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COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 5 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
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ANNEX 5

CHEMICAL SUBSTANCES USED IN PPP OR BP, IDENTIFIED AS ENDOCRINE DISRUPTORS UNDER EACH OF THE 4 OPTIONS

Contents

The present screening was performed in the framework of a study contracted by the Commission and carried out in the context of an impact assessment to evaluate the impacts associated to options for criteria to identify endocrine disruptors under the regulations on plant protection products and biocidal products. The screening was based on available evidence (no additional testing) and needed to be carried out in a limited time. The screening methodology was developed for the purpose of the screening exercise. The results of the screening therefore do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

1. INTRODUCTION

An external contractor under supervision of the Joint Research Center (JRC), European Commission) screened the available evidence of approximately 600 chemicals (listed in Annex 4) with a method developed by the JRC and summarised in Annex 3. The screening started in May 2015 and sequentially covered active substances used in plant protection products (PPP) and biocidal products (BP), as well as a selection of substances falling under REACH Regulation, the cosmetic products Regulation and the Water Framework Directive (WFD).

The new criteria to identify endocrine disruptors (EDs) are requested by the legislation on PPP and BP and will be applicable to these two sectors. This is why this impact assessment (IA) focuses on these two sectors. However, it is acknowledged that the new criteria may also have repercussions on other EU legislation containing specific provisions regarding EDs (for example REACH and the WFD). Therefore, the screening is carried out also on a selection of substances falling under REACH Regulation, the Cosmetic Products Regulation and the WFD.

The work is expected to last until end of May 2016. Results for active substances used in PPP and BP were available by February 2016 and are reported below, while the screening of the chemicals falling under REACH, the cosmetics products Regulation and WFD was still on-going when this report was drafted.

The results for substances used in PPP and BP constitute the basis for this IA and give an estimation of which substances are expected to fall under each of the four options for the criteria to identify EDs, as outlined in the roadmap. The screening results do not substitute evaluations of individual substances to be carried out under the respective chemical legislations and do not pre-empt the regulatory conclusions that may eventually be drawn.

The contractor was selected following public procurement rules using the Framework Contract (FWC) SANCO/2012/02/011 (Specific Contract SANTE/2015/E3/001). The contractor is bound by conflict of interest and confidentiality rules.

The methodology, the results of the screening, and the contractor's details will be published once the screening is finalised, which is expected by end June 2016.

The results of the screening on PPP and BP were based on the extensive data sets available in the approval/renewal dossiers, plus several studies from the public scientific literature stored in EU and international databases. Most of these studies were considered in the screening. Due to time constraints, a minority of them (most from US-EPA EDSP and ToxCast ER model databases and some from EU EASIS database) could not be included in the screening by February 2016 and were therefore not considered in the results used for this IA. These additional data were anyhow considered in a refinement of the results that will be published in the final study report expected by end June 2016.

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

2. SCREENING RESULTS FOR ACTIVE SUBSTANCES USED IN PPP

A total of 324 active substances used as PPP were screened. The selection of the chemicals for the IA screening exercise is explained in Annex 4. As of January 1, 2016, there are 482 substances approved in the EU market; 147 fungicides, 123 herbicides, 98 insecticides, and 114 other type of pesticides (Figure 1).

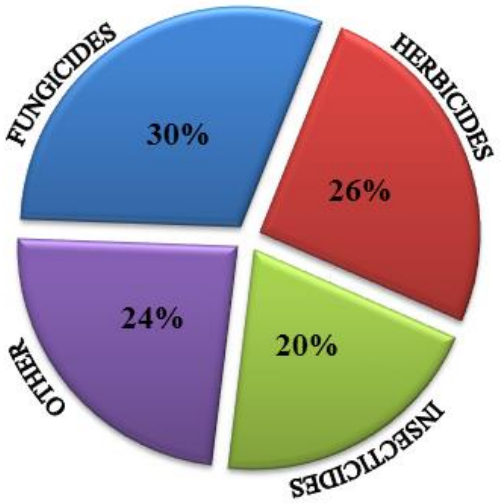

Figure 1. Approved active substances to be used in PPP in the EU, by 01/01/2016.

The screened active substances identified as potential EDs under each of the options are summarised in Figure 3 and listed in Table 2 (Option 1, Option 2, Option 3 Category I, Option 4). Table 3 also gives the chemical class according to Annex III in Regulation (EC) No 1185/2009 (Regulation on pesticides statistics)[1].

The results of the screening were filtered for other "cut off" criteria:

1. none of the substances identified as potential ED were classified or to be classified as M1 nor persistent in the environment. Substances persistent in the environment were identified using the results of the study reported in "Ad-hoc study to support the initial establishment of the list of candidates for substitution as required in Article 80(7) of Regulation (EC) No 1107/2009"[2] .

[1] Pesticides are generally divided into three broad groups; insecticides, herbicides and fungicides. To further refine the categorisation, pesticides can be divided into chemical classes, as done in Regulation EC No 1185/2009. This may be of importance if most or all substances within the same chemical class will be banned, because then the likelihood of finding an appropriate substitute to fight a certain pest decreases.

[2] Arcadia International (2013). Ad-hoc study to support the initial establishment of the list of candidates for substitution as required in Article 80(7) of Regulation (EC) No 1107/2009. Framework Contract for evaluation and evaluation related services - Lot 3: Food Chain. Final Report, retrieved from: http://ec.europa.eu/food/plant/pesticides/approval_active_substances/docs/cfs_final_report_072013_en.pdf.

2. substances which are classified or to be classified as C1, or R1 were flagged and excluded from the analysis of the impacts in the different policy areas (in particular agriculture and trade). In this way, substances which are already having regulatory consequences under Regulation (EC) No 1107/2009 under consideration of other "cut off" criteria are not double counted (Figure 2 and Table 3).

The screening of chemical substances used in PPP or BP resulted in the same number of active substances identified as potential EDs under Option 2 and Option 3 Category I, while the number of substances identified under Option 4 is a subset of these. Option 1 (interim criteria) identifies almost twice as many substances than Option 2 or Option 3 Category I, but only a small overlap (5 substances) exists between them, see table 2 for more details.

A total of 37 substances are identified under Option 1 as potential ED, but are not overlapping with the substances identified under Options 2, 3 Category I, or 4. Consequently they are considered to be **false positives** because they are identified as potential EDs under Option 1 without appearing to have ED properties according to Options 2, 3 and 4 (Table 1). This is because the approach followed for Option 1 and Options 2, 3 Category I, and 4 differ: while the interim criteria are based on potential categorisation of substances as suspected of being carcinogenic (C2) or suspected of being toxic for reproduction (R2), Options 2 to 4 are based on implementation of the WHO definition of EDs (adverse effects, mode of action and causal link).

