



Article

EU Chemical Plant Protection Products in 2023: Current State and Perspectives

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Abstract: Agrochemicals are synthetic or hemi-synthetic crop protection substances which are supervised by the EU Regulation EC 1107/2009, which give rise to plant protection products (PPP) with market authorizations. Most of these active substances of chemical origin were transferred from the previous Annex I of Directive 91/414/EEC to Part A of Regulation EU 540/2011, with newly approved active substances mainly being listed in Part B or E, while renewed substances were moved from Part A to Part B or E. In this study, approved agrochemicals from the early part of 2023 are organized into categories, families, functions, usages, treated crop categories, regulatory characteristics, and maximum residue limits (MRLs). Perspectives regarding their evolution are also described together with pending approvals.

Keywords: Regulation EC 1107/2009; active substances; plant protection products (PPP); chemicals

1. Introduction: The Chemical Viewpoint

Although natural compounds from plant or natural origin have long been used for crop protection [1], around the Second World War [2] chemicals massively supplanted previous plant protection products [3], even including some natural minerals which were already produced by industrial-scale chemistry such as copper compounds [4]. Plant protection products (PPP) such as active substances (AS) mainly of chemical origin increased in the second part of 20th century up to more than 1250 authorized plant protection products, finally reducing to 556 AS [5] by the end of the previous Directive 91/414/EEC, before the entry into force of the new PPP Regulation EC 1107/2009 [6].

Many challenges [7,8] and criticisms [9] have been directed at agrochemicals, even though developments in their evaluation and limitations in their usages are constantly increasing [10–12]. Although not specific to synthetic pesticides, the fight against resistance is one issue; the main challenge for these chemicals is the goal of reducing their use, as highlighted in many EU programs, i.e., Green Deal and current Sustainable Use of Pesticide Regulation (SUR). This reduction should not be understood only as a reduction in doses, but also as a reduction in uses, impact [11,13,14], residues, and unintended effects. Lastly, this goal is translated in practice by a reduction in the number of substances, which albeit not the main object of the initial criticisms, is the practical effect.

Even though the past developments in the reduction in the use of agrochemicals is well documented [5], the perspective of their pending evolution is important for understanding further likely plant protection developments in the near future. For this analysis, centered on an actual fingerprint extrapolated in early 2023, explained by the previous modifications [5], we can trace a direction and imagine probable scenarios for the next few years. On the basis of previous data, augmented with the characteristics of chemical AS, values for each AS were determined for agrochemicals. The initial values and data were crops, functions, all regulatory events including dates of approval, number of extensions, number of renewals, legal end date of approval, parts A to E of Implementing Regulation (EU) No. 540/2011 [15,16], initial and actual maximum residue limits (MRLs), and MRL



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class [5]. Subsequently, new data has been added, such as AS category qualifications such as succinate dehydrogenase inhibitor (SDHI) fungicides and neonicotinoids insecticides (NN). Later, AS status, i.e., low-risk candidates for substitution and basic AS, was added. For other purposes, organic production (OP) status was then listed together with “transformed” AS characteristics, corresponding to natural or biorational AS being further transformed (i.e., UV-protectant moiety), which is important for this specific allowance in OP. Therefore, this update, compared to our previous work on biocontrol agent (BCA) AS, allows us to categorize agrochemicals as closely as possible in this paper.

It is indeed important to measure and trace developments with these chemical AS in order to anticipate their gradual, even inevitable disappearance, in view of recent analyses [5]. Clearly, this perspective can and should boost substitution efforts, in order to avoid arriving at situations of orphan uses and impasse, firstly by BCA AS, and then probably without chemical AS in the longer term. It is clear that the BCA AS, particularly living organisms, are likely to lower the pressure on ecosystems, which is highly desirable.

1.1. Definitions

Active substances (AS) are all phytopharmaceutical active materials (i.e., active substances) under the PPP EC Regulation 1107/2009 (Art. 2) [6], including chemicals, microorganisms, and semiochemicals, which confer a general or specific action against organisms that are harmful to agricultural production or to plants, parts of plants, or plant products. These active substances are further classified into categories (A to E) that correspond to the relevant parts of Implementing Regulation (EU) No. 540/2011 [15].

