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PART 6/16

**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}  
{SWD(2016) 212 final}

## ANNEX 5

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

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*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 prejudice 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

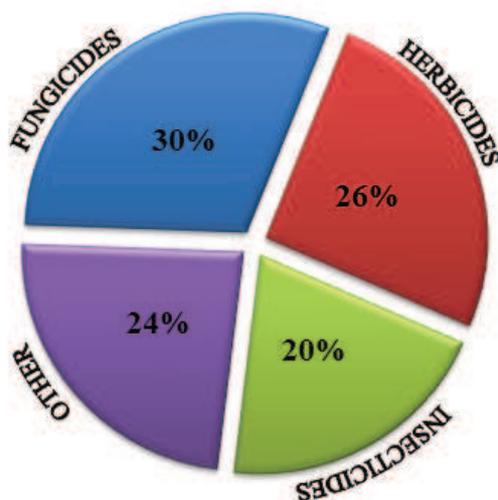
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additional data were anyhow considered in a refinement of the results that will be published in the final study report expected by end June 2016.

## 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)<sup>1</sup>.

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

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<sup>1</sup> 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.

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establishment of the list of candidates for substitution as required in Article 80(7) of Regulation (EC) No 1107/2009"<sup>2</sup>.

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.

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<sup>2</sup> 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](http://ec.europa.eu/food/plant/pesticides/approval_active_substances/docs/cfs_final_report_072013_en.pdf).

Additional information available on:

[http://ec.europa.eu/food/plant/pesticides/approval\\_active\\_substances/index\\_en.htm](http://ec.europa.eu/food/plant/pesticides/approval_active_substances/index_en.htm)

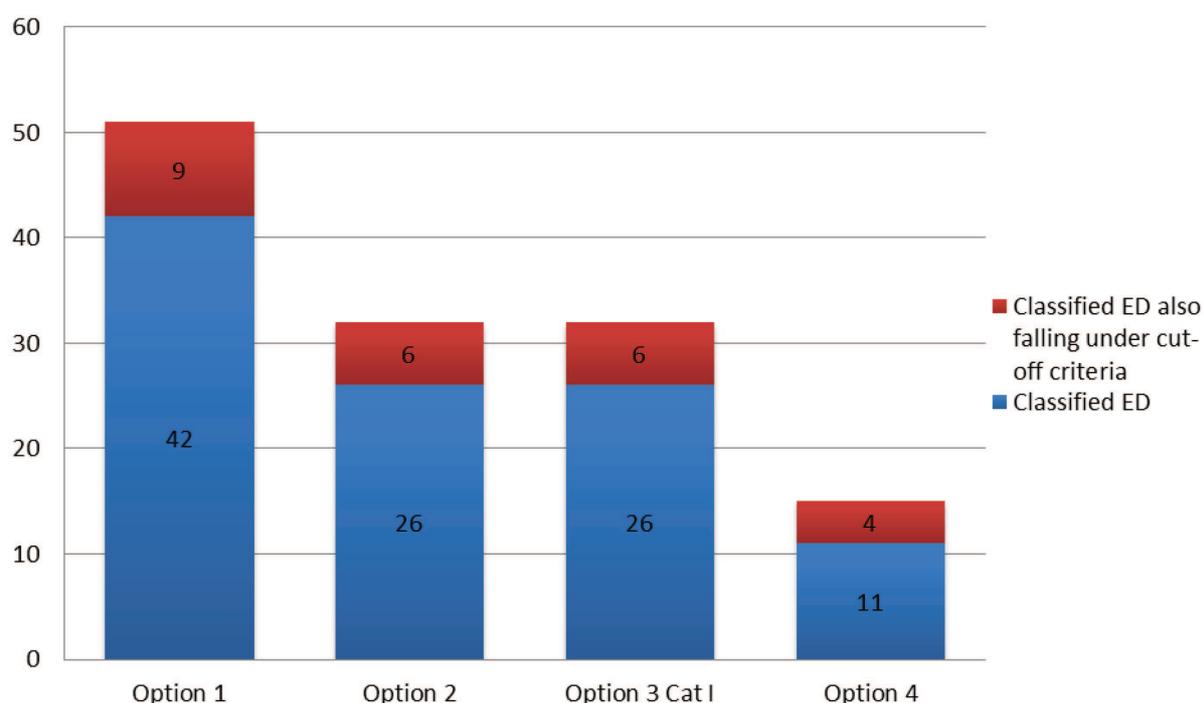
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Option 3 introduces the concept of additional categories, which would have no direct regulatory consequences. The substances identified under Option 3 Category I, Category II and Category III are reported in Table 4.