The results also show that Option 1 (interim criteria) did not identify all active substances that were considered ED under Options 2, 3 Category I, or 4. These 21 substances are **false negatives** because substances identified as potential ED using the WHO definition are not identified under Option 1 (Table 1).

A graphic illustration of the overlap between the options can be seen in Figure 4. The figure shows that all substances identified by Option 4 represent a subset of the substances identified under Option 2 (equivalent to those under Option 3 Category I). It also clear that most of the substances identified under Option 1 do not overlap with those identified under Option 2, 3 Category I, and 4 (thus being either false negatives or false positives as explained above). Finally, all substances falling under the cut-off criteria overlap with substances under Option 1, while only a subset of them overlaps with substances under Option 2, 3 Cat I and 4.

Option 3 introduces the concept of additional categories, which would have no direct regulatory consequences. The substances identified under Option 3 Category I, Category II and Category III are reported in Table 4.

Additional information available on:
http://ec.europa.eu/food/plant/pesticides/approval_active_substances/index_en.htm

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

Table 1. False positive and false negatives identified for Option 1 by the screening.

	PPP	BP
False positives (identified under Option 1 but not under Options 2 to 4)	37	13
False negatives (identified under Options 2 to 4 but not under Option 1)	21	2

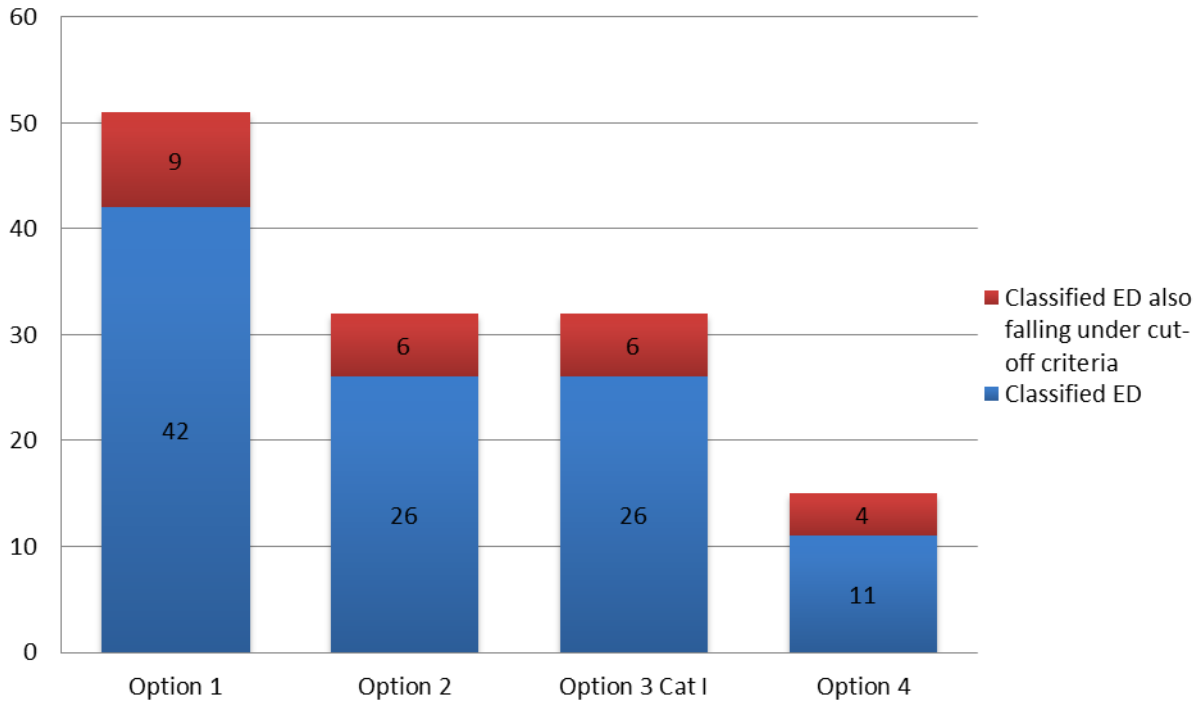

Figure 2. Number of active substances used in PPP identified as potential EDs under each of the four options: Option 1, Option 2, Option 3 Category I, Option 4. Substances identified as potential ED and also classified as C1 or R1 are reported separately in this figure.

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

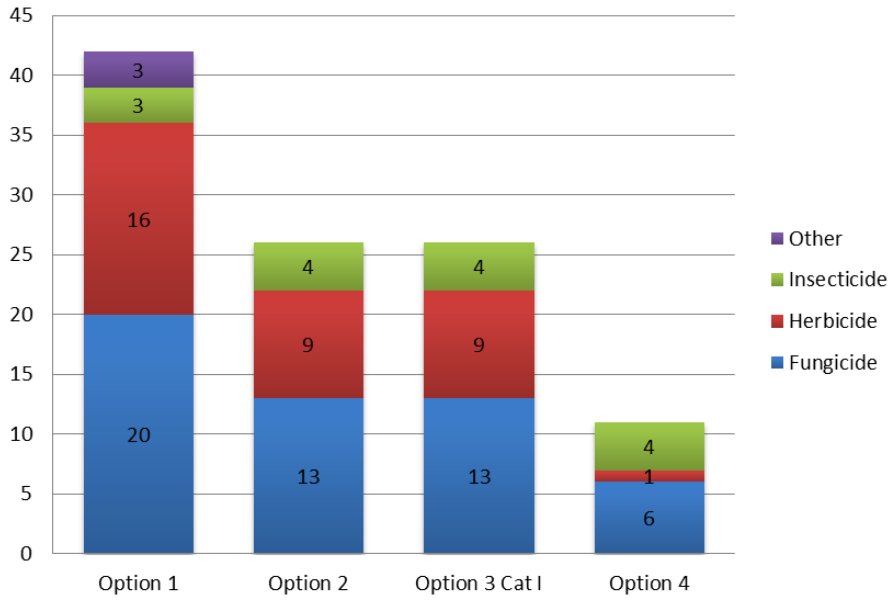

Figure 3. Number of substances classified as potential ED by PPP major group excluding substances that are classified as C1 or R1.