Pesticides, defined as plant protection products, are formulated active substances (phytopharmaceuticals) adopted and marketed in the EU legislation/regulation, although pesticides in the literature sometimes also include biocides. Market authorizations under the PPP regulation are further considered at the national level in European countries, although zonal authorizations are described in this PPP regulation [6].

Biorational AS or biocontrol agents (BCA) AS are semiochemicals (even synthetic AS equivalent to natural sources), substances of natural origin (mineral, plant, microbial, or animal), and substances of biological origin (microorganisms). Generally, when considering the global sum of PPPs, AS strictly structurally identical to natural substances, even obtained synthetically, such as chemical mediators/semiochemicals, are considered as BCAs [6]. By extension, a few AS obtained by light or biological transformation, such as vinegar or calcinated kaolin, and purified to single-molecule AS (thymol) are considered to be BCA AS.

Agrochemicals are, therefore, exogenous PPPs from chemical/synthetic origin and are distinguished from other PPPs of natural origin, although they are active substances with the same regulatory status and approval pathway. Agrochemical AS are opposed to these BCA AS by their exogenous status, and they do not occur naturally in environment. A few PPPs containing exogenous agrochemical AS in traps with no contact with crops (i.e., deltamethrin) are considered as BCA AS and are even allowed in organic production [17] precisely because they are only used in traps.

All approved active substances (AS) with a defined function (Table 1), such as herbicide (HB) and insecticide (IN), corresponding to their mode of action (MOA) have been approved through the same regulatory pathway since 2011 (submission, evaluation, vote, approval, and then market authorization) and are only distinguishable by their regulatory position [15] in Regulation 540/2011 (Parts A to E) granting them a different duration of approval (from 7 to 15 years) and different conditions of access to market authorization. There are all **active substances** (AS), although their specific status (low-risk, basic, candidate for substitution, or “regular” active substance) is used for convenience [6]. Along regular PPP market authorization, only low-risk PPPs are mentioned as low-risk products, while basic substances have no market authorization.

Table 1. Functions of the chemicals.

Usages	Chemical	Rank
Fungicides	79	2
Insecticides	37	3
Elicitors	1	9
Herbicides	90	1
Plant growth regulators	21	4
Molluscicides	1	9
Nematicides	4	6
Plant activators	1	9
Repellents	2	8
Acaricides	14	5
Attractants	0	14
Rodenticides	3	7
Soil treatments	1	9
Desiccants	0	14
Bactericides	1	9
Total	255	-

Plant growth regulators (PGs) are PPP AS in EU with specific MOA, which are used to modify plant growth such as increasing branching, suppressing shoot growth, increasing frequency of flowering, removing excess fruit, or altering fruit maturity [16]. Similarly, plant activators (PAs) at EU PPP regulation are substances that activate a plant's immune system in response to invasion by pathogens.

Elicitors or plant strengtheners (ELs) are compounds or mixtures of compounds, different from plant growth regulators (PGs) or plant activators (PAs), that can be applied to cultivated plants, and then managed by PPP regulation, in order to “boost their vigor, resilience, and performance” [18,19].

1.2. Data Mining

All these categories are based on AS functions (i.e., IN, FU, etc.) and linked agricultural uses [20], previously indicated on each AS page in the EU Pesticide Database v2.2 but now removed in the latest revision (v3) of this database [21], which also indicates all the implementing regulations corresponding to the regulatory movements of the AS (approval, renewal, extension, and modifications) and its MRL.

Agricultural uses [20] or usages in plant protection are defined by cultivation practices, roughly managed by the pairing of the crop vs. bioaggressor (insect/pathogen), and linked to function; they are listed in the corresponding good agricultural practices (GAP) table in the review reports in the EU Pesticide database v3 [21].

2. The Regulatory Standpoint

Newly approved agrochemical AS (chemical active substances) ($n = 275$) under the new PPP Regulation in June 2011 were all directed to Part A of Regulation EU 540/2011 [15,22]; the chemicals approved later than this are mainly listed in Part B or E, while renewed substances were moved from Part A to Part B or E depending on their status. After an important increase until 2018, their negative evolution [5] was triggered by the removal of the most risky targeted substances, especially endocrine disruptors, and candidates for substitution (CfS) driven by Article 24 of the PPP regulation [23].