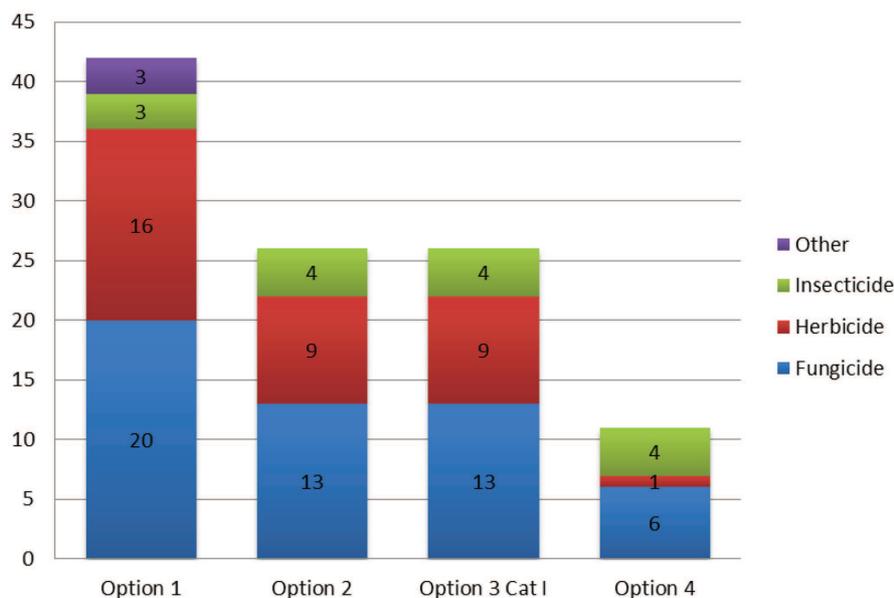
**Table 1. False positive and false negatives identified for Option 1 by the screening.**

|  | PPP | BP |
|--|-----|----|
| <b>False positives</b><br>(identified under Option 1 but not under Options 2 to 4) | 37  | 13 |
| <b>False negatives</b><br>(identified under Options 2 to 4 but not under Option 1) | 21  | 2  |

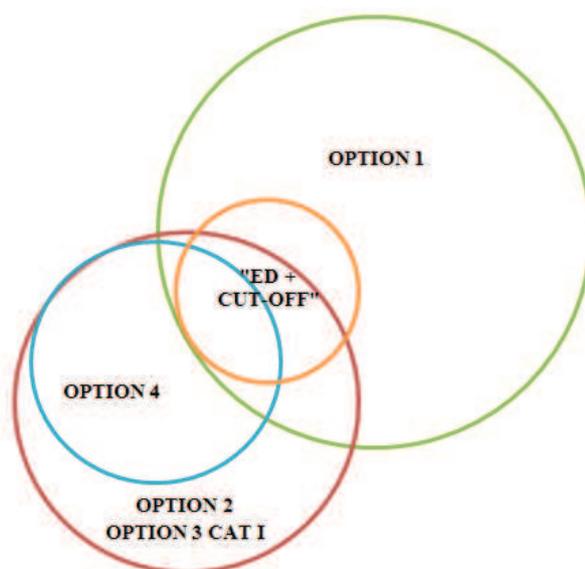


**Figure 2. Number of active substances used in PPP identified as potential EDs under each of the four options: Option 1, Option 2, Option 3 Category I, Option 4. Substances identified as potential ED and also classified as C1 or R1 are reported separately in this figure.**

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**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.**