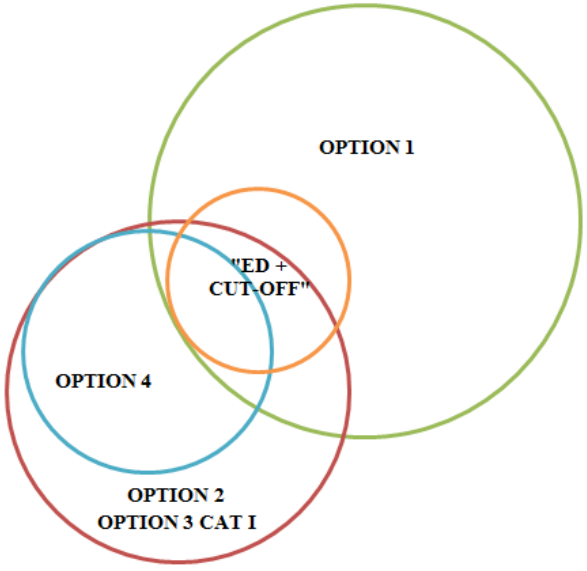

Figure 4. Overlap of active substances used as PPP screened in the framework of this IA and identified as potential ED under the four options: Option 1, Option 2, Option 3 Category I, and Option 4. The circle "ED + cut off" represents substances that are identified as potential ED and also classified as C1 or R1 and therefore falling under the cut-off criteria in the PPP Regulation.

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

Table 2. Active substances used in PPP identified as potential ED during the screening study (substances identified as potential ED and classified as C1 or R1 are excluded)

Option 1 (total 42)	Option 2 and Option 3 Cat I (total 26)	Option 4 (total 11)
1-Naphthylacetamide	2,4-D	8-hydroxyquinoline
1-Naphthylacetic acid	8-hydroxyquinoline	Cypermethrin
8-hydroxyquinoline	Boscalid	Fenamidone
Abamectin	Cypermethrin	Flubendiamide
Benthiavalicarb	Desmedipham	Malathion
Bromoxynil	Fenamidone	Mancozeb
Captan	Flubendiamide	Metiram
Chlorotoluron	Iprodione	Pendimethalin
Cycloxydim	Lenacil	Spirodiclofen
Cymoxanil	Malathion	Tetraconazole
Dazomet	Mancozeb	Ziram
Dimoxystrobin	Maneb	
Fenbuconazole	Metiram	
Fenpropimorph	Myclobutanil	
Fluazifop-P-butyl	Oxadiazon	
Fluazinam	Pendimethalin	
Flupyrsulfuron-methyl	Propyzamide	
Halosulfuron methyl	Spirodiclofen	
Hymexazol	Tebuconazole	
Indolylbutyric acid	Tepraloxydim	
Ipconazole	Tetraconazole	
Isoproturon	Thiophanate-methyl	
Isopyrazam	Thiram	
Isoxaflutole	Tralkoxydim	
Maneb	Triflusulfuron	
Metam	Ziram	
Metconazole		
Metribuzin		
Myclobutanil		
Prochloraz		
Profoxydim		
Prothioconazole		
Pymetrozine		
Quinoclamine		
Quizalfop-P		
Spirotetramat		
Spiroxamine		
Tebuconazole		
Tembotrione		
Tepraloxydim		
Thifensulfuron-methyl		
Triadimenol		

Table 3. Active substances used as PPP identified as potential EDs under each of the four options: Option 1, Option 2 and Option 3 Category I, Option 4. Substances that are classified as C1 or R1 are identified and reported in the column "ED + cut off".

Note: A cell containing a "1" indicates that the substance was identified as potential ED under the respective option. An empty cell indicates that the substance was NOT identified as ED under the respective option. False positives are substances identified under Option 1, but not under Option 2 and Option 3 Category I (e.g. Abamectin). False negatives are those substances identified under Option 2 and Option 3 Category I but not identified under Option 1 (e.g., Malathion).

	Substance	Option 1	Option 2 + Option 3 Cat I	Option 4	"ED + cut-off "	Chemical class
INSECTICIDE	**Abamectin**	**1**				INSECTICIDES PRODUCED BY FERMENTATION
	Malathion		**1**	**1**		ORGANOPHOSPHORUS INSECTICIDES
	Flubendiamide		**1**	**1**		PYRAZOLE (PHENYL-) INSECTICIDES
	Cypermethrin		**1**	**1**		PYRETHROID INSECTICIDES
	Pymetrozine (A)	**1**				PYRIDINE INSECTICIDES
	Thiacloprid	**1**			**1**	PYRIDYLMETHYLAMINE INSECTICIDES
	Spirodiclofen		**1**	**1**		TETRONIC ACID INSECTICIDES
	Spirotetramat	**1**				UNCLASSIFIED INSECTICIDES-ACARICIDES
FUNGICIDE	**Cymoxanil**	**1**				ALIPHATIC NITROGEN FUNGICIDES
	Boscalid		**1**			AMIDE FUNGICIDES
	Prochloraz	**1**				AMIDE FUNGICIDES
	Isopyrazam	**1**				ANILIDE FUNGICIDES
	Thiophanate-methyl		**1**			BENZIMIDAZOLE FUNGICIDES
	Benthiavalicarb	**1**				CARBAMATE FUNGICIDES
	Cyproconazole	**1**	**1**	**1**	**1**	CONAZOLE FUNGICIDES
	Epoxiconazole	**1**	**1**	**1**	**1**	CONAZOLE FUNGICIDES
	Fenbuconazole	**1**				CONAZOLE FUNGICIDES
	Ipconazole	**1**				CONAZOLE FUNGICIDES
	Metconazole	**1**				CONAZOLE FUNGICIDES
	Myclobutanil	**1**	**1**			CONAZOLE FUNGICIDES
	Prothioconazole	**1**				CONAZOLE FUNGICIDES
	Tebuconazole	**1**	**1**			CONAZOLE FUNGICIDES
	Tetraconazole		**1**	**1**		CONAZOLE FUNGICIDES
	Triadimenol	**1**				CONAZOLE FUNGICIDES
	Triflumizole	**1**	**1**	**1**	**1**	CONAZOLE FUNGICIDES
	Iprodione		**1**			DICARBOXIMIDE FUNGICIDES
	Fluazinam	**1**				DINITROANILINE FUNGICIDES
	Mancozeb		**1**	**1**		DITHIOCARBAMATE FUNGICIDES
	Maneb	**1**	**1**			DITHIOCARBAMATE FUNGICIDES
	Metiram		**1**	**1**		DITHIOCARBAMATE FUNGICIDES
	Thiram		**1**			DITHIOCARBAMATE FUNGICIDES
	Ziram		**1**	**1**		DITHIOCARBAMATE FUNGICIDES
	Fenamidone		**1**	**1**		IMIDAZOLE FUNGICIDES
	Fenpropimorph	**1**				MORPHOLINE FUNGICIDES
	Metam	**1**				OTHER SOIL STERILANTS
	Hymexazol	**1**				OXAZOLE FUNGICIDES