The actual number of approved agrochemicals has now reduced to 234 AS with many non-renewals, some withdrawals, and no more newly approved chemicals since 2019 [5]. The last EU candidates to be dismissed were 1,3-dichloropropene and chloropicrin, while there is an ongoing application (napropamid-M) being voted for non-approval. The published EFSA (European Food Safety Authority) evaluation outcomes report being somewhat negative for some ongoing applications about EU pending active substances (i.e., dimethyl disulfide), or even adverse for asulam-sodium, which already exhibits endocrine disruption

properties; therefore, approvals of these AS are also doubtful. Other EU pending chemical active substances including BAS 684 H, benzobicyclon, bixlozone, dimpropyridaz, fenquinotrione, fluazaindolizine, fluindapyr, fluoxapiprolin, indaziflam, inpyrfluxam (S-2399), ipflufenquin, isoflucypram, metyltetraprole, OptiCHOS, picarbutrazox, pydiflumetofen, and florylpicoxamid have no published EFSA evaluation outcome; thus, no prognosis can be surmised for them.

3. Chemicals, All to Be Banned?

Synthetic pesticides and agrochemicals are often decried with good evidence for their toxicity and ecotoxicity for some families [24–27], but sometimes without understanding the reality behind the word “chemicals”. First of all, synthetic agrochemicals are obtained from petroleum, also a natural substance [28], even if, in the collective unconscious, it is not perceived as such, and the undifferentiated opprobrium against “chemicals” is not always justified [17]. In particular, in certain specific cases, pesticides are not sprayed onto crops without an MRL [29] and biomimetic substances, such as semiochemicals and some synthetic/hemisynthetic equivalents of natural substances, are even allowed in organic production (OP) [30]. Thus, it is rather the concept of natural/present in nature/habitual substance versus substance exogenous to the environment that must be considered [31].

4. Current Status

Agrochemicals used for all crop usages and including all functions of crop protection as previously described [30] still represent more than half of the allowed EU pesticides (52%). The main families are sulfonylureas, aryloxyacides, carbamates, triazoles, pyridines, pyrethrins, and diphenyl-ethers, while organochlorines and organo-phosphorates are in decline.

4.1. Functions

Although many herbicides have been removed [5], this function is still the most abundant group among the synthetic chemical AS (Table 1). Appearing just behind the fungicides in the table and far behind the insecticides are the plant growth regulators and the acaricides, along with some representatives of other functions (Figure 1).

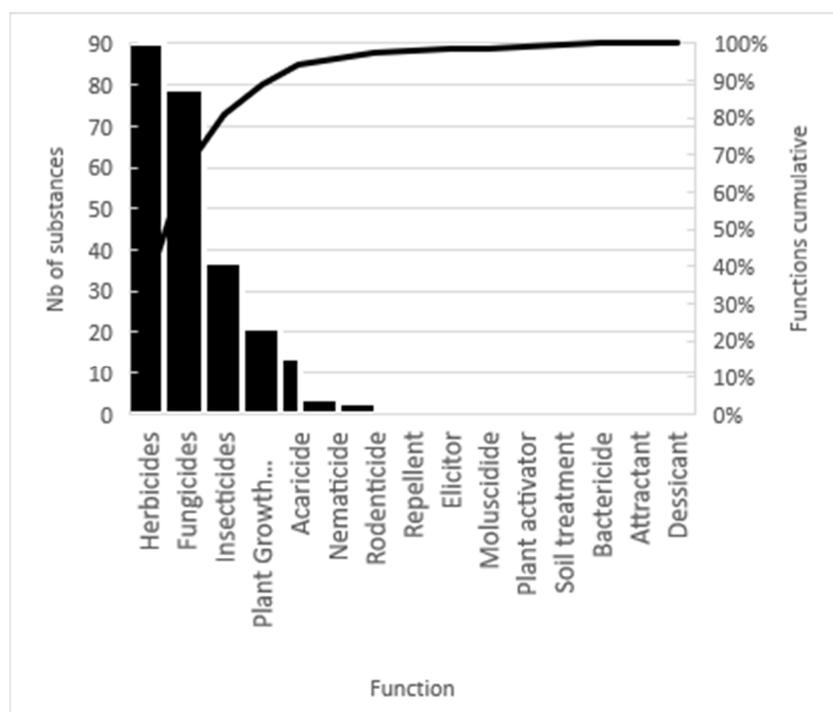


Figure 1. Cumulative functions of chemicals.

