this way, European industry can ensure its share of the growing world market for safer products and move to more sustainable production and sustainable agriculture.

I believe that this public consultation is not really for the public

The consultation is aimed at the concerns of certain industry sectors, and ignores important questions for citizens, society and companies interested in replacing EDCs with safer alternatives. For example, what will be the benefits of stricter controls for EDCs? How much will we save in terms of reduced health care costs? What are the business opportunities for innovative solutions?

I believe the micro and macro-economic, social, political and environmental benefits of reducing our exposure to EDCs should be included in impact assessments

The following reports and studies made an attempt to cost the benefits of stricter controls for EDCs and reduced human exposure. These should be integrated in the Commission's impact assessment:

- The cost of inaction – A socioeconomic analysis of costs linked to effects of endocrine disrupting substances on male reproductive health, Nordic Council report, November 2014
- Health costs in the EU - How much is related to EDCs, Health and Environment Alliance (HEAL), June 2014
- L. Trasande, Further Limiting Bisphenol A in Food Uses Could Provide Health and Economic Benefits, Health Affairs, January 2014

I believe regulatory option A, no change in the law, is the best way forward

I am opposed to the European Commission's proposed regulatory options B and C to make changes to established EU laws. These are unacceptable because they would undermine the democratically agreed rules in the EU pesticides law adopted by the elected European parliamentarians and national governments in 2009.

The EU pesticides and biocidal laws already contain provisions for exemptions so that no changes are necessary or useful.

I believe policy makers should act on the existing scientific evidence

Scientists have repeatedly voiced concerns about EDCs because it is likely that they are contributing to the dramatic increases of serious diseases and health disorders such as reproductive and fertility problems, breast, prostate and testicular cancers, effects on brain development and nervous system problems, and obesity and diabetes.

Recent biomonitoring studies from across Europe have shown that people in the general population are typically contaminated with several chemicals. Special care should be taken to reduce exposures before and during pregnancy, in early childhood and during puberty.

Many people come into contact with EDCs on a daily basis including from consumer products, indoor air, water, food or from the workplace. Wildlife is also suffering from exposure to hormone disrupters and impaired reproduction and development linked to EDCs has been reported in many species, including fish, birds, otters and even polar bears.

The following studies highlight the levels of certain chemicals in urine and hair, found several EDCs in children and their mothers.

- EU biomonitoring project
- M. Casas et al. Exposure to brominated flame retardants, perfluorinated compounds, phthalates and phenols in European birth cohorts. International Journal of Hygiene and Environmental Health 216 (2013) 230-242.
- O. Leino et al. Pollutant concentrations in placenta. Food and Chemical Toxicology 54 (2013) 59-69.

This corresponds to Question 4.1 – Provide any other data or information that could help the Commission to conduct its impact assessment in the EU public consultation

---

More information

EDC-Free Europe campaign

- EDC-Free Europe campaign website with information on EDCs and food, daily life, health, pregnancy and children and the workplace.
- EDC-Free Europe campaign call

Useful resources

- Endocrination: new film exposing lobby battle on EDCs by Stephane Horel – English and French
- Towards an EDC Free Europe: 5 minute video explaining where EDCs are found and why we are concerned by HEAL and PAN Europe
- Consumer Guide on EDCs from Pesticide Action Network
- Frequently Asked Questions on EDCs (CHEM Trust)
- New video by Corporate Europe Observatory "The corporate lobby tour"
- "State of the Science of EDCs" Report by the United Nations Environment Programme (UNEP) and World Health Organisation (WHO), June 2014
- European Commission page on EDCs

Other ways to take action:

- Take Action now for an EDC-Free Future! – EN – FR – ES – DE
- Is this disrupting me? photo gallery
- Petitions on EDCs
- Support the campaign as an individual or Organisation

9.3. Abbreviations

BPR	EU Biocidal Product Regulation (Regulation (EU) No 528/2012)
CLP	Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of substances and mixtures
CMR	Carcinogenic, Mutagenic or Toxic for Reproduction

EC	European Commission
ECHA	European Chemicals Agency
ED	Endocrine Disruptor
EDC	Endocrine Disrupting Chemical
EFSA	European Food Safety Authority
EU	European Union
FCM	Food Contact Material
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
In vitro	Experiments done outside living organisms
In vivo	Experiments in living organisms
In silico	Experiments performed on computer or via computer simulation
MoA	Mode of Action
MRL	Maximum Residue Limit
MS	Member State
NGO	Non-Governmental Organisation
NOEL	No Observed Effect Level
OECD	Organisation for Economic Co-operation and Development
PBT	Persistent, Bioaccumulative and Toxic
PPP	Plant Protection Product
PPPR	EU Plant Protection Product Regulation (Regulation (EC) No 1107/2009)
RA	Risk Assessment
REACH	Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemical
SME	Small and Medium Enterprises
SPS	Sanitary and Phytosanitary measures
WTO	World Trade Organization
vPvB	very Persistent and very Bioaccumulative