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

	Substance	Option 1	Option 2 + Option 3 Cat I	Option 4	"ED + cut-off "	Chemical class
	Captan	**1**				PHTHALIMIDE FUNGICIDES
	8-hydroxyquinoline	**1**	**1**	**1**		QUINOLINE FUNGICIDES
	Dimoxystrobin	**1**				STROBILURINE FUNGICIDES
	Spiroxamine	**1**				UNCLASSIFIED FUNGICIDES
HERBICIDE	**Propyzamide**		**1**			AMIDE HERBICIDES
	Halosulfuron methyl	**1**				ANILIDE HERBICIDES
	Fluazifop-P-butyl	**1**				ARYLOXYPHENOXY- PROPIONIC HERBICIDES
	Quizalofop	**1**				ARYLOXYPHENOXY- PROPIONIC HERBICIDES
	Desmedipham		**1**			BIS-CARBAMATE HERBICIDES
	Carbetamide	**1**			**1**	CARBAMATE HERBICIDES
	Cycloxydim	**1**				CYCLOHEXANEDIONE HERBICIDES
	Tepraloxydim**	**1**	**1**			CYCLOHEXANEDIONE HERBICIDES
	Tralkoxydim		**1**			CYCLOHEXANEDIONE HERBICIDES
	Pendimethalin		**1**	**1**		DINITROANILINE HERBICIDES
	Profoxydim	**1**				DINITROANILINE HERBICIDES
	Isoxaflutole	**1**				ISOXAZOLE HERBICIDES
	Bromoxynil	**1**				NITRILE HERBICIDES
	Dazomet	**1**				OTHER SOIL STERILANTS
	2,4-D		**1**			PHENOXY HERBICIDES
	Flupyrsulfuron-methyl	**1**				SULFONYLUREA HERBICIDES
	Thifensulfuron-methyl	**1**				SULFONYLUREA HERBICIDES
	Triflusulfuron		**1**			SULFONYLUREA HERBICIDES
	Metribuzin	**1**				TRIAZINONE HERBICIDES
	Amitrole	**1**	**1**	**1**	**1**	TRIAZOLE HERBICIDES
	Tembotrione	**1**				TRIKETONE HERBICIDES
	Flurochloridone	**1**	**1**		**1**	UNCLASSIFIED HERBICIDES
	Oxadiazon		**1**			UNCLASSIFIED HERBICIDES
	Quinoclamine	**1**				UNCLASSIFIED HERBICIDES
	Lenacil		**1**			URACIL HERBICIDES
	Isoproturon	**1**				UREA HERBICIDES
	Linuron	**1**	**1**		**1**	UREA HERBICIDES
	Chlorotoluron	**1**				UREA HERBICIDES
OTHER	**1-Naphthylacetamide**	**1**				OTHER PHYSIOLOGICAL PLANT GROWTH REGULATORS
	1-Naphthylacetic acid	**1**				OTHER PHYSIOLOGICAL PLANT GROWTH REGULATORS
	Indolylbutyric acid	**1**				OTHER PHYSIOLOGICAL PLANT GROWTH REGULATORS
	Difenacoum	**1**			**1**	RODENTICIDES

** Tepraloxydim non-approved on the 31/05/2015

Table 4. Active substances used in PPP identified under each of the categories of Option 3 during the screening of substances (substances identified under Category I, II, or III and also classified as C1 or R1, or persistent are included in the table and flagged with an asterisk).

Cat I (32)	Cat II (84)		Cat III (46)
2,4-D	1-Naphthylacetamide	Ipconazole	Azoxystrobin
8-Hydroxyquinoline	1-Naphthylacetic acid	Isoproturon	Benfluralin
Amitrole*	2,4-DB	Isoxaflutole	Beta-Cyfluthrin
Boscalid	Abamectin	lambda-Cyhalothrin	Bifenox
Cypermethrin	Acrinathrin	Meptyldinocap	Bupirimate
Cyproconazole*	Azadirachtin	Metaldehyde	Captan
Desmedipham	Azimsulfuron	Metazachlor	Carfentrazone-ethyl
Epoxiconazole*	Benthiavalicarb	Methoxyfenozide	Chlorpyrifos
Fenamidone	Bifenthrin	Oryzalin	Clofentezine
Flubendiamide	Bixafen	Oxasulfuron	Clomazone
Flurochloridone*	Bromoxynil	Paclobutrazol	Cyazofamid
Iprodione	Bromuconazole	Penflufen	Cyhalofop-butyl
Lenacil	Buprofezin	Penthiopyrad	Cyprodinil
Linuron*	Carbetamide	Pethoxamid	Daminozide
Malathion	Carboxin	Phenmedipham	Difenoconazole
Mancozeb	Chlorothalonil	Picolinafen	Diuron
Maneb	Chlorpropham	Prochloraz	Etofenprox
Metiram	Chlorpyrifos-methyl	Profoxydim	Famoxadone
Myclobutanil	Chlorsulfuron	Prohexadione	Fenoxaprop-P
Oxadiazon	Clethodim	Propaquizafop	Fenoxycarb
Pendimethalin	Clodinafop	Propiconazole	Fludioxonil
Propyzamide	Clothianidin	Propineb	Flumioxazin*
Spirodiclofen	Cycloxydim	Proquinazid	Fluoxastrobin
Tebuconazole	Cyflumetofen	Prosulfuron	Fluroxypyr
Tepraloxydim	Cymoxanil	Prothioconazole	Flutolanil
Tetraconazole	Dazomet	Pymetrozine	Folpet
Thiophanate-methyl	Deltamethrin	Pyraflufen-ethyl	Forchlorfenuron
Thiram	Dicamba	Pyridaben	Haloxyfop-P
Tralkoxydim	Diclofop	Pyridalyl	Hexythiazox
Triflumizole*	Diethofencarb	Pyriproxyfen	Imazalil
Triflusulfuron	Difenacoum*	Quizalofop-P-ethyl	Imidacloprid
Ziram	Diflufenican	Quizalofop-P-tefuryl	Isoxaben
	Dimethoate	Rimsulfuron	MCPA
	Dimethomorph	Sedaxane	MCPB
	Esfenvalerate	Silthiofam	Mecoprop
	Etoxazole	Spiromesifen	Mecoprop-P
	Etridiazole	Spirotetramat	Methyl octanoate
	Fenazaquin	Spiroxamine	Oxamyl
	Fenbuconazole	Tembotrione	Oxyfluorfen
	Fenhexamid	Terbuthylazine	Penconazole
	Fipronil	Thiabendazole	Phosmet
	Flonicamid	Thiacloprid*	Picoxystrobin
	Fluazifop-P	Thiamethoxam	Pirimiphos-methyl
	Fluazinam	Thifensulfuron-methyl	Propamocarb
	Flufenacet	Triadimenol	Pyraclostrobin
	Glyphosate	Triticonazole	Pyrimethanil
	Hymexazol	Tritosulfuron	tau-Fluvalinate
	Indolylbutyric acid	Valifenalate	Tefluthrin
			Tolclofos-methyl
			Tribenuron
			Trifloxystrobin
			Zoxamide

