

# *The Slow Decrease of Active Substance Candidates for Substitution in the Framework of the European Pesticide Regulation (EC) No 1107/2009*

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*The specific status of active substance candidates for substitution (CfS) is detailed by Article 24 of plant protection Commission Regulation EC No 1107/2009 (PPP Regulation). The criteria of candidates for substitution are now clearly defined: low acceptable daily intake/acute reference dose/acceptable operator exposure level or two persistent, bio-accumulative or toxic criteria, or by nature of the critical effects: non-active isomers, carcinogen 1A/1B, toxic for reproduction 1A/1B or endocrine disruption properties, with these later properties now being well characterised. The total number of active substances CfS has been in constant evolution since 2011, with the first batch of candidates for substitution being published in 2015 and updated since then. After a slow decrease, growth is again observed, with another list of active substances being granted this status. CfS are substances targeted by the PPP Regulation that are supposed to be cancelled or non-renewed at the active substance level or substituted at the market authorisation level. CfS are also supposed to be replaced by substances with better toxicological profiles. However, after five years of implementation of the status, their number, which is intended to decrease, remains high, at sixty residual CfS. We exhibit here their evolution.*

## I. INTRODUCTION

Article 24 of plant protection EC Commission Regulation No 1107/2009 (PPP Regulation) introduced in 2009<sup>1</sup> a new concept in crop protection substances as well as a specific status for active substances as candidates for substitution (CfS).<sup>2</sup> This

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<sup>1</sup> Commission Regulation (EC) 1107/2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309/1.

<sup>2</sup> S Jess, S Kildea, A Moody, G Rennick, AK Murchie and LR Cooke, "European Union policy on pesticides: implications for agriculture in Ireland" (2014) 70(11) Pest Management Science 1646.

new category of substances was undoubtedly introduced with the objective of reducing pesticide impacts following civil society concerns.<sup>3</sup> Active substances can be registered as one of the four types: standard substances (approved for ten years), basic substances (not a substance of concern, no time limit for approbation, etc.), low-risk substances (low risk to human and animal health and the environment, approved for fifteen years, etc.) and CfS (cut-off criteria imposed and only approved for seven years maximum, etc.).<sup>4</sup> The establishment of this statute with the first CfS only came late in 2015 after the entry into force of the PPP Regulation in 2011.<sup>5</sup>

The regulatory definition of CfS included two parts: (1) “An active substance complying with the criteria provided for in Article 4 shall be approved, for a period not exceeding seven years, as a candidate for substitution if it meets one or more of the additional criteria laid down in point 4 of Annex II. By way of derogation from Article 14(2), the approval may be renewed once or more for periods not exceeding seven years”; and (2) “Without prejudice to paragraph 1, Articles 4 to 21 shall apply. Candidates for substitution shall be listed separately in the Regulation referred to in Article 13(4)”. Numerous criteria were defined for the classification of CfS, mainly referring to point 4 of Annex II to the PPP Regulation<sup>6</sup>: being carcinogen category 1A or 1B or toxic for reproduction category 1A or 1B; having endocrine-disrupting properties; having a low acceptable daily intake (ADI), acute reference dose (ARfD) or acceptable operator exposure level (AOEL); having two properties from being persistent, bio-accumulative or toxic (PBT); and containing a significant proportion of non-active isomers or inducing critical effects. At the present time, the endocrine-disrupting properties refer to point 3.6.5 of Annex II to the PPP Regulation, but are not fully settled. Substances that the approval document (Implementing Regulation) is referring to in terms of Article 80(7) of the PPP Regulation should also be verified for CfS status during full approval and inclusion in Part B of Regulation (EU) No 540/2011.<sup>7</sup> Once granted CfS status, some restrictions apply when renewal of the approval is involved. The renewal duration is reduced to a maximum of seven instead of fifteen years.

The first wave of qualification took place in 2015 with an impressive official total of seventy-seven CfS, in reality corresponding to eighty-one active substances (copper compounds are not considered as active substances).

## II. MATERIAL AND METHODS

The evolution of the agrochemical substances panel was followed using the Commission implementing regulations amending Implementing Regulation (EU) No 540/2011. These

<sup>3</sup> S Miles, M Brennan, S Kuznesof, M Ness, C Ritson and LJ Frewer, “Public worry about specific food safety issues” (2004) 106(1) *British Food Journal* 9.

<sup>4</sup> EC 2009, *supra*, note 1; Jess et al, *supra*, note 2.

<sup>5</sup> EC 2009, *supra*, note 1; Commission Regulation (EC) 540/2011 as regards the list of approved active substances. *OJ L* 153/1.

<sup>6</sup> EC 2009, *supra*, note 1.

<sup>7</sup> DC Robin and PA Marchand, “Evolution of Regulation (EU) No 540/2011 since its entry into force” (2019) 7 *Journal of Regulatory Science* 1.

regulations were used to trace the history of agrochemical substances since 2011 to the present day and took into account all of the approvals, approval extensions and renewals of the substances, together with their approved periods. The European Union (EU) Pesticides Database<sup>8</sup> was also used to follow Commission Implementing Regulation No 2015/408 updates.<sup>9</sup> The EU Pesticides Database is also used to determine the disappearance of substances without any implementing regulation (end of approval, CfS qualification during evaluation). Review reports on each active substance published on each page in the EU Pesticides Database were also taken in consideration. The EU Pesticides Database was moving to its v.2.1 revision at the end of 2020, consisting of a large update to its active substances data. Constant follow-up and analysis of all regulation implementations were conducted regarding the evolution of all substances in the different Parts (A to E) of Regulation EC 540/2011. The results show the allocations into Part A (in 2011), Part B (from 2011) and Part E (from 2015); since all CfS are not registered in the dedicated Part E, this analysis includes the disappearance of non-supported substances (end of approval without a regulatory event). Later, some CfS were identified in the evaluation outcomes from the European Food Safety Authority (EFSA) during renewals. The resulting material data are exhibited in Table 1. Thus, ninety-four active substances were granted CfS since 2015 at diverse levels, and their functions are detailed in Table 1.

### III. RESULTS

#### 1. Overall evolution of candidate for substitution substances since 2011

With the entry into force in 2011 of the Commission Implementing Regulation (EU) No 540/2011, 398 substances were immediately approved. At the present time, approximately 467 substances<sup>10</sup> have been permitted, which represents a significant increase compared to the initial number; however, the maximum number of substances was 502.<sup>11</sup> To understand the calculation of the total number of substances, it should be mentioned that many blocks of microorganism active substances (lists of strains in a single substance) were converted at various points into individual approvals (ie during renewals).

Thus, CfS represent at their entry time (2015) more than 16% of the total number of substances. Recently, two newly approved substances (flumetralin and benzovindiflupyr) were directly granted this CfS status, entering directly in Part E.<sup>12</sup> In 2017, 8-hydroxyquinoline was also granted CfS status. It has to be noted that Part

<sup>8</sup> EU Pesticides Database <<http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN>> (last accessed 24 November 2020), replaced by EU Pesticides Database v.2.1 <<https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/active-substances/?event=search.as>> (last accessed 9 April 2021).

<sup>9</sup> Commission Implementing Regulation (EU) 2015/408 on implementing Article 80(7) of Regulation (EC) No 1107/2009 concerning the placing of plant protection products on the market and establishing a list of candidates for substitution OJ L 67/18.

<sup>10</sup> EU Pesticides Database, *supra*, note 8.

<sup>11</sup> DC Robin and PA Marchand, "Biocontrol active substances: evolution since the entry in vigour of Reg. 1107/2009" (2019) 75(4) *Pest Management Science* 950.

<sup>12</sup> Robin and Marchand, *supra*, note 7.