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**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)**

| <b>Option 1<br/>(total 42)</b> | <b>Option 2 and Option 3 Cat I<br/>(total 26)</b> | <b>Option 4<br/>(total 11)</b> |
|--------------------------------|---|--------------------------------|
| 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            | Tepraloxymid                                      |                                |
| Ipconazole                     | Tetraconazole                                     |                                |
| Isoproturon                    | Thiophanate-methyl                                |                                |
| Isopyrazam                     | Thiram  |                                |
| Isoxaflutole                   | Tralkoxydim                                       |                                |
| Maneb                          | Triflurosulfuron                                  |                                |
| Metam                          | Ziram   |                                |
| Metconazole                    |   |                                |
| Metribuzin                     |   |                                |
| Myclobutanil                   |   |                                |
| Prochloraz                     |   |                                |
| Profoxydim                     |   |                                |
| Prothioconazole                |   |                                |
| Pymetrozine                    |   |                                |
| Quinoclamine                   |   |                                |
| Quizalofop-P                   |   |                                |
| Spirotetramat                  |   |                                |
| Spiroxamine                    |   |                                |
| Tebuconazole                   |   |                                |
| Tembotrione                    |   |                                |
| Tepraloxymid                   |   |                                |
| Thifensulfuron-methyl          |   |                                |
| Triadimenol                    |   |                                |

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**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                        |
|--------------------|--------------------|----------|---------------------------|----------|-----------------|---------------------------------------|
| <b>INSECTICIDE</b> | 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  |
| <b>FUNGICIDE</b>   | 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                   |
|                    | Ipreconazole       | 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                    |

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

\*\* Tepraloxym non-approved on the 31/05/2015

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**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          |
| Tepraloxymid       | Cymoxanil             | Prothioconazole       | Flutolanil          |
| Tetraconazole      | Dazomet               | Pymetrozine           | Folpet              |
| Thiophanate-methyl | Deltamethrin          | Pyraflufen-ethyl      | Forchlorfenuron     |
| Thiram             | Dicamba               | Pyridaben             | Haloxyp-P           |
| Tralkoxydim        | Diclofop              | Pyridalyl             | Hexythiazox         |
| Triflumizole*      | Diethofencarb         | Pyriproxyfen          | Imazalil            |
| Triflurosulfuron   | 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             |
|                    | Fonicamid             | 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     |

*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 prejudice 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.*

| Cat I (32) | Cat II (84) | Cat III (46) |
|------------|-------------|--------------|
|            |             | Zoxamide     |

### 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 substances 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<sup>3</sup>, or fulfilling the exclusion criteria (Article 5(1) of the BP Regulation<sup>4</sup>). 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.

<sup>3</sup> This refers to the substances also approved for use in PPP.

<sup>4</sup> 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 Bioaccumulative according to Annex XIII to Regulation (EC) No 1907/2006).

*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.*

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.

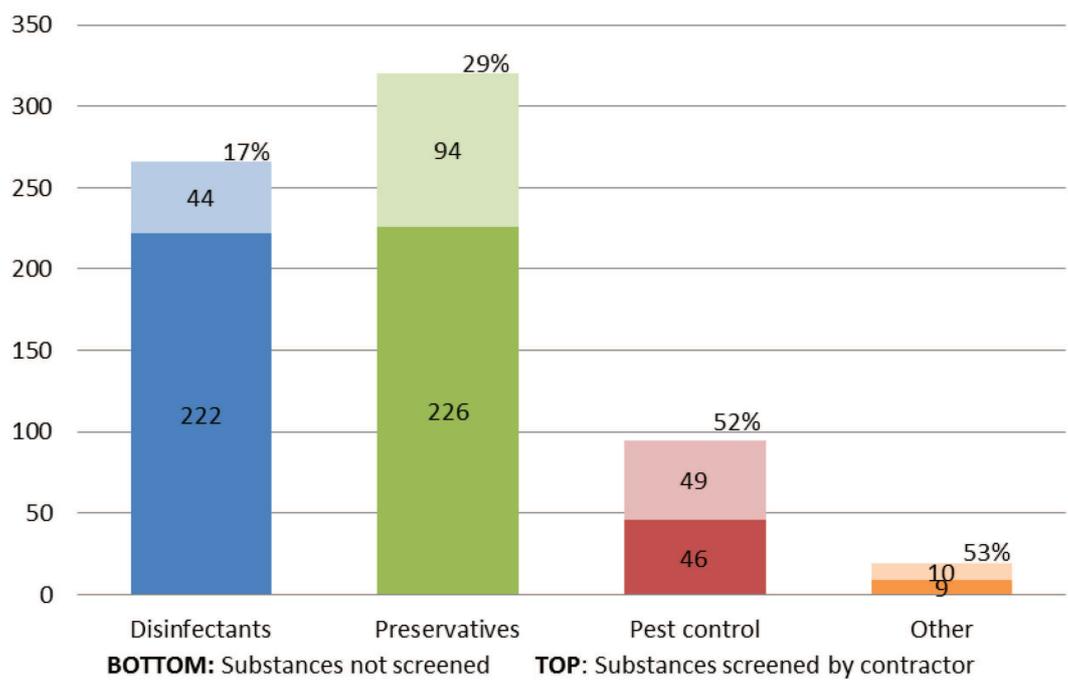
From Table 6 it becomes clear that of the substances identified as potential ED under Option 2, Option 3 Category I and Option 4, one (Cyproconazole) is currently fulfilling the exclusion criteria. However, taking into account the screening cannot be considered representative for the active substances/product 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<sup>5</sup> on iodine that the concept of endocrine disruption is not meaningful for essential elements as iodine.