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

3. SCREENING RESULTS FOR ACTIVE SUBSTANCES USED IN BP

A total of 98 active substances contained in BP or used in treated articles were screened. Only the substances of which sufficient information was available, i.e. active substances that were approved at EU level or where an opinion of the BP Committee of ECHA was available, were screened.

Active substances and BP are approved or authorised for 22 product types. Therefore the total number of active substances per product type is of relevance. In total 700 active substance and product type combinations are approved or under review of which 266, 320, 95 and 19 for disinfectants, preservatives, pest control, and other, respectively.

A significant number of these active subsatnces is currently under review. In this review programme the existing active substances that were on the market on 14 May 2000, and are supported by companies, are included. These substances will be assessed in the review programme and, if they fulfill the required conditions, approved in accordance with a working schedule linked to groups of product types. Each year, up to 2024, about 50 dossiers will be examined.

The number and type of substances screened is directly linked to the set up of the review working programme. This implies that the screening is not representative for the active substances/product types distribution currently available on the market. For example, only 17% of the active substances used in disinfectants are screened in comparison with 52% of the pest control substances (see Figure 5). This is caused by the priority given for pest control substances in the review programme of active substances. Therefore, any result of the screening should be very cautiously interpreted for the potential impact on all product types on the market as it is not possible to judge how representative the screening results are within and across the product groups.

The screened substances identified as potential EDs under each of the options are listed in Table 5 (Option 1, Option 2 and Option 3 Category I, and Option 4).

Substances identified as potential ED under each of the options considered for the screening may also fall under the so called "cut-off criteria" mentioned in Section 2 of this Annex[3], or fulfilling the exclusion criteria (Article 5(1) of the BP Regulation[4]). The substances fulfilling these criteria are listed in Table 6; in the same table the substances identified as potential EDs and being used in both PPP and BP are also indicated.

[3] This refers to the substances also approved for use in PPP.

[4] Article 5(1) of BP Regulation: CMR, PBT, vPvB or having endocrine-disrupting properties (C=carcinogen category 1A or 1B; M= mutagen category 1A or 1B; R=toxic for reproduction category 1A or 1B; substances meet the criteria for being Persistent Bioaccumulative and Toxic or very Persistent and very Biocaccumulative according to Annex XIII to Regulation (EC) No 1907/2006).

Option 3 introduces the concept of additional categories. The substances identified under Option 3 in the Category I, Category II and Category III are reported in Table 6. For Categories I, II and III, 5, 26 and 8 substances were identified respectively.

In total 16 biocidal substances were identified as potential ED under Option 1, five substances under Option 2 and 3 Category I, and three substances under Option 4. The number of false positives and false negatives show the same trend for BP as for PPP. A total of 13 substances are identified under Option 1 for BP but not under Option 2 and 3 Cat I (false positives). The interim criteria failed to identify two substances that have endocrine modes of actions (false negatives) that were identified as potential EDs under Option 2 and 3 Cat I.

From Table 6 it becomes clear that of the substances identified as potential ED under Option 2, Option 3 Category I and Option 4, one (Cyproconazole) is currently fulfilling the exclusion criteria. However, taking into account the screening cannot be considered representative for the active substances/product types currently available on the market, it is challenging to extrapolate this result to all BP substances.

Further, iodine (used as disinfectant) is identified as potential ED under Options 2 and 3 Category I. Iodine is a physiologically essential element and needed for maintaining hormone homeostasis. It is required for the synthesis of the thyroid hormones, which control metabolism and play an important role in reproduction, growth and development. This means that both iodine deficiency as well as excess iodine can affect thyroid hormone levels and is to be considered as an endocrine effect. However, as essential element it differs from typical xenobiotic substances, which are not needed for the functioning of the human or animal body. ECHA stated in the assessment report[5] on iodine that the concept of endocrine disruption is not meaningful for essential elements as iodine.

[5] Assessment report on iodine, available on the section of ECHA website providing information on biocidal active substances: http://echa.europa.eu/web/guest/information-on-chemicals/biocidal-active-substances.

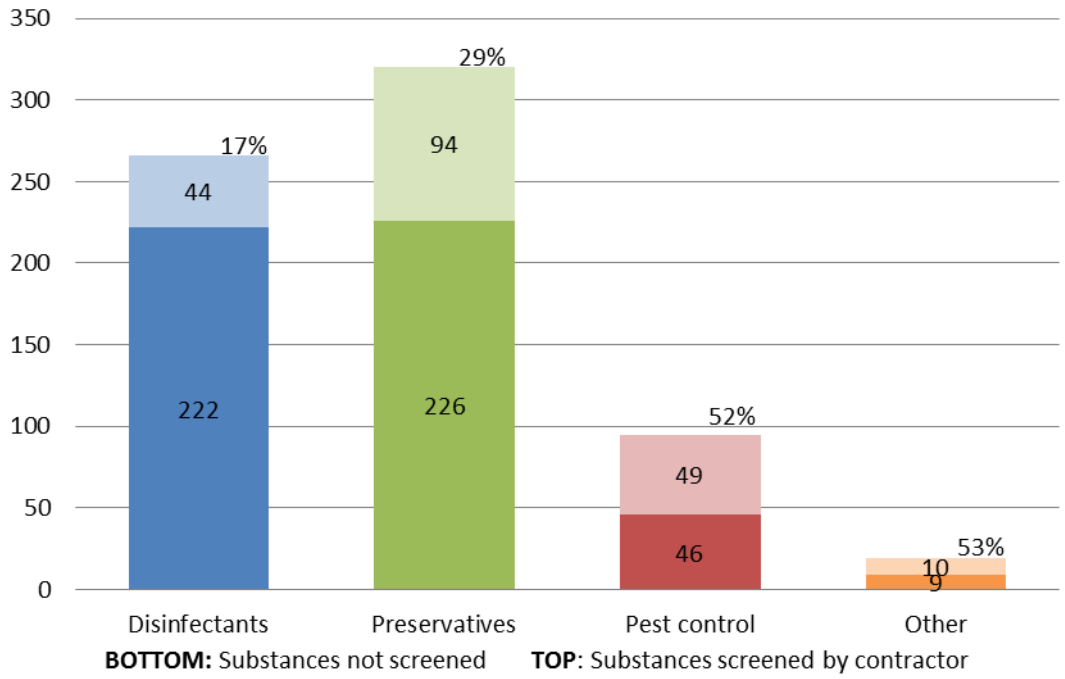

Figure 5. Number of biocidal active substances arranged by major group of product types, included (bottom) and not included (top) in the screening.