**Table 1.** Candidates for substitution substances in the PPP Regulation: functions, entryway (A or G) and entry date.

Candidate for substitution	Entry	Year	Regulatory exclusion	No. of criteria	Criteria	Function(s)
1-Methyl-cyclopropene	G	2015		1	Low ADI/ARfD/AOEL	PG
8-Hydroxyquinoline, including oxyquinoleine	G	2017		1	Repr. 1B – H360D	FU
Aclonifen	G	2015		1	Two PBT criteria, Carc. 2 – H351	HB
Alpha-cypermethrin (a.k.a. alphamethrin)	G	2015		2	Low ADI/ARfD/AOEL, Acute Tox. 3 – H301	IN
Amitrole (aminotriazole)	G	2015	NR	3	Low ADI/ARfD/AOEL, two PBT criteria	HB
Benzovindiflupyr	G	2016		1	Acute Tox. 3 – H331	FU
Bifenthrin	G	2015	NR	1	Carc. 2 – H351	IN AC
Bordeaux mixture	G	2015		2	Two PBT criteria	BA FU
Bromadiolone	G	2015	NR	2	Low ADI/ARfD/AOEL, Repr. 1B – H360D	RO
Bromuconazole	G	2015		2	Two PBT criteria	FU
Carbendazim	G	2015	E	2	Muta. 1B – H340, Repr. 1B – H360FD	FU
Carbetamide	G	2020	NR	2	Carc. 2 – H351 Repr. 1B – H360FD	HB
Chlorotoluron	G	2015		2	Two PBT criteria + endocrine disruptor	HB
Copper compounds	G	2015		2	Two PBT criteria	BA FU
Copper hydroxide	G	2015		2	Two PBT criteria	BA FU
Copper oxide	G	2015		2	Two PBT criteria	BA FU
Copper oxychloride	G	2015		2	Two PBT criteria	BA FU
Cyproconazole	G	2015	NR	2	Two PBT criteria	FU
Cyprodinil	G	2015		2	Two PBT criteria	FU
Diclofop	G	2015			Low ADI/ARfD/AOEL	HB
Difenacoum	G	2015	E	1	Low ADI/ARfD/AOEL, two PBT criteria (Repr. 1B – H360D)	RO
Difenoconazole	G	2015		2	Two PBT criteria	FU
Diflufenican	G	2015		2	Two PBT criteria	HB

**Table 1.** (Continued)

Candidate for substitution	Entry	Year	Regulatory exclusion	No. of criteria	Criteria	Function(s)
Dimethoate	G	2015	NR	1	Low ADI/ARfD/AOEL, two PBT criteria	IN AC
Dimoxystrobin	G	2015		3	Low ADI/ARfD/AOEL, two PBT criteria + potential endocrine disruptor	FU
Diquat (dibromide)	G	2015	NR	1	Low ADI/ARfD/AOEL, two PBT criteria	HB DE
Emamectin	G	2020		1	Low ADI/ARfD/AOEL	IN
Epoxiconazole	G	2015	E	2	Two PBT criteria, Carc. 2 – H351, Repr. 1B – H360Df + endocrine disruptor	FU
Esfenvalerate	G	2015		2	Two PBT criteria	IN
Ethoprophos	G	2015	NR	1	Low ADI/ARfD/AOEL	NE IN
Etofenprox	G	2015		2	Two PBT criteria	IN
Etoxazole	G	2015		2	Two PBT criteria	IN
Famoxadone	G	2015	NR	3	Two PBT criteria, low ADI/ARfD/AOEL	FU
Fenamiphos (a.k.a. phenamiphos)	G	2015	NR	1	Low ADI/ARfD/AOEL	NE
Fenbutatin oxide	G	2015	W	1	Low ADI/ARfD/AOEL	AC
Fludioxonil	G	2015		2	Two PBT criteria	FU
Flufenacet (formerly fluthiamide)	G	2015		2	Two PBT criteria	HB
Flumetralin	A	2015		2	Two PBT criteria	PG
Flumioxazine	A	2015		2	Low ADI/ARfD/AOEL, Repr. 1B – H360D	HB
Fluometuron	G	2015		1	Low ADI/ARfD/AOEL	HB
Fluopicolide	G	2015		2	Two PBT criteria	FU
Fipronil	G	2015	E	1	Low ADI/ARfD/AOEL	IN
Fluquinconazole	G	2015		3	Two PBT criteria, low ADI/ARfD/AOEL	FU
Flurochloridone	G	2020		1	Potential endocrine disruptor	HB
Gamma-cyhalothrin	G	2020		1	Low ADI/ARfD/AOEL	IN
Glufosinate	G	2015	E	2	Repr. 1B – H360FD, low ADI/ARfD/AOEL	HB
Haloxyfop-P (Haloxyfop-R)	G	2015	E	1	Low ADI/ARfD/AOEL	HB
Halosulfuron methyl	G	2020				HB

**Table 1.** (Continued)

Candidate for substitution	Entry	Year	Regulatory exclusion	No. of criteria	Criteria	Function(s)
Imazamox	G	2015		2	Two PBT criteria	HB
Imazosulfuron	G	2015	NR, Appl W	1	Low ADI/ARfD/AOEL	HB
Ipconazole	G	2020		1	Low ADI/ARfD/AOEL	FU
Isoproturon	G	2015	NR	2	Two PBT criteria, Carc. 2 – H351	HB
Isopyrazam	G	2015		2	Two PBT criteria	FU
Lambda-cyhalothrin	G	2015		3	Two PBT criteria, low ADI/ARfD/AOEL	IN
Lenacil	G	2015		2	Two PBT criteria	HB
Linuron	G	2015	NR	1	Toxic for reproduction 1A/1B, Carc. 2 – H351, Repr. 1B – H360Df	HB
Lufenuron	G	2015	E	1	Low ADI/ARfD/AOEL	IN
Mecoprop	G	2015	E, Appl W	1	Non-active isomers	HB
Metalaxyl	G	2015		1	Non-active isomers	FU
Metam (including metam-potassium and metam-sodium)	G	2015		1	Low ADI/ARfD/AOEL	FU IN HB
Metconazole	G	2015		2	Low ADI/ARfD/AOEL, Repr. 2 – H361d	FU PG
Methomyl	G	2015	E	1	Low ADI/ARfD/AOEL	IN
Methoxyfenozide	G	2015		2	Two PBT criteria	IN
Metribuzin	G	2015		2	Two PBT criteria	HB
Metsulfuron-methyl	G	2015		2	Two PBT criteria	HB
Molinate	G	2015	E	2	Carc. 2 – H351, low ADI/ARfD/AOEL	HB
Myclobutanil	G	2015	NR	2	Two PBT criteria	FU
Nicosulfuron	G	2015		2	Two PBT criteria	HB
Oxadiazon	G	2015	E	2	H361d and toxic	HB
Oxadiargyl	G	2015	E	2	H361d and toxic	HB
Oxadiazon	G	2015	E	1	Low ADI/ARfD/AOEL	HB
Oxamyl	G	2015		1	Low ADI/ARfD/AOEL	IN NE
Oxyfluorfen	G	2015		2	Two PBT criteria	HB

**Table 1.** (Continued)

Candidate for substitution	Entry	Year	Regulatory exclusion	No. of criteria	Criteria	Function(s)
Paclobutrazol	G	2015		2	Two PBT criteria	PG
Pendimethalin	G	2015		2	Two PBT criteria	HB
Pirimicarb	G	2015		2	Two PBT criteria	IN
Prochloraz	G	2015		2	Two PBT criteria	FU
Profoxydim	G	2015		1	Endocrine disruptor	HB
Propiconazole	G	2015	NR	2	Two PBT criteria, Repr. 1B – H360D	FU
<i>Propoxycarbazone</i>	<i>G</i>	<i>2015</i>			<i>Proposal deletion of the list of CfS</i>	<i>HB</i>
Prosulfuron	G	2015		2	Two PBT criteria	HB
Quinoxifen	G	2015	NR	3	P, B and toxic or PBT	FU
Quizalofop-P-tefuryl	G	2015		2	Carc. 2 – H351, Repr. 2 – H361fd + Repr. 1B – H360D	HB
Sulcotrione	G	2015		1	Low ADI/ARfD/AOEL	HB
Tebuconazole	G	2015		1	Repr. 2 – H361d	FU
Tebufenpyrad	G	2015		1	Low ADI/ARfD/AOEL	AC
Tembotrione	G	2020		2	Low ADI/ARfD/AOEL, Repr. 2 – H361d	HB
Tepraloxymid	G	2015	E	2	Repr. 2 – H361fd, Carc. 2 – H351, low ADI/ARfD/AOEL	HB
Thiacloprid	G	2015	NR	2	Repr. 1B – H360FD, Carc. 2 – H351	IN
Tri-allate	G	2015		2	Two PBT criteria	HB
Triasulfuron	G	2015	NR	2	Two PBT criteria, potential low ADI/ARfD/AOEL and incomplete genotoxicity assessment	HB
Tribasic copper sulphate	G	2015		2	Two PBT criteria	BA FU
Triazoxide	G	2015		1	Low ADI/ARfD/AOEL	FU
Warfarin (a.k.a. coumaphene)	G	2015	E	1	Repr. 1A – H360D	RO
Ziram	G	2015		2	Two PBT criteria	FU RE

Italics represent an ongoing process.