With 255 functions for 234 chemical AS, this represents barely more than one function per substance, and the cumulative curve (Figure 1) is decreasing rapidly; the cumulative curve is relatively restricted to four functions. The rank of the functions is also indicated in Table 1. It is remarkable that whole sections of plant protection needs are barely if at all addressed by chemical AS (i.e., soil treatment ST), desiccant DE, and bactericide BA), while others are over-represented (fungicides FU and insecticides IN).

It is quite noticeable that whole sections of plant protection such as attractants, rodenticides, soil treatments, desiccants, bactericides, molluscicides, nematocides, plant activators (PAs), repellents (ERs), or even elicitor (ELs) are not considered currently by chemical AS, leading to many orphan uses for chemical AS. We must add a caveat to this conclusion that it does not only mean that they have not been considered by the chemical AS in the past, but that the chemical AS which previously possessed these functions were not renewed or have never been approved and used (or not) under derogations (Articles 53 of PPP regulation).

4.2. Crop Usages

Agrochemicals used for all crop usages appear relatively balanced compared to functions (Table 2, Figure 2), with a slight bias toward market gardening and arable crops. With 529 crop usages for 234 chemicals, this represents about 2.25 crop uses per substance. The rank of these functions is also indicated in Table 2.

Table 2. Crop usages of the chemicals.

Crop Usages	Chemical	Rank
Viticulture	70	5
Arboriculture	69	6
Market gardening	120	1
Horticulture	73	4
Cereals	82	3
Arable crops	115	2
Total	529	-

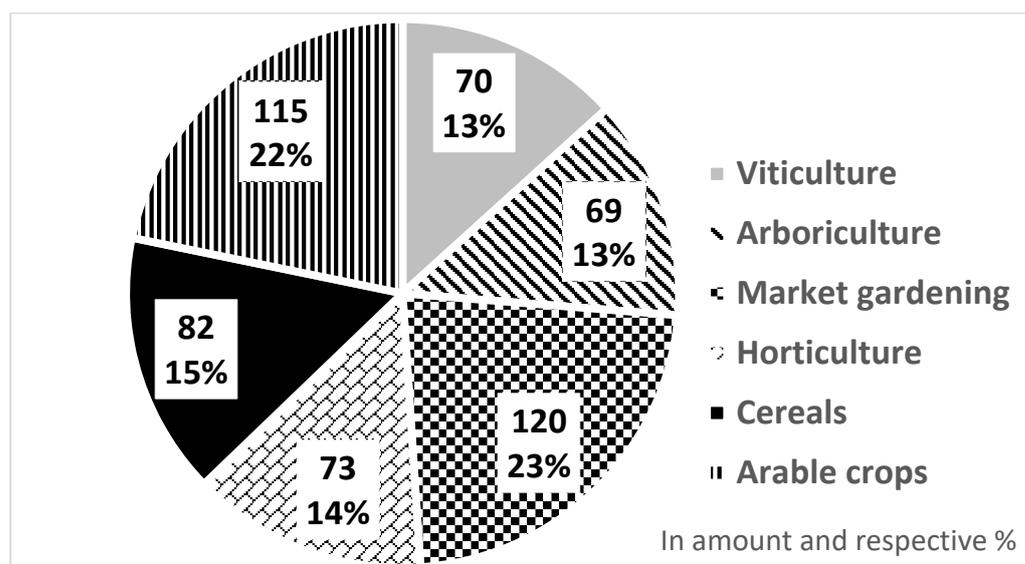


Figure 2. Crop usages of chemicals as a percentage.

Half of the agrochemical substances are dedicated to market gardening and arable crops (one-fourth each), while about one-seventh each are used for viticulture, arboriculture, horticulture, and cereal crops (Table 2). This proves that no crop is neglected by chemical substances; conversely, since these chemical AS are decreasing, many uses will be lost with each substance (>2 per AS).

4.3. Links between Functions and Crop Usages

Repertition of crops is largely accounted for by four crops corresponding to 13–15% of the chemicals and two crops with one-fourth of the agrochemicals. These analyses and comparisons are more easily understandable with a cross-sectional matrix of functions and crops (Table 3).