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

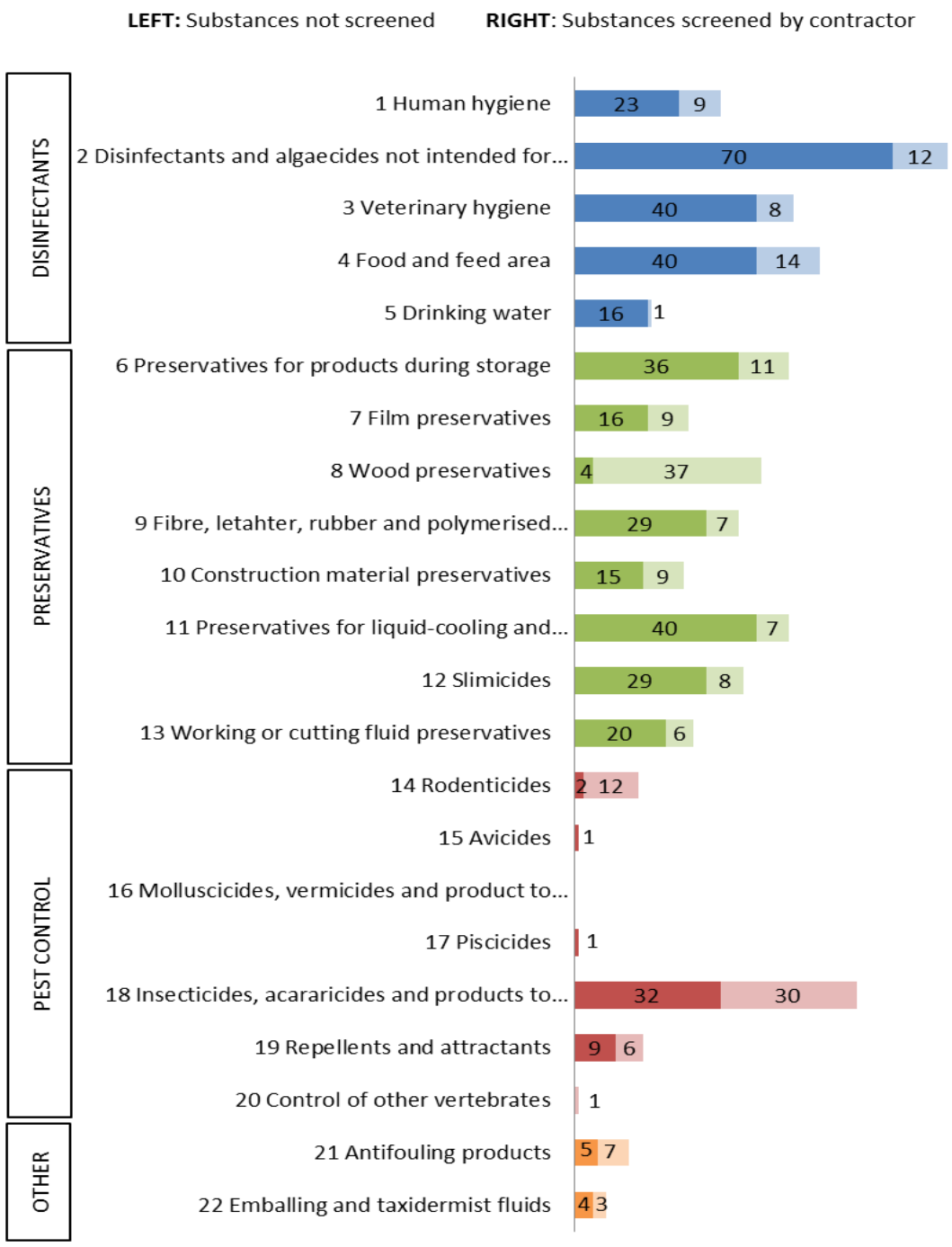

Figure 6. Number of biocidal active substances arranged by product type included and not included in the screening.

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

Table 5. Biocidal active substances identified under Options 1, Option 2 and 3 Cat I, and Option 4 as potential EDs.

Option 1 (16)	Option 2 and Option 3 Cat I (5)	Option 4 (2)
Abamectin (aka avermectin)	Cypermethrin	Cypermethrin
Boric acid	Cyproconazole	Cyproconazole
Boric oxide	Iodine	Zineb
Copper pyrithione	Tebuconazole	
Creosote	Zineb	
Cyproconazole		
Dazomet		
Difenacoum		
Disodium octaborate tetrahydrate		
Disodium tetraborate		
Disodium tetraborate decahydrate		
Disodium tetraborate pentahydrate		
Fenpropimorph		
Tebuconazole		
Thiacloprid		
Zineb		

Table 6. Biocidal active substances identified as potential EDs under the three categories of Option 3.

Option 3 Cat I (5)	Option 3 Cat II (26)	Option 3 Cat III (8)
Cypermethrin	4,5-Dichloro-2-octylisothiazol-3(2H)-one	1R-trans phenothrin
Cyproconazole	Abamectin (aka avermectin)	Chlorophacinone
Iodine	Bifenthrin	DDACarbonate
Tebuconazole	Boric acid	Didecyldimethylammonium chloride; DDAC
Zineb	Boric oxide	Etofenprox
	Clothianidin	Fenoxycarb
	Copper pyrithione	Folpet
	Dazomet	Imidacloprid
	DCPP	
	Deltamethrin	
	Dichlofluanid	
	Difenacoum	
	Disodium octaborate tetrahydrate	
	Disodium tetraborate	
	Disodium tetraborate decahydrate	
	Disodium tetraborate pentahydrate	
	Fipronil	
	Glutaraldehyde	
	Hydrogen cyanide	
	Lambda-Cyhalothrin	
	Permethrin	
	Propan-2-ol	
	Propiconazole	
	Pyriproxyfen	
	Thiabendazole	
	Thiamethoxam	

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

Table 7. Biocidal active substances identified as potential EDs under option 1, option 2 and option 3 Cat I, and option 4 and the associated product types.