A = approved as CfS (others were granted (G) after approval); AC = acaricide; ADI = acceptable daily intake; AOEL = acceptable operator exposure level; Appl W = application withdrawn; ARfD = acute reference dose; BA = bactericide; Carc. = carcinogenic; DE = desiccant; E = end of approval; FU = fungicide; HB = herbicide; IN = insecticide; Muta. = mutagenic; NE = nematocidal; NR = non-renewal; PBT = persistent, bio-accumulative and toxic; PG = plant growth regulator; RE = repulsive; Repr. = reprotoxic; RO = rodenticide; Tox. = toxicity; W = withdrawal.

E of Implementing Regulation (EU) No 540/2011 was not implemented with substances qualified under Implementing Regulation (EU) No 2015/408. Later evolutions of Implementing Regulation (EU) No 2015/408 show the addition to the CFS list of 8-hydroxyquinoline<sup>13</sup> and 1-methylcyclopropene.<sup>14</sup> A further list of CFS (seven active substances) was published in 2020, transferring seven more substances into the annex of Implementing Regulation (EU) No 2015/408.<sup>15</sup> Finally, thiacloprid was qualified as a CFS during its renewal process and thus does not appear in Table 1, but is present in Figure 1. Thus, ninety-four active substances were granted CFS status since 2015 at diverse levels detailed in Table 1, and their evolution is shown in Figure 1.

The different movements of CFS between Parts A, B and E and their reglementary status are described in Table 2. Some were initially granted when present in Part A and some when present in Part B (after renewal). The CFS present in Part E were granted during renewal (from Part A or Part B) or by direct approval as CFS.

Previously, fenbutatin oxide<sup>16</sup> was already withdrawn and oxadiargyl's<sup>17</sup> approval ended in 2014 from Part A before the publication of the first list. The first non-renewed active substance was triasulfuron,<sup>18</sup> whereas the first CFS removed from Part A by simple end of approval was carbendazime.<sup>19</sup> The first active substance qualified as a CFS in the PPP Regulation by Implementing Regulation (EU) No 2015/408<sup>20</sup> renewed from Part A was esfenvalerate in 2015, therefore opening the way to Part E of the PPP regulation. Flumetralin<sup>21</sup> was the first For CFS to undergo direct entry in

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<sup>13</sup> Commission Implementing Regulation (EU) 2017/2065 confirming the conditions of approval of the active substance 8-hydroxyquinoline, as set out in Implementing Regulation (EU) No 540/2011 and modifying Implementing Regulation (EU) 2015/408 as regards the inclusion of the active substance 8-hydroxyquinoline in the list of candidates for substitution. C/2017/7430. OJ L 295/40.

<sup>14</sup> Commission Implementing Regulation (EU) 2019/1085 renewing the approval of the active substance 1-methylcyclopropene, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011, and amending the Annex to Commission Implementing Regulation (EU) 2015/408. OJ L 171/110.

<sup>15</sup> Commission Implementing Regulation (EU) 2020/1295 amending Implementing Regulation (EU) 2015/408 as regards the inclusion of the active substances carbetamide, emamectin, flurochloridone, gamma-cyhalothrin, halosulfuron-methyl, ipconazole and tembotrione in the list of candidates for substitution. C/2020/6239. OJ L 303/18.

<sup>16</sup> Commission Implementing Regulation (EU) No 486/2014 of 12 May 2014 withdrawing the approval of the active substance fenbutatin oxide, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending Commission Implementing Regulation (EU) No 540/2011. OJ L 138/70.

<sup>17</sup> Commission Regulation (EU) No 186/2014 of 26 February 2014 amending Regulation (EU) No 823/2012 as regards the expiry dates of the approval of the active substances ethoxysulfuron, oxadiargyl and warfarin. OJ L 57/22.

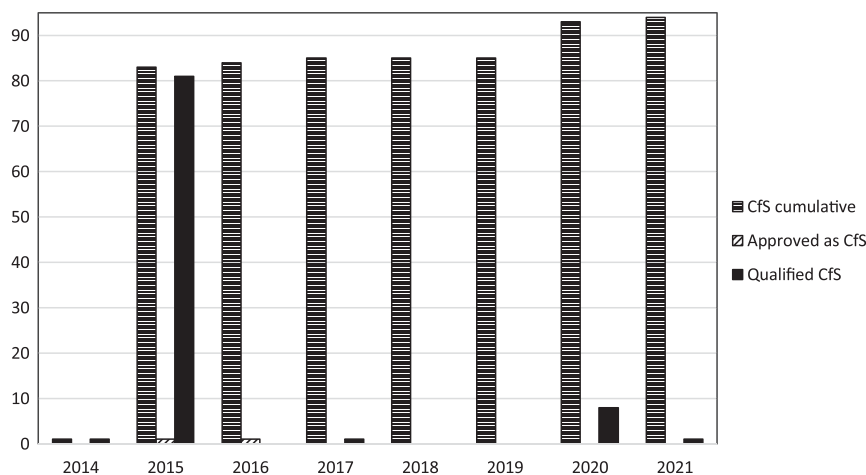
<sup>18</sup> Commission Implementing Regulation (EU) 2016/864 of 31 May 2016 concerning the non-renewal of approval of the active substance triasulfuron, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending Commission Implementing Regulation (EU) No 540/2011. OJ L 144/32.

<sup>19</sup> Commission Implementing Regulation (EU) No 542/2011 of 1 June 2011 amending Implementing Regulation (EU) No 540/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances to take into account Directive 2011/58/EU amending Council Directive 91/414/EEC to renew the inclusion of carbendazim as active substance. OJ L 153/189.

<sup>20</sup> EU 2015, *supra*, note 9.

<sup>21</sup> Commission Implementing Regulation (EU) 2015/2105 of 20 November 2015 approving the active substance flumetralin, as a candidate for substitution, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending Commission Implementing Regulation (EU) No 540/2011. OJ L 305/31.





**Figure 1.** Number of candidates for substitution (CfS) by type of entry and cumulative sum between 2014 and 2020.

Part E in 2015. Surprisingly, propoxycarbazone<sup>22</sup> was renewed from Part A into Part B in 2017 and CfS qualifications were abandoned during its renewal. These qualification changes resulted from the risk assessment conclusions of the renewal evaluation,<sup>23</sup> and the abandonment of the CfS qualification was officially requested in 2021.<sup>24</sup>

Exits (by suppression, withdrawal, end of approval or disqualification) from Implementing Regulation (EC) No 540/2011 since 2014 are shown in Figure 2, while the cumulative sum of CfS entries (via approval or qualification) and resultant annual effective numbers of CfS are exhibited in Figure 3. These show a relative high number of granted CfS since 2014 (ninety-four active substances) compared to the approved maximum number of active substance (502), as well as a slow decrease of the still-approved CfS (sixty active substances) from the total granted CfS; thus, only 30% (thirty-four active substances) have been removed (Figure 2).