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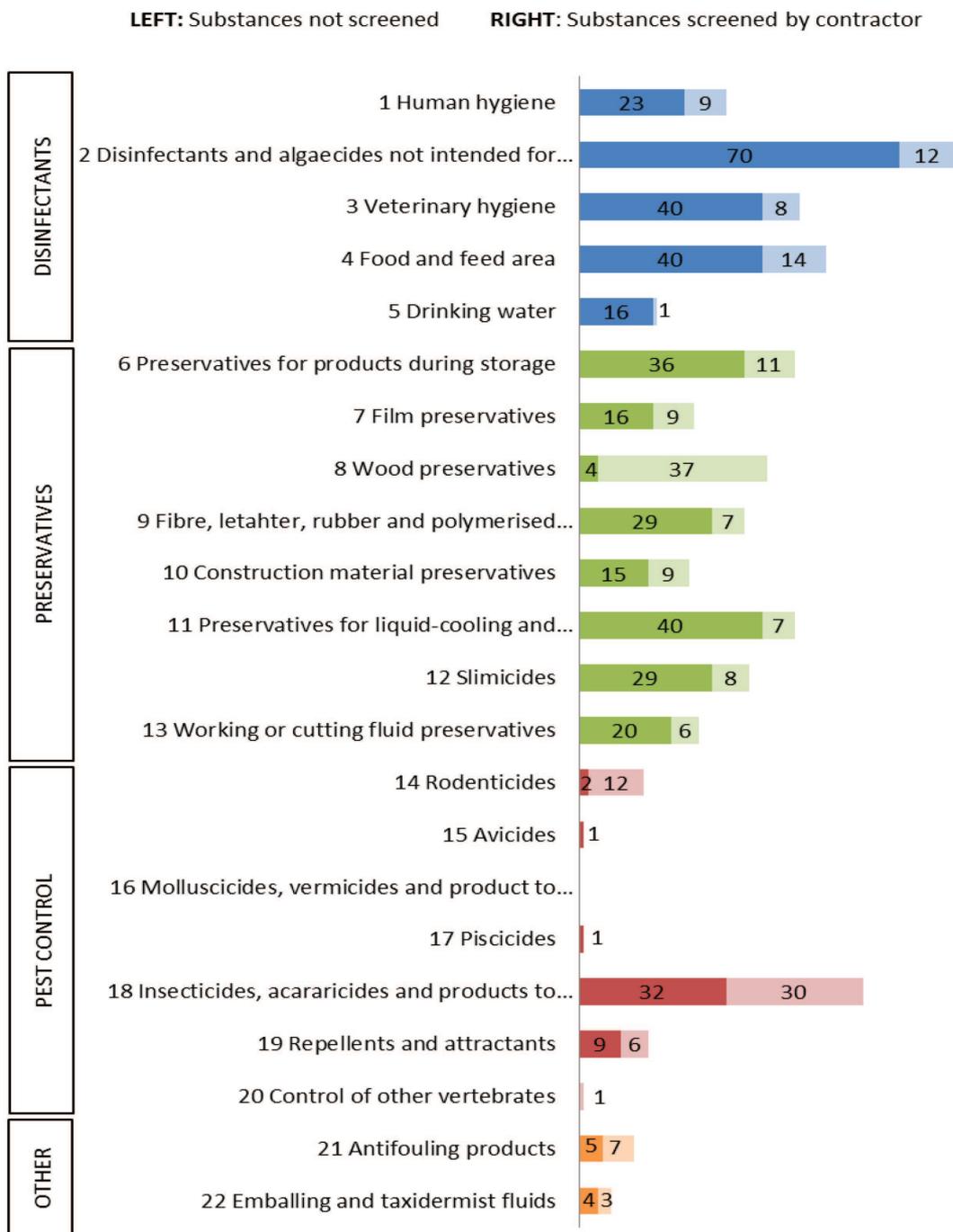
<sup>5</sup> Assessment report on iodine, available on the section of ECHA website providing information on biocidal active substances: <http://echa.europa.eu/web/guest/information-on-chemicals/biocidal-active-substances>.