Table 3. Comparison matrix of the chemicals between functions and crop usages.

Crop/Function *	Viticulture	Arboriculture	Market Gardening	Horticulture	Cereals	Arable Crops
FU	42 (2, 1)	23 (5, 1)	48 (1, 1)	22 (6, 1)	28 (3, 2)	27 (4, 2)
HB	14 (6, 2)	16 (5, 3)	33 (3, 2)	22 (4, 1)	38 (2, 1)	63 (1, 1)
IN	10 (6, 3)	18 (2, 2)	24 (1, 3)	18 (2, 3)	10 (6, 3)	12 (4, 3)
PG	5 (6, 4)	5 (6, 4)	7 (2, 4)	6 (3, 4)	6 (3, 4)	11 (1, 4)

* FU: fungicide, HB: herbicide, IN: insecticide, PG: plant growth regulator. Number of chemical active substances (rank in function, rank in crops); the most important values are in bold.

Fungicides are mostly dedicated to market gardening and viticulture uses; herbicides are mainly used for arable crops, cereals, and market gardening; insecticides are mainly used for market gardening, arboriculture, and horticulture; plant growth regulators are slightly more devoted to arable crops and market gardening. In a similar manner, viticulture and market gardening are primarily covered by fungicides, arboriculture and horticulture are primarily covered by insecticides, and cereals and arable crops are primarily covered by herbicides. These disparities are materialized by two ranks in Table 3 for crops and functions. Table 3 shows that some crops require either some functions (viticulture) or a varied panel of PPP solutions (arboriculture and horticulture).

4.4. Maximum Residue Limits

Agrochemical residues are also an issue of concern, with maximum residue limits (MRLs) being defined to limit their toxicological and ecotoxicological impacts as PPPs. They are defined for each active substance and most crops, at least by default [5,29,30]. Each MRL is affixed to one of the annexes of Regulation EC 396/2005, although very few (around 1%) chemicals are without an MRL (Annex IV) or are assigned an MRL by default (0.01 mg/kg) in Annex V (3%), while the vast majority (95%) of chemicals with defined MRLs are assigned to Annexes II and III (Figure 3). Therefore, the initial issue of concern regarding chemical PPP residues is clearly validated by the reality of the MRLs for a large majority.

These results confirm the general impression that almost all chemical AS produce residues of concern. These residues and their metabolites are also largely responsible for non-renewals of approved chemical AS, and even sometimes for initial non-approvals in Europe (i.e., 1,3-dichloropropene and chloropicrin). This applies here to chemicals AS agricultural pesticides, but similar fears are also expressed for the global change [32].