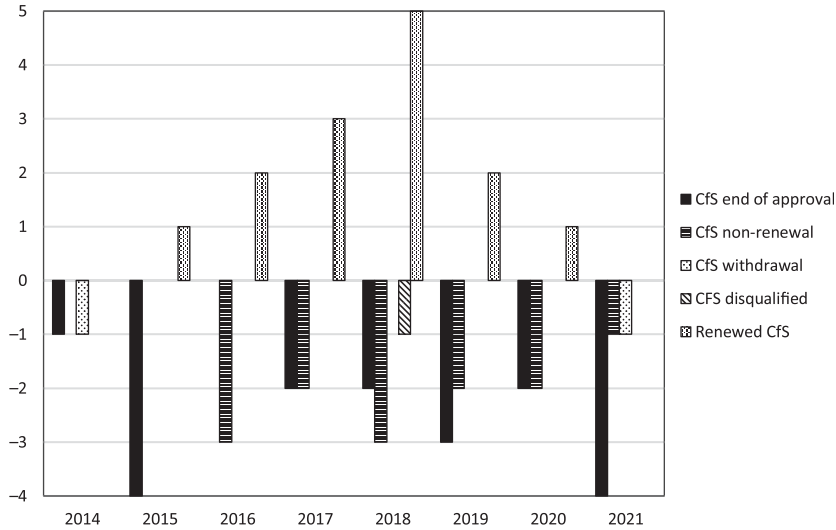
In the meantime, fifteen CfS were renewed between 2014 and 2020 (Figure 2 and Table 2)<sup>25</sup> for a maximum of seven years, as described in Article 24, instead of a

<sup>22</sup> Commission Implementing Regulation (EU) 2017/1115 of 22 June 2017 renewing the approval of the active substance propoxycarbazone in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. C/2017/4216. OJ L 162/38.

<sup>23</sup> EFSA (European Food Safety Authority), “Conclusion on the peer review of the pesticide risk assessment of the active substance propoxycarbazone (variant evaluated propoxycarbazone-sodium)” (2016) 14(10) EFSA Journal 4612.

<sup>24</sup> Exchange of views of the Committee on a draft Commission Implementing Regulation (EU) correcting Implementing Regulation (EU) 2015/408 as regards the deletion of the active substance propoxycarbazone from the list of candidates for substitution in Standing Committee on Plants, Animals, Food and Feed section Phytopharmaceuticals – Legislation of 19–20 May 2021 (SANTE/10304/2021).

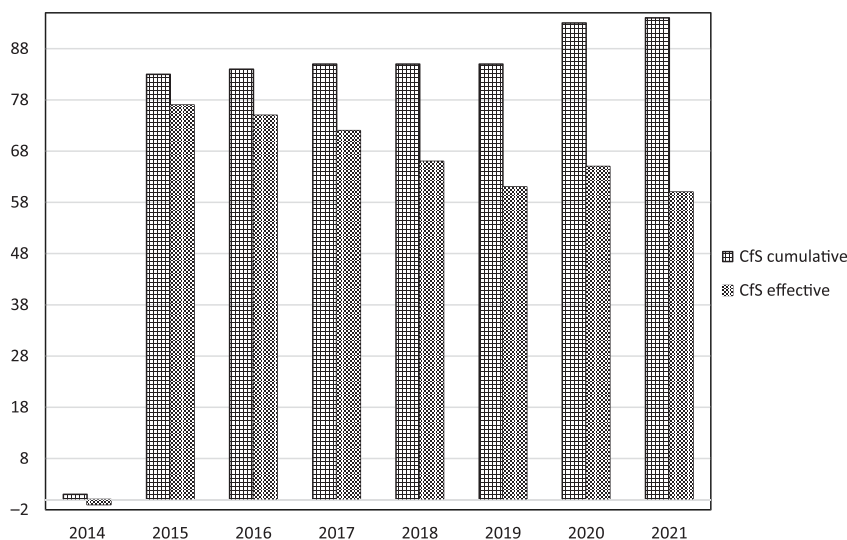
<sup>25</sup> Commission Implementing Regulation (EU) 2015/2047 of 16 November 2015 renewing the approval of the active substance esfenvalerate, as a candidate for substitution, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. OJ L 300/8; Commission Implementing Regulation (EU) 2016/146 of 4 February 2016 renewing the approval of the active substance lambda-cyhalothrin, as a candidate for substitution, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the



**Figure 2.** Evolution of candidates for substitution (CfS) between 2014 and 2020.

*Note:* Number and type of CfS suppression (under) and renewal (above).

Annex to Implementing Regulation (EU) No 540/2011 OJ L 30/7; Commission Implementing Regulation (EU) 2016/139 of 2 February 2016 renewing the approval of the active substance metsulfuron-methyl, as a candidate for substitution, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Implementing Regulation (EU) No 540/2011 OJ L 27/7; Commission Implementing Regulation (EU) 2017/1531 of 7 September 2017 renewing the approval of the active substance imazamox, as a candidate for substitution, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. C/2017/6036. OJ L 232/6; Commission Implementing Regulation (EU) 2017/1114 of 22 June 2017 renewing the approval of the active substance pendimethalin, as a candidate for substitution, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. C/2017/4198. OJ L 162/32; Commission Implementing Regulation (EU) 2017/375 of 2 March 2017 renewing the approval of the active substance prosulfuron, as a candidate for substitution, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. C/2017/1300. OL L 58/3; Commission Implementing Regulation (EU) 2018/755 of 23 May 2018 renewing the approval of the active substance propyzamide, as a candidate for substitution, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. C/2018/2636. OL L 128/4; Commission Implementing Regulation (EU) 2019/1690 of 9 October 2019 renewing the approval of the active substance alpha-cypermethrin, as a candidate for substitution, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. C/2019/7134. OL L 259/2; Commission Implementing Regulation (EU) 2019/158 of 31 January 2019 renewing the approval of the active substance methoxyfenozide, as a candidate for substitution, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. C/2019/696. OL L 31/21; and Commission Implementing Regulation (EU) 2020/2105 of 15 December 2020 renewing the approval of the active substance etoxazole as a candidate for substitution in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. C/2020/8809. OJ L 425/96.



**Figure 3.** Cumulative entries and effective approved numbers of candidates for substitution (CfS) between 2014 and 2020.

maximum of fifteen years for regular active substances. These renewals also maintain a high number of approved CfS, as shown in Figure 3, even if they represent few active substances per year (copper compounds account for five in 2018).<sup>26</sup>

## 2. Type of substances, classes and functions affected

The major type of substances granted CfS are chemicals (eighty-seven active substances, 93.5%), whereas natural substances are few (six active substances, 6.5%), only being represented by the copper compounds family (five active substances) and, more recently, emamectin (Figure 4).<sup>27</sup> The corresponding classes covering many of the distinguished specific chemical structures are listed in Table 3.

Functions covered by CfS detailed in Table 1 are mainly herbicides (thirty-eight active substances), fungicides (thirty active substances) and insecticides (nineteen active substances) accounting for 81% of the usages, and only few bactericides (five active substances), acaricides (four active substances), rodenticides, plant growth regulators and nematocides (three active substances reach), desiccants and repulsives (one active substances each) (Figure 5). The sum of the corresponding usages (106) is higher the total CfS (94); thus, the number of lost usages and functions for each removed CfS is greater than one.