*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 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 prejudice 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 prejudice 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;<br>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 prejudice 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 |
|--------------------------------|-----------------------------------|----------|-----------------------------|----------|-------------|-----------------------|-----------------|-----------------------------|
| <b>BIOCIDES AND PESTICIDES</b> | 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               |
| <b>BIOCIDES</b>                | 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     |
|                                | <b>TOTAL</b>                      |          | <b>16</b>                   | <b>5</b> | <b>3</b>    | <b>3</b>              | <b>10</b>       |                             |

*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 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<sup>6</sup> as included in BP Regulation<sup>7</sup>.**

|                                | Substance                  | Option 3<br>Cat I | Option 3<br>Cat II | Option 3 Cat<br>III | Cut-off<br>PPP | BP Exclusion<br>criteria | Product Type<br>No | Main group                  |
|--------------------------------|----------------------------|-------------------|--------------------|---------------------|----------------|--------------------------|--------------------|-----------------------------|
| <b>BIOCIDES AND PESTICIDES</b> | 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 |

<sup>6</sup> 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).

<sup>7</sup> 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

*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 3<br>Cat I | Option 3<br>Cat II | Option 3 Cat<br>III | Cut-off<br>PPP | BP Exclusion<br>criteria | Product Type<br>No              | Main group                                |
|-----------------|--|-------------------|--------------------|---------------------|----------------|--------------------------|---------------------------------|---|
| <b>BIOCIDES</b> | 1R-trans phenothrin                                  |                   |                    | 1                   |                |                          | 18                              | PEST CONTROL                              |
|                 | 4,5-Dichloro-2-octylisothiazol-3(2H)-<br>one (DCOIT) |                   | 1                  |                     |                |                          | 7; 8; 9; 10; 11; 21             | PRESERVATIVES; OTHER BIOCIDAL<br>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<br>PRODUCTS |
|                 | Didecyldimethylammonium chloride;<br>DDAC            |                   |                    | 1                   |                |                          | 1; 2; 3; 4; 6; 8; 10;<br>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;<br>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         |   |
| <b>TOTAL</b>    |  | <b>5</b>          | <b>26</b>          | <b>8</b>            | <b>3</b>       | <b>9</b>                 |                                 |   |

*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.*

#### 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.<sup>8</sup> 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<sup>9</sup>. 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<sup>10</sup>; EFSA 2013<sup>11</sup>). Therefore, the present screening was limited to the available evidence related to modes of actions along these four modalities (see also Annex 3).<sup>12</sup> 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.

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<sup>8</sup> 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.

<sup>9</sup> 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.

<sup>10</sup> 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](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2012)22&doclanguage=en)

<sup>11</sup> 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.

<sup>12</sup> 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.

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*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.*

OECD Guidance<sup>13</sup> 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<sup>9</sup> 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

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<sup>13</sup> OECD Work Related to Endocrine Disruptors, available on:  
<http://www.oecd.org/env/ehs/testing/oecdworkrelatedtoendocrinedisrupters.htm>

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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<sup>14</sup> and BP<sup>15</sup> 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.

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<sup>14</sup> European Commission, DG SANTE. EU Legislation on PPP, available on:  
[http://ec.europa.eu/food/plant/pesticides/legislation/index\\_en.htm](http://ec.europa.eu/food/plant/pesticides/legislation/index_en.htm)

<sup>15</sup> ECHA Guidance on biocides legislation, available on:  
<http://echa.europa.eu/guidance-documents/guidance-on-biocides-legislation>

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