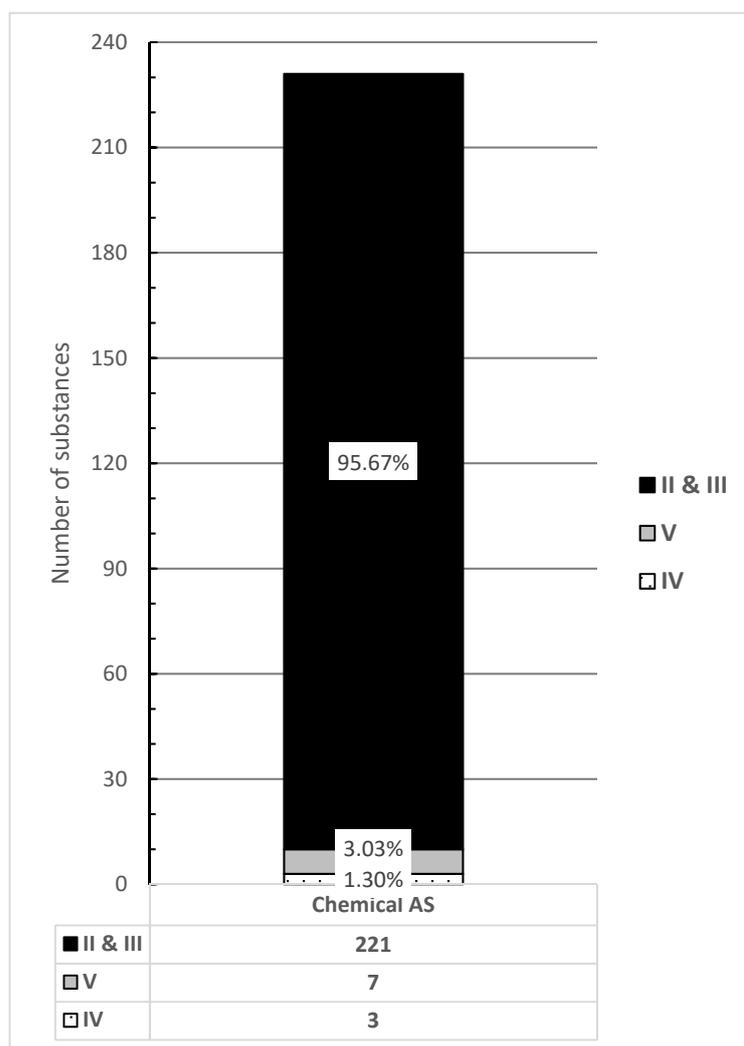


Figure 3. Maximum residue limits of agrochemicals.

5. Future Trends for Agrochemicals

With few de novo potential approvals and no actual approvals since 2019 [5], the constant pressure on some families of synthetic pesticides, i.e., neonicotinoids and SDHI [26,33,34], and the negative EFSA outcomes for the most recently evaluated chemicals [29], the evolution of agrochemicals next year is likely to reflect a further decrease in the number of approved active substances for this plant protection category.

The latest AIR (active ingredient renewal) programs [5] will affect many chemicals (ca. 40 AS for AIR V and VI plus overdue substance evaluation), with many approvals ending in 2023 and 2024. Subsequently, many chemical active substances are undergoing EU renewal with many charges and pressures bearing on them. These questions are mainly linked to substances of concern, starting with candidates for substitution (CfS) [23] and potential or suspected endocrine disruptors. Some chemical AS are already programmed for withdrawal (i.e., ipconazole), non-renewal (i.e., dimoxystrobin and oxamyl), official vote for non-renewal (i.e., benfluralin in December 2022), or offline status in the foreseeable future (i.e., ziram, metam, prosulfuron, prosulfocarb, and flurochloridone), but clearly there may be more.

The evolution of the curve, even if real over the 2017–2022 period (each semester (S)) with a particularly high R^2 regression coefficient, is directly linked to the 4 years since 2018 with an average loss of almost 20 synthetic chemical AS per year. This extrapolation is not a strict forecast, as the same decline for 2023 cannot yet be predicted, although the elements

highlighted in this work tend to suggest that it is a good forecast of developments, with only 224 chemical AS predicted to be in use by the first semester of 2023.

In fact, 128 synthetic chemical AS have an implied end of approval in 2023 (Table 4), with many chemical AS (97) due to end in 2022 being postponed for a year. This makes 2023 the year involving the greatest number of renewal considerations (end of approval). These adjournments are responsible for the stagnation and tapering off of the curve in 2023.

Table 4. Chemical AS end of approval year in number.

Year	Number of Chemical AS Concerned
2023	128
2024	46
2025	23
2026	4
2027	1
2028	2
2029	4
2030	5
2031	6
2032	9
2033	7
2034	5
Total	240

As a result of the end of approvals and if we consider that only 50% of these chemical AS will not be renewed, this leaves fewer than 120 approved chemical AS in the next 10 years; hence, from 234 in 2022, in a few years, there will only be around 115 chemical AS left. Therefore, as negative as the curve in Figure 4 may appear, it seems to be a relatively reasonable projection. Indeed, of the 340 total chemical AS originally approved, only 234 are still approved (a decrease of 106), and, of the chemical AS that have been re-evaluated, 57 have been renewed and are still approved, while, 108 have not been or will not be renewed. Since 2011, this rate of non-renewal has, therefore, been 50% overall for chemical AS, confirming our pessimistic forecast. An analysis comparing the cases to the substances in OP from the toxicological point of view is moreover in progress, unsurprisingly coming to a similar conclusion [35].