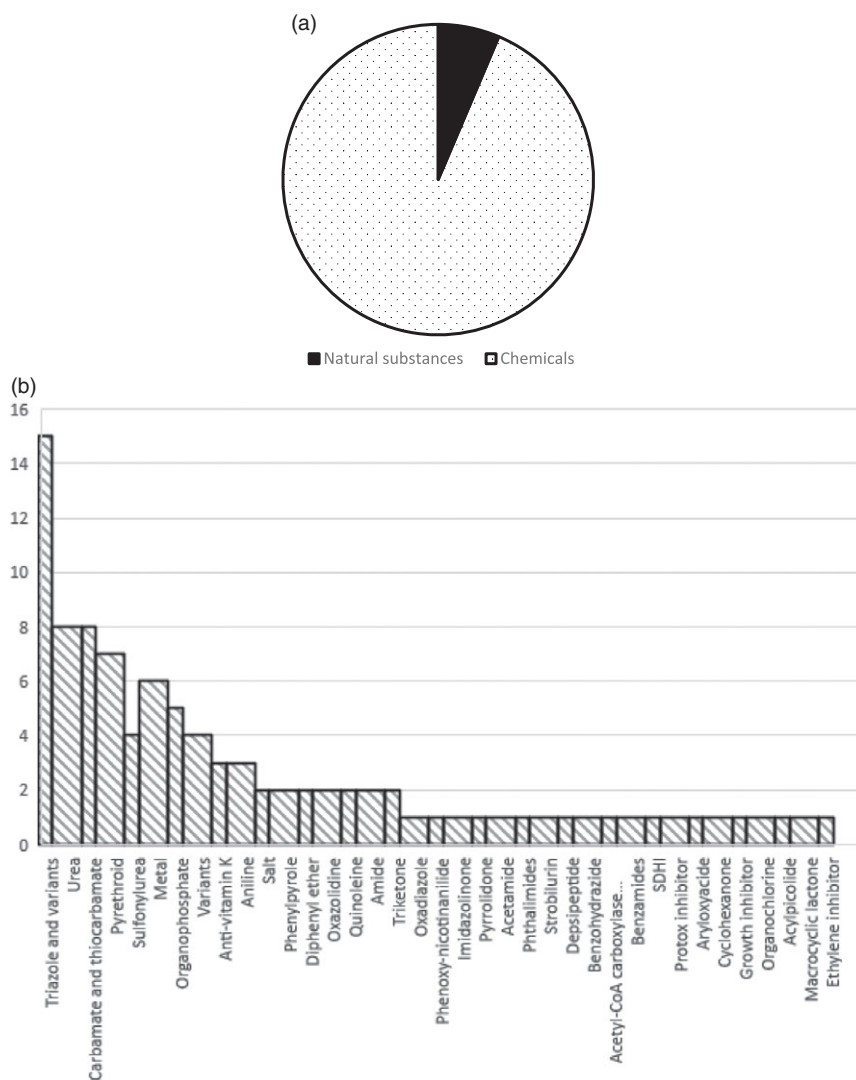
<sup>26</sup> Commission Implementing Regulation (EU) 2018/1981 of 13 December 2018 renewing the approval of the active substances copper compounds, as candidates for substitution, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. C/2018/8449. OJ L 317/16.

<sup>27</sup> Robin and Marchand, *supra*, note 11; EU 2020, *supra*, note 13.

**Table 2.** Evolution of candidates for substitution (Cfs) in the PPP Regulation.

Reg. 540/2011 status	Approved in Part A	Approved in Part B		Not approved			Approved in Part E by		
	Regulatory position by year	Unchanged since 2011	Renewed before Cfs qualification	Renewed without Cfs qualification	Non-renewal	Withdrawal	End of approval	Renewal	Approval
2014					Fenbutatin oxide				
2015	1-Methylcyclopropene, aclonifen, bromuconazole, chlorotoluron, cyprodinil, diclofop, difenoconazole, diflufenican, dimoxystrobine, epoxiconazole, etofenprox, fludioxonil, flufenacet, flumioxazin, fluometuron, fluopicolide, fluquinconazole, isopyrazam, lenacil, metalaxyl, metam, metconazole, metribuzine, nicosulfuron, oxamyl, oxyfluorfen, paclobutrazol, pirimicarb, prochloraz, profoxydim, sulcotrione, tebuconazole, tebufenpyrad, tri-allate, triazoxide, ziram			Triasulfuron			Carbendazime, molinate, oxadiargyl, tepraloxim, warfarin	Esfenvalerate	Flumetralin
2016				Amitrole		Isoproturon		Lambda-cyhalothrin, metsulfuron-methyl	Benzovindiflupyr
2017	Quizalofop-P-tefuryl		8-Hydroxyquinoline, including oxyquinoline	Imazosulfuron, linuron		Fipronil, mecoprop		Imazamox, pendimethalin, pro-sulfuron	
2018			Propoxycarbazone	Propiconazole, quinoxifen		Glufosinate, oxadiazon		Copper compounds = 5 active substances (copper hydroxide, copper oxide, copper oxychloride, Bordeaux mixture, tribasic copper sulphate), propyzamide	
2019				Bifenthrin, dimethoate, diquat, ethoprophos		Difenacoum, lufenuron, methomyl		Methoxyfenozide	
2020	Flurochloridone		Emamectin, gamma-cyhalothrin, halosulfuron methyl, ipconazole, tembotrione	Fenamiphos, thiacloprid		Haloxypop-P, epoxyconazole		Etoxazole	
2021				<i>Famoxadone</i>	<i>Alpha-cypermethrin</i>	<i>Bromadiolone, carbemide, cyproconazole, myclobutanil</i>		<i>Cypermethrin</i>	
No.	39	7	1	13	2	18	15	2	
Total no.	47			33			17		

Italics represent an ongoing reglementary event.



**Figure 4.** Characteristics of candidates for substitution. (a) Type of candidates for substitution. (b) Classes of candidates for substitution.

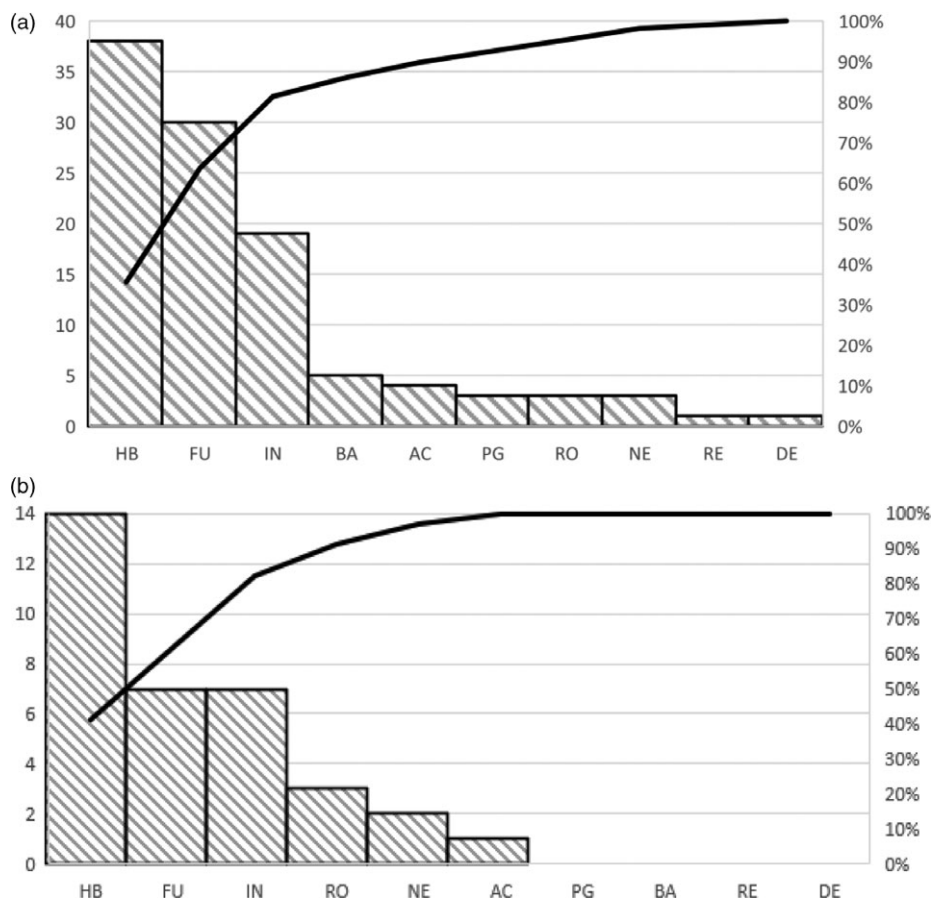
Suppressed functions, following non-approval status of CfS for all removal issues (thirty-four active substances), are different from the CfS profile. In the great majority, herbicide functions (fourteen active substances), mainly insecticide (seven active substances) and fungicide (seven active substances) functions, account for approximately 82% of the usages, while other functions (rodenticide and nematicide (three and two active substances each) and acaricide (1 active substance) functions) are negligible (Figure 5b), although some removals may create orphan uses. Indeed, the disappearance, for example, of ziram (after that of thiram and pepper dust) could create a situation where there would be no more repellents for mammals.