Note: A cell containing a "1" indicates that the substance was identified as potential ED under the respective option. An empty cell indicates that the substance was NOT identified as potential ED under the respective option. False positives are substances identified under Option 1, but not under Option 2 and Option 3 Category I (e.g. Abamectin). False negatives are those substances identified under Option 2 and Option 3 Category I but not identified under Option 1 (e.g., Malathion).

	Substance	Option 1	Option 2 and Option 3 Cat I	Option 4	Cut-off PPP	BP Exclusion criteria	Product Type No	Main group of product types
BIOCIDES AND PESTICIDES	Abamectin (aka avermectin)	1					18	PEST CONTROL
	Cypermethrin		1	1			8; 18	PRESERVATIVES; PEST CONTROL
	Cyproconazole	1	1	1	1	1	8	PRESERVATIVES
	Dazomet	1					6; 8; 12	PRESERVATIVES
	Difenacoum	1			1	1	14	PEST CONTROL
	Fenpropimorph	1					8	PRESERVATIVES
	Tebuconazole	1	1				7; 8; 10	PRESERVATIVES
	Thiacloprid	1			1	1	8	PRESERVATIVES
BIOCIDES	Boric acid	1				1	8	PRESERVATIVES
	Boric oxide	1				1	8	PRESERVATIVES
	Copper pyrithione	1					21	OTHER BIOCIDAL PRODUCTS
	Creosote	1				1	8	PRESERVATIVES
	Disodium octaborate tetrahydrate	1				1	8	PRESERVATIVES
	Disodium tetraborate	1				1	8	PRESERVATIVES
	Disodium tetraborate decahydrate	1				1	8	PRESERVATIVES
	Disodium tetraborate pentahydrate	1				1	8	PRESERVATIVES
	Iodine		1				1; 3; 4; 22	DISINFECTANTS. OTHER
	Zineb	1	1	1			21	OTHER BIOCIDAL PRODUCTS
	TOTAL	**16**	**5**	**3**	**3**	**10**		

Table 8. Biocidal active substances identified as potential EDs under the three categories of Option 3, the associated product types, the applicability of cut-off values for PPP and the exclusion[6] as included in BP Regulation[7].

	Substance	Option 3 Cat I	Option 3 Cat II	Option 3 Cat III	Cut-off PPP	BP Exclusion criteria	Product Type No	Main group
BIOCIDES AND PESTICIDES	Abamectin (aka avermectin)		1				18	PEST CONTROL
	Bifenthrin		1				8	PRESERVATIVES
	Clothianidin		1				8; 18	PRESERVATIVES; PEST CONTROL
	Cypermethrin	1					8; 18	PRESERVATIVES; PEST CONTROL
	Cyproconazole	1			1	1	8	PRESERVATIVES
	Dazomet		1				6; 8; 12	PRESERVATIVES
	Deltamethrin		1				18	PEST CONTROL
	Difenacoum		1		1	1	14	PEST CONTROL
	Etofenprox			1			8; 18	PRESERVATIVES; PEST CONTROL
	Fenoxycarb			1			8	PRESERVATIVES
	Fipronil		1				18	PEST CONTROL
	Folpet			1			6; 7; 9	PRESERVATIVES
	Imidacloprid			1			18	PEST CONTROL
	Lambda-Cyhalothrin		1				18	PEST CONTROL
	Propiconazole		1				7; 8; 9	PRESERVATIVES
	Pyriproxyfen		1				18	PEST CONTROL
	Tebuconazole	1					7; 8; 10	PRESERVATIVES
	Thiabendazole		1		1		7; 8; 9; 10	PRESERVATIVES
	Thiamethoxam		1				8,18	PRESERVATIVES; PEST CONTROL

[6] Article 5 of BP Regulation: CMR, PBT, vPvB or ED (C=carcinogen Category IA or 1B; M= mutagen category 1A or 1B; R=toxic for reproduction category 1A or 1B; Persistent Bioaccumulative Toxic or vPvB according to Annex XIII to Regulation (EC) No 1907/2006).

[7] In addition to exclusion criteria the BP Regulation provides that active substances should be designated as candidate for substitution if they have intrinsic hazardous properties. Article 10(1) of the BP Regulation stipulates the criteria for designating a substance as a candidate for substitution

	Substance	Option 3 Cat I	Option 3 Cat II	Option 3 Cat III	Cut-off PPP	BP Exclusion criteria	Product Type No	Main group
BIOCIDES	1R-trans phenothrin			1			18	PEST CONTROL
	4,5-Dichloro-2-octylisothiazol-3(2H)-one (DCOIT)		1				7; 8; 9; 10; 11; 21	PRESERVATIVES; OTHER BIOCIDAL PRODUCTS
	Boric acid		1			1	8	PRESERVATIVES
	Boric oxide		1			1	8	PRESERVATIVES
	Chlorophacinone			1		1	14	PEST CONTROL
	Copper pyrithione		1				21	OTHER BIOCIDAL PRODUCTS
	DCPP		1				1; 2; 4	DISINFECTANTS
	DDACarbonate			1			8	PRESERVATIVES
	Dichlofluanid		1				7; 8; 21	PRESERVATIVES; OTHER BIOCIDAL PRODUCTS
	Didecyldimethylammonium chloride; DDAC			1			1; 2; 3; 4; 6; 8; 10; 11; 12	PRESERVATIVES; DISINFECTANTS
	Disodium octaborate tetrahydrate		1			1	8	PRESERVATIVES
	Disodium tetraborate		1			1	8	PRESERVATIVES
	Disodium tetraborate decahydrate		1			1	8	PRESERVATIVES
	Disodium tetraborate pentahydrate		1			1	8	PRESERVATIVES
	Glutaraldehyde		1				1; 2; 3; 4; 6; 11; 12; 13	DISINFECTANTS; PRESERVATIVES
	Hydrogen cyanide		1				8; 14; 18	PRESERVATIVES; PEST CONTROL
	Iodine	1					1; 3; 4; 22	DISINFECTANTS. OTHER
	Permethrin		1				8; 18	PRESERVATIVES; PEST CONTROL
	Propan-2-ol		1				1; 2; 4	DISINFECTANTS
	Zineb	1					21	OTHER BIOCIDAL PRODUCTS
	TOTAL	**5**	**26**	**8**	**3**	**9**		

4. CONCLUSIONS

The results presented in this Annex show that it was possible to screen the evidence available for PPP and BP chemicals with the aim to estimate which substances would fall under different options for the criteria to identify EDs.[8] This was possible not only for Option 1 (interim criteria under PPP and BP legislation), but also for the other three options which are based on the WHO definition (Options 2, 3 and 4). This means that it is possible to use scientific evidence available on EDs (test methods and results) and interpret it for an estimate on whether they may be identified as EDs.