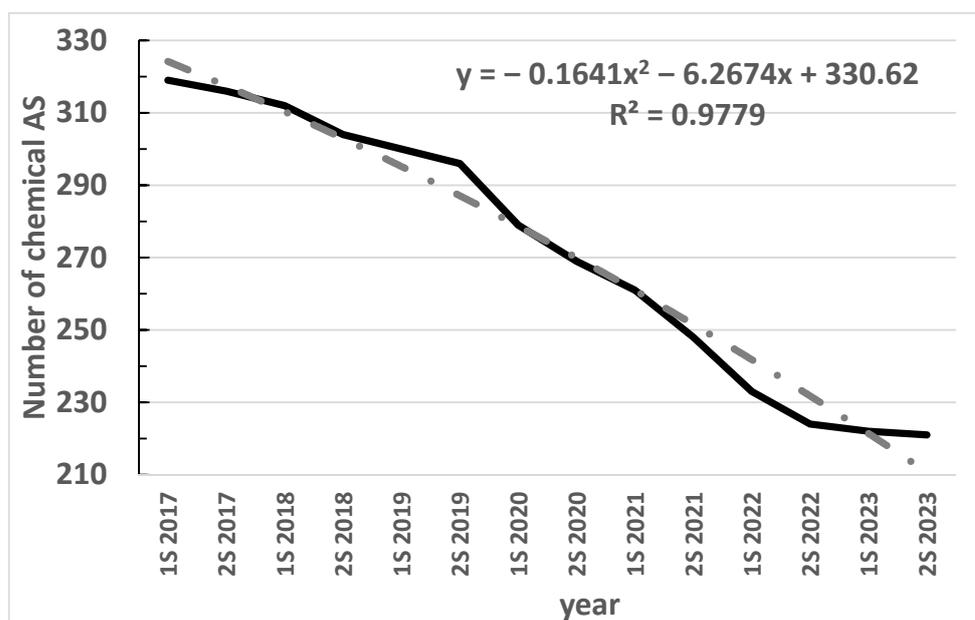


Figure 4. Hypothetical evolution of synthetic agrochemicals.

In parallel, in order to provide elements to justify these negative forecasts, we can highlight the **high** number of extensions of approval periods for chemical AS due for re-evaluation, especially in 2022 (97) or already published in 2023 (49), and the systematic request to study the endocrine-disrupting (ED) properties of all AS (including some BCA AS), which will inevitably generate critical results for ED criteria for a significant number of chemical AS, likely leading to further non-renewals. AS with end of approval in the next 2 years are listed in Table 5. In addition to the information about these 97 ongoing renewal processes in 2022, 166 chemical AS have their end of approval in 2023 and 2024.

Table 5. Chemical AS with end of approval year in 2023 or 2024.

AS		
1-Naphthylacetamide (1-NAD)	Fenoxaprop-P	Paclobutrazol
1-Naphthylacetic acid (1-NAA)	Fenpropidin	Penconazole
2,5-Dichlorobenzoic acid methylester	Fenpyrazamine	Pendimethalin
2-Phenylphenol	Fenpyroximate	Penoxsulam
6-Benzyladenine	Flonicamid	Phenmedipham
8-Hydroxyquinoline \$	Fluazifop-P	Phosphane
Acequinocyl	Fluazinam	Picloram
Aclonifen \$	Flubendiamide	Pirimicarb \$
Aluminium phosphide	Fludioxonil	Pirimiphos-methyl
Ametoctradin	Flufenacet \$	Prohexadione
Amidosulfuron	Flumetralin \$	Propamocarb
Aminopyralid	Fluometuron \$	Propaquizafop
Amisulbrom	Fluopicolide \$	Proquinazid
Azoxystrobin	Fluopyram	Prosulfocarb £
Beflubutamid	Fluoxastrobin	Prosulfuron £,\$
Benfluralin #	Flurochloridone £,\$	Prothioconazole
Bensulfuron	Fluroxypyr	Pyraclostrobin
Benthiavalicarb	Flutolanil	Pyridaben
Benzovindiflupyr \$	Folpet	Pyrimethanil
Bifenox	Formetanate	Quinmerac
Boscalid	Fosetyl €	Quizalofop-P
Bromuconazole	Fosthiazate	Quizalofop-P-ethyl
Bupirimate	Glyphosate	Quizalofop-P-tefuryl
Buprofezin	Halosulfuron-methyl \$	Rimsulfuron €
Calcium carbide	Hexythiazox	S-Metolachlor
<i>Captan</i> *	Hymexazol	Sintofen