**Table 3.** Class of all candidates for substitution (by amount rank).

Class or chemical structure	Substances
Triazole and variants	Bromuconazole, cyproconazole, difenoconazole, epoxiconazole, fluquinconazole, metconazole, propiconazole, tebuconazole, amitrole, triazoxide, myclobutanil, epoxiconazole, ipconazole, metribuzine, paclobutrazol
Urea	Fluometuron, imazosulfuron, prosulfuron, lufenuron, chlorotoluron, linuron, isoproturon, prochloraz
Carbamate and thiocarbamate	Pirimicarb, carbendazime, ziram, metam, methomyl, tri-allate, molinate, oxamyl
Pyrethroid	Esfenvalerate, lambda-cyhalothrin, gamma-cyhalothrin, bifenthrin, alpha-cypermethrin
Sulphonylurea	Nicosulfuron, triasulfuron, metsulfuron-methyl, halosulfuron methyl
Metal	Copper compounds = 5 active substances (copper hydroxide, copper oxide, copper oxychloride, Bordeaux mixture, tribasic copper sulphate), fenbutatin oxide
Organophosphate Variant	Lenacil, ethoprophos, fenamiphos, dimethoate, glufosinate Benzovindiflupyr, propoxycarbazone, quizalofop-P-tefuryl, haloxyfop-P
Anti-vitamin K	Difenacoum, warfarin, bromadiolone
Aniline	Flumetralin, cyprodinil, pendimethalin
Salt	Diquat, mecoprop
Phenylpyrole	Fludioxonil, fipronil
Diphenyl ether	Etofenprox, aclonifen
Oxazolidine	Famoxadone, oxadiargyl
Quinoleine	8-Hydroxyquinoline incl. oxyquinoleine, quinoxifen
Amide	Carbetamide, tebufenpyrad
Triketone	Tembotrione, sulcotrione
Oxadiazole	Oxadiazon
Phenoxy-nicotinilide	Diflufenican
Imidazolinone	Imazamox
Pyrrolidone	Flurochloridone
Acetamide	Flufenacet
Phthalimides	Flumioxazin
Strobilurin	Dimoxystrobine
Depsipeptide	Metalaxyl
Benzohydrazide	Methoxyfenozide
Diverse	Profoxydim, propyzamide, isopyrazam, oxyfluorfen, diclofop, tepraloxym, etoxazole, thiacloprid, fluopicolide, emamectin, 1-methylcyclopropene

#### IV. DISCUSSION

The evolution of CfS shown in the various figures in this paper demonstrates erratic and non-linear changes. Qualifications as CfS are given mainly in steep increments, whereas decreases are slow and at the individual level for each active substance. Thus, lot of movement has been observed since the first qualification as a CfS – only a few



**Figure 5.** Attributes of candidates for substitution. (a) Functions for candidates for substitution. (b) Functions of removed candidates for substitution.

AC = acaricide; BA = bactericide; DE = desiccant; FU = fungicide; HB = herbicide; IN = insecticide; NE = nematicide; PG = plant growth regulator; RE = repulsive; RO = rodenticide.

reductions have been enacted (withdrawal, end of approval or non-renewal), including the ongoing process for haloxyfop-P and later the end of approval for ziram. A significant number of CfS (fourteen active substances) were renewed (from Part A to B or E), including the recent renewal for etoxazole.<sup>28</sup> A lot of renewals of CfS are still pending, and considering the increasing evaluation time for these substances, this generates numerous extended approval periods (cf. chlorotoluron,<sup>29</sup> dimoxystrobin

<sup>28</sup> Commission Implementing Regulation (EU) 2020/2105 renewing the approval of the active substance etoxazole as a candidate for substitution. OJ L 425/96.

<sup>29</sup> Commission Implementing Regulation (EU) 2020/1511 of 16 October 2020 amending Implementing Regulation (EU) No 540/2011 as regards the extension of the approval periods of the active substances amidosulfuron, bifenox, chlorotoluron, clofentezine, clomazone, cypermethrin, daminozide, deltamethrin, dicamba, difenoconazole, diflufenican, fenoxaprop-P, fenpropidin, fludioxonil, flufenacet, fosthiazate, indoxacarb, lenacil, MCPA, MCPB, nicosulfuron, paraffin oils, picloram, prosulfocarb, sulphur, triflusalufuron and tritosulfuron. C/2020/7046. OJ L 344/18.

and oxamyl<sup>30</sup> or ziram),<sup>31</sup> although some non-renewals are in progress (cf. famoxadone).<sup>32</sup>

Since all CfS were used in the field as approved active substances, the effective (substances now non-approved) or the possible (ongoing regulatory process) and programmed loss (regulations stipulating that CfS are supposed to be removed/substituted) of these CfS active substances and therefore the loss of these functions and usages may be problematic for some agricultural sectors, leading to orphan uses (see above). A few examples may be detailed, such as the loss of many CfS herbicides as well as non-CfS herbicides, reducing the diversity of active substances, therefore automatically increasing the use and therefore the volume (in tonnes) of the few remaining herbicides and thus the occurrence of their residues.<sup>33</sup> In the meantime, other non-PPP integrated pest management (IPM) techniques are being implemented in fields to overcome chemical herbicide reductions or as direct replacements, but initial thermic solutions, first developed in organic production, are in decline due to CO<sub>2</sub> emissions concerns. In fact, mechanical weeding is rapidly taking over, but electrical weeding systems are also promising.

Similarly, organic food production may be heavily affected by the evolution of copper compounds as CfS.<sup>34</sup> Furthermore, follow-up on the evolution of CfS is not easy to conduct, since only twelve CfS entries are listed in Part E of Regulation (EC) No 540/2011, accounting for sixteen material active substances (due to the copper compound family including copper hydroxide, copper oxide, copper oxychloride, tribasic copper sulphate and Bordeaux mixture), whereas another sixty-four active substances are candidate for substitution. This means that a majority of the CfS were not considered for evaluation during renewal operations and still remain in Parts A and B of Regulation (EC) No 540/2011.

<sup>30</sup> Commission Implementing Regulation (EU) 2021/52 of 22 January 2021 amending Implementing Regulation (EU) No 540/2011 as regards the extension of the approval periods of the active substances benfluralin, dimoxystrobin, fluzainam, flutolanil, mecoprop-P, mepiquat, metiram, oxamyl and pyraclostrobin. C/2021/291. OJ L 23/13.

<sup>31</sup> Commission Implementing Regulation (EU) 2021/566 of 30 March 2021 amending Implementing Regulation (EU) No 540/2011 as regards the extension of the approval periods of the active substances abamectin, *Bacillus subtilis* (Cohn 1872) strain QST 713, *Bacillus thuringiensis* subsp. Aizawai strains ABTS-1857 and GC-91, *Bacillus thuringiensis* subsp. Israeliensis (serotype H-14) strain AM65-52, *Bacillus thuringiensis* subsp. Kurstaki strains ABTS 351, PB 54, SA 11, SA12 and EG 2348, *Beauveria bassiana* strains ATCC 74040 and GHA, clodinafop, clopyralid, *Cydia pomonella* Granulovirus (CpGV), cyprodinil, dichlorprop-P, fenpyroximate, fosetyl, mepanipyrim, *Metarhizium anisopliae* (var. anisopliae) strain BIPESCO 5/F52, metconazole, metrafenone, pirimicarb, *Pseudomonas chlororaphis* strain MA342, pyrimethanil, *Pythium oligandrum* M1, rimsulfuron, spinosad, *Streptomyces* K61 (formerly “*S. griseoviridis*”), *Trichoderma asperellum* (formerly “*T. harzianum*”) strains ICC012, T25 and TV1, *Trichoderma atroviride* (formerly “*T. harzianum*”) strain T11, *Trichoderma gamsii* (formerly “*T. viride*”) strain ICC080, *Trichoderma harzianum* strains T-22 and ITEM 908, triclopyr, trinexapac, triticonazole and ziram. C/2021/2028. OJ L 118/1.