Criteria under options 2, 3 and 4 are based on the widely agreed WHO/IPCS definition of an ED[9]. The WHO/IPCS definition is characterised by three elements: a chemical can be defined an ED; 1) if it shows an adverse effect in an intact organism (generally from in vivo animal testing); 2) if it is able to interfere with the endocrine/hormonal system (mechanistic data show the substance can act via an endocrine/hormonal mode of action); and 3) if a plausible link can be established between the endocrine mode of action and the adverse effect observed for the substance.

OECD test methods are available for four of the various endocrine modalities: the androgen (A), the oestrogen (E), the thyroid (T) and the (S) steroidogenesis modalities (often referred to as EATS modalities) (OECD 2012[10]; EFSA 2013[11]). Therefore, the present screening was limited to the available evidence related to modes of actions along these four modalities (see also Annex 3).[12] Similarly, the evidence available could only be assessed for vertebrate wildlife species, because the endocrine system of invertebrates is not well understood and test capable of discriminating adverse effects by an endocrine mode of action are not yet available.

[8] The screening study also includes screening of substances falling under REACH, Cosmetics Regulation, or Water Framework Directive (see Annex 4). The results of the screening of these substances were neither available nor relevant in the context of this impact assessment report. They will be available once the report of the screening study will be published.

[9] WHO/IPCS. 2002. Definition of an Endocrine Disruptor: 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.

[10] OECD Guidance Document On Standardised Test Guidelines For Evaluating Chemicals For Endocrine Disruption Series on Testing and Assessment No. 150, ENV/JM/MONO(2012)22. Retrieved from: http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2012)22&doclanguage=en

[11] EFSA Scientific Committee; Scientific Opinion on the hazard assessment of endocrine disruptors: scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment. EFSA Journal 2013;11(3):31323. doi: 10.2903/j.efsa.2013.3132.

[12] A detailed description of the methodology applied in the screening will be published at the same time the Commission would propose draft measures to specify scientific criteria for the determination of endocrine-disrupting properties.

OECD Guidance[13] was used to interpret results on adverse effect and mechanistic data related to endocrine disruption. A decision tree based on information taken from the OECD GD 150[9] was used to decide whether or not enough evidence is available to categorise a substance as a potential ED (and if relevant as ED Cat I, II or III). In addition, as mentioned in Annex 3 to this Report - where the methodology applied to this screening is described - a limited weight of evidence approach based on expert judgement was necessary to evaluate the evidence available and ultimately decide whether or not a substance can be identified as a potential ED (or, if relevant, as potential ED Category II or III under Option 3). It is stressed that the weight of evidence approach could only be used to a limited extent compared to standard regulatory assessment because of the time constraints and the level of expertise of the present project.

This limited weight of evidence approach used was based, among others, on the following considerations:

a) the magnitude and nature of the adverse effects;

b) the pattern and coherence of adverse effects observed at different doses within and between studies of a similar design and across different species;

c) the weight of certain studies with respect to others: e.g. long term/chronic/repeated-dose studies versus short term/acute studies; *in vivo* tests versus *in vitro* tests; studies with clear study-design versus poorly detailed studies;

d) the biological plausibility of a causal relationship between the induced endocrine activity and the adverse effect(s);

e) the presence of overt toxicity together with the potential ED-related effects;

f) the data available on the human relevance of the effects and mode of action observed.

Thus, for instance, an isolated effect of low magnitude in one species not observed in other studies of similar design with the same species (provided the effect had been measured) would have lower weight than a case where a clear pattern of effects was seen across a number of studies and in more than one species. As this largely depends on expert judgement, this part could not be codified into the decision tree. When potential ED-related effects were observed in the presence of overt toxicity, these effects were not considered to be informative of an endocrine mode of action.

As mentioned above, some additional data could only be considered at a late stage of the screening and could therefore not be included in the results used for the IA. These additional data may refine to a limited extent the final results, in that a few substances have changed categorisation: some became identified as potential EDs, while they were

[13] OECD Work Related to Endocrine Disrupters, available on: http://www.oecd.org/env/ehs/testing/oecdworkrelatedtoendocrinedisrupters.htm

not before; others became unclassified or potential EDs Cat II or III, while they were potential EDs Cat I before. For instance, using new data from EDSP/EASIS databases and/or from the ToxCast ER prediction model, the following substances were identified as potential EDs under Option 2 and 3 Category I: flutolanil, prochloraz, pyriproxyfen, 2-phenylphenol, propiconazole, metalaxyl. For prochloraz the categorisation is elevated because of data relevant for both human health and wildlife, while for the other five substances the updated categorisation is related to data relevant for wildlife only (fish/amphibian) data. The refined results will be published in the final report of the screening, which is expected to be published by end June 2016.

The fact that additional data can affect the outcome of the screening shows how availability of experimental data can influence the conclusions with respect to the identification of a substance as an ED. To this respect, PPP and BP are based on pre-market approval ("positive list") which relies on data-rich dossiers. This pre-market approval system described above is considered as one of the strictest worldwide and the data requirements are very detailed and require extensive in vivo testing.

On the other hand, in the relatively new field of endocrine disruption, test methods to detect an endocrine mode of action have been recently developed. When these test methods are internationally validated (e.g.at OECD level), the data requirements for PPP[14] and BP[15] are updated. Studies from the public literature can provide additional weight to the body of evidence.

The screening results for PPP and BP provided in this IA - together with those refined in the final screening report to be published by end June 2016 - have a degree of uncertainty associated to any assessment in a complex field like the one of endocrine disruption. This uncertainty is determined by several factors, including the expert judgement involved in each decision, the availability of scientific evidence on the various chemicals, the developments in test methods and guidance to interpret their results.

[14] European Commission, DG SANTE. EU Legislation on PPP, available on: http://ec.europa.eu/food/plant/pesticides/legislation/index_en.htm

[15] ECHA Guidance on biocides legislation, available on: http://echa.europa.eu/guidance-documents/guidance-on-biocides-legislation

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.