<sup>32</sup> Exchange of views of the Committee on a draft Commission Implementing Regulation (EU) concerning the non-renewal of approval of the active substance famoxadone, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending Commission Implementing Regulation (EU) No 540/2011 (Draft Review Report SANTE/12986/2019 Rev. 1) during Standing Committee on Plants, Animals, Food and Feed Section Phytopharmaceuticals – Legislation of 24–25 March 2021.

<sup>33</sup> EFSA (European Food Safety Authority), CL Carrasco and PP Medina, “The 2019 European Union report on pesticide residues in food” (2021) 19(4) EFSA Journal 6491.

<sup>34</sup> PA Marchand, “Novel plant protection regulation: new perspectives for organic production?” (2018) 4(1) Organic Farming 3.



This study shows that gaining access to complete information (harmonised risk indicator (HRI) effective national values, pesticides weight sales, explanations of the amendment of the EU HRI curve) is not easy, although our survey is continuous and accurate (using the EU Pesticides Database, regulations and EFSA outcomes). Complete follow-up of CfS requires full EU website analyses since previous versions of the EU Pesticides Database using simple research numbered only seventy-three CfS in the EU Pesticides Database v.2.0 (approved/non-approved), whereas ninety-four active substances were officially granted CfS status. EU regulatory processes and sometimes individual active substance evolutions also must be investigated in order to gather all of the data. An update after the recent qualification of seven CfS active substance included eighty-one active substances, and the actual EU Pesticides Database v.2.1 now exhibits ninety-one CfS active substances. Thus, only two active substances labelled as CfS (triasulfuron and 1-methyl-cyclopropene) are still missing from the EU Pesticides Database.

### 1. Subcategories of candidates for substitution

Seven subcategories taken in consideration for CfS correspond to specific criteria.<sup>35</sup> No scale is mentioned regarding risk or danger (ie from medium to high), thus they have the same risk weight for all of the CfS classifications. From the twenty-nine CfS removed through non-renewal, withdrawal or expiry of approval, some were representative of only one criterion (ie dimethoate, methomyl, etc.), but several exhibited two criteria (ie diquat) and some three criteria (ie epoxiconazole), although some single-criterion examples such as “PBT” are already a proof of the presence of two negative properties from being persistent, bio-accumulative or toxic. Table 1 describes the granted criteria for these actual non-approved CfS with information founded in implementing regulations, EFSA outcomes and the EU Pesticides Database. Table 1 shows thirteen non-renewals, fourteen ends of approval and one withdrawal, with the results exhibited in Figure 2 (under the baseline).

Moreover, CfS examples that are still approved meet one (ie cyprodinil), two (ie chlorotoluron) or three (ie dimoxystrobin) criteria, still with the same ambiguity regarding PBT with two risk points. This is exhibited in Figure 2 (above the baseline) and confirms the absence of priority between CfS categories and numbers of criteria retained for managing the existing CfS in terms of conducting removal or renewal.

### 2. Implications of candidates for substitution in Directive (EC) No 128/2009

The political action at the European level includes, amongst others, Directive 2009/128/EC,<sup>36</sup> which encourages a reduction in pesticide risks, and is also a triggering factor for CfS decreases.<sup>37</sup> In fact, the multiplication factor for CfS in the

<sup>35</sup> Point 4 in Annex II of PPP Regulation, *supra*, note 1.

<sup>36</sup> Directive 2009/128/EC establishing a framework for Community action to achieve the sustainable use of pesticides. OJ L 309/71–86.

<sup>37</sup> DC Robin and PA Marchand, “Evolution of Directive (EC) No 128/2009 of the European Parliament and of the Council establishing a framework for Community action to achieve the sustainable use of pesticides” (2019) 7 *Journal of Regulatory Science* 1.

calculation of harmonised risk indicators (HRI1 and HRI2) is very high, as the multiplication factor is  $\times 16$  for CfS,<sup>38</sup> while the multiplication factors are  $\times 1$  for low-risk substances,  $\times 8$  for regular active substances and zero for basic substances (versus a very high multiplication factor ( $\times 64$ ) for non-approved substances).<sup>39</sup> The slow decrease of CfS and the discontinuous but permanent increase of CfS due to inclusion through different entryways are described by Figure 3. This, coupled with steep arrival increments for the new qualification of CfS approved substances (eight in 2020), is generating an increase in HRI1, directly linked to CfS number. The increase in HRI1 is a worrying sign as the expectation and goal was for a decrease of this value over time (in terms of the number of risky substances and corresponding sales volumes).

### 3. Future evolution

The quantity of CfS is still high and the currently observed decreases are not efficient, although twenty-eight CfS have been removed by various means. The ongoing renewal processes for a few CfS are not going to decrease radically the total number of CfS, since the criteria for endocrine disruptors are now published,<sup>40</sup> and already seven new ones have been qualified for the CfS list in 2020, and other new CfS qualifications will clearly occur.<sup>41</sup> However, a significant decrease in CfS numbers may occur in 2021 as a lot of qualified CfS were approved for ten years in 2011 at the entry of the PPP Regulation. Perspectives are given in Tables 4 and 5. Short-term perspectives for CfS with end of approval before July 2021<sup>42</sup> are given in Table 4 (along with an attempt to predict outcomes from implementing regulation drafts, EFSA outcomes and Plants, Animals, Food and Feed (PAFF) Committee agendas), while mid-term perspectives for CfS are detailed in Table 5. The existence of a recent EFSA outcome is a good indication of the willingness for renewal from the applicant, while the number of extensions of approval is also a good indication of an ongoing evaluation process for renewal, at least from the point of view of the applicant. The number of extensions of approval voted for in 2020<sup>43</sup> is detailed in order to give greater clarity regarding the issues facing these CfS. Thus, in 2021, twenty-seven CfS were pending, with a possible end of approval; however, massive extensions of the approval periods for these CfS were voted for in January and March 2021. At the same time, some CfS exits are ongoing, such as

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<sup>38</sup> MC Vekemans and PA Marchand, "The European pesticides Harmonised Risk Indicator 1: a clarification of its displayed rendering" (2021) Risk Analysis, accepted with corrections for publication.

<sup>39</sup> PA Marchand, "Basic substances: an approval opportunity for Low Concern Natural Products under EU pesticide regulation" (2015) 71(9) Pest Management Science 1197.

<sup>40</sup> Commission Regulation (EU) 2018/605 amending Annex II to Regulation (EC) No 1107/2009 by setting out scientific criteria for the determination of endocrine disrupting properties. C/2018/2229. OJ L 101/33.

<sup>41</sup> EU 2021, *supra*, notes 31 and 32.

<sup>42</sup> EU Pesticides Database, *supra*, note 8.

<sup>43</sup> EU 2020, *supra*, notes 29–31.

**Table 4.** Candidates for substitution (CfS) end of approval pending in 2021: short-term perspectives for CfS.

Approved in Part A/B	End of approval <sup>44</sup>	Extension of approval <sup>45</sup>	Probable end
<i>Bromadiolone</i>	31 May 2021	0	No recent EFSA outcome, <b>end of approval</b>
<i>Carbetamide</i>	31 May 2021	0	CfS qualified in 2020, no recent EFSA outcome, <b>end of approval</b>
<i>Cyproconazole</i>	31 May 2021	0	no recent EFSA outcome, <b>end of approval</b>
<i>Myclobutanil</i>	31 May 2021	0	No recent EFSA outcome, <b>end of approval</b>
<i>Famoxadone</i>	30 June 2021	6 including 1 in 2020	<i>Ongoing non-renewal</i>
Profoxydim	31 July 2021	0	No recent EFSA outcome, potential end of approval

Italics represent an ongoing reglementary event.

Bold text represent a definitive issue.

EFSA = European Food Safety Authority.

for alpha-cypermethrin, which was recently renewed in 2019<sup>46</sup> and is now proposed for withdrawal.<sup>47</sup> Again, the CfS amount is increasing, with the active substance cypermethrin qualified as a CfS during the undergoing of renewal in 2021.<sup>48</sup>

Table 5 details CfS with end of approval before the end of 2021 (from July to December), including the recent extension to the approval period. It also shows the number of extensions<sup>49</sup> of approval for each CfS for similar reasons as in Table 4. Conclusions regarding the issues are more uncertain in Table 5 than in Table 4, but clearly extensions of approval represent a good indication of the willingness of the applicants to pursue renewal, especially those voted for twice in 2020 and 2021.

All of these considerations increase constantly the number of non-desired substances in specific crop protection systems (labelled with “no pesticide residues”, labelled with no carcinogenic, mutagenic and reprotoxic (CMR) substances, IPM, organic production, etc.), and their non-uses may also impact their availability for plant protection due to

<sup>44</sup> EU Pesticides Database, *supra*, note 8.

<sup>45</sup> EC 2011, *supra*, note 5.

<sup>46</sup> EU 2019, *supra*, note 25.

<sup>47</sup> Exchange of views of the Committee on a draft Commission Implementing Regulation (EU) withdrawing the approval of the active substance alpha-cypermethrin in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending Commission Implementing Regulation (EU) No 540/2011. (SANTE/12548/2020) during Standing Committee on Plants, Animals, Food and Feed Section Phytopharmaceuticals – Legislation of 25–26 January 2021.

<sup>48</sup> Exchange of views of the Committee on a draft Commission Implementing Regulation (EU) concerning renewing the approval of the active substance cypermethrin as a candidate for substitution in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011 (Draft Review Report SANTE 2018-11527 Rev. 6). (SANTE/10590/2021) during Standing Committee on Plants, Animals, Food and Feed Section Phytopharmaceuticals – Legislation of 19–21 May 2021.

<sup>49</sup> EC 2009, *supra*, note 1; EC 2011, *supra*, note 4.

**Table 5.** Mid-term end of approval for candidates for substitution (CfS) in 2021 and recently extended to 2022.

<b>Approved in Part A/B</b>	<b>End of approval<sup>50</sup></b>	<b>Extension of approval<sup>51</sup></b>	<b>Probable end</b>
Triazoxide	30 September 2021	0	
Chlorotoluron	31 October 2021	5 including 1 in 2020	
Fludioxonil	31 October 2021	3 including 1 in 2020	
Flufenacet	31 October 2021	5 including 1 in 2020	
Quizalofop-P-tefuryl	30 November 2021	1	
8-Hydroxyquinoline, including oxyquinoleine	31 December 2021	0	
Difenoconazole	31 December 2021	3	
Etofenprox	31 December 2021	0	
Fluquinconazole	31 December 2021	0	
Lenacil	31 December 2021	3 including 1 in 2020	
Nicosulfuron	31 December 2021	3 including 1 in 2020	
Tri-allate	31 December 2021	0	
Dimoxystrobine	31 January 2022	5 including 1 in 2021	Recent extension of approval until 31 January 2022
Oxamyl	31 January 2022	4 including 1 in 2021	Recent extension of approval until 31 January 2022
Metconazole	30 April 2022	5 including 1 in 2021	Recent extension of approval until 30 April 2022
Pirimicarb	30 April 2022	5 including 1 in 2021	Recent extension of approval until 30 April 2022
Ziram	30 April 2022	6 including 1 in 2021	CfS (ED) properties contested, potential for renewal
Flurochloridone	31 May 2022	1 in 2021	Recent extension of approval until 31 May 2022
Flumioxazin	30 June 2022	7 including 1 in 2021	Recent extension of approval until 30 June 2022
Metribuzine	31 July 2022	5 including 1 in 2021	
Tebuconazole	22/8/31	3 including 1 in 2021	

ED = endocrine disruptor substance.

decreases of sales,<sup>52</sup> complications in renewals and a global desire to abandon the use of these substances.<sup>53</sup> Therefore, when looking at Table 4, it is clear that a large number of

<sup>50</sup> EU Pesticides Database, *supra*, note 8.

<sup>51</sup> EC 2011, *supra*, note 5.

<sup>52</sup> Vekemans and Marchand, 2021, *supra*, note 38.

<sup>53</sup> MR Ragaganni, M Magliuolo, M Picciolo, L Nencini, T Galassi and F Mazzini, "Future availability of pesticides in the integrated pest management agricultural programme in Italy in accordance with the application of the new European Regulation 1107/2009 concerning the placing of plant protection products on the market: impact of the application of

CfS may be suppressed through re-evaluation processes or abandoned by applicants in 2021, this now being effective for bromadiolone, carbetamide and cyproconazole, whose approval ends without regulatory event.<sup>54</sup> Accordingly, in the second batch of CfS taken into consideration in 2021 (Table 5), the issue may also lead to quite a few ends of approval or non-renewals, such as for famoxadone. Indeed, it is also quite confusing to observe in the same PAFF Committee an extension of the period and a proposal for non-renewal or a suppression of the extension of the period, giving rise to an end of approval, but this may be the result of a renewal application withdrawal from the applicant side after the first results of re-evaluation.<sup>55</sup> Finally, these constraints may trigger an effective removal of dangerous pesticides and a real “substitution” of these pesticides corresponding to a paradigm change, including an agroecology approach in order to reduce the dependence on chemical pest control, as well as the adoption of higher-level IPM methodologies or increasing interest in organic farming.<sup>56</sup> However, these choices and new constraints may also contribute to a cost increase for moving from crop protection using traditional chemicals to biocontrol agents, as mentioned previously.<sup>57</sup>

## V. CONCLUSIONS

This study has documented the overall evolution of CfS substances. Firstly, the legislator’s initial desire to introduce this new category of active substances was respected. Secondly, endocrine disruption criteria were published, increasing the total amount of substances granted CfS status. We show that although ninety-one CfS are listed in the EU Pesticides Database (approved or not), ninety-four were actually granted this status from 2014 to 2020 through regulation or during evaluation processes for approval or renewal. However, the slow growth of biocontrol substances included in Implementing Regulation (EU) No 540/2011 (EC 2011) did not allow for an acceleration of the disappearance of the corresponding targeted CfS. The massive initial entry followed by continuous CfS qualifications is maintaining a high level of still-approved CfS (sixty active substances), which was not necessarily the initial intention. Thus, Article 24 was effective at targeting active substances of concern, but was insufficient to remove them from use in practice according to Sustainable Uses of Pesticides Directive EC No 128/2009 (SUD) (EC 2009b), since only thirty CfS were removed. The actual amount of approved CfS may decrease rapidly in 2021 since approvals for ten years in the PPP Regulation occur in 2011 (EC 2009), and dozens of substances are under renewal procedures. The

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cut-off criteria and selection criteria for substances that are candidates for substitution. Report RT/2011/8/ENEA (2011) Agenzia Nazionale per le Nuove tecnologie, l’Energia e lo Sviluppo economico sostenibile (ENEA) 1.

<sup>54</sup> EU Pesticides Database, *supra*, note 8.

<sup>55</sup> EU 2021, *supra*, note 32.

<sup>56</sup> J Riedo, FE Wettstein, A Rösch, C Herzog, S Banerjee, L Büchi et al, “Widespread occurrence of pesticides in organically managed agricultural soils – the ghost of a conventional agricultural past?” (2021) 55(5) *Environmental Science and Technology* 2919.

<sup>57</sup> MM Steingrimsdóttir, A Petersen and P Fantke, “A screening framework for pesticide substitution in agriculture” (2018) 192 *Journal of Cleaner Production* 306.

implementation of the endocrine disruptor criteria will also be a triggering factor, although it could lead to new CfS approvals.<sup>58</sup> The constant and massive decline in regular active substances or CfS (more than eighty in fewer than four years) and the loss of corresponding usages were not anticipated nor followed by substantial replacement of them with biocontrol agents, but more agroecology-compatible tools may overcome the pure plant protection product solution against bioaggressors.

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<sup>58</sup> EU 2018, *supra*, note 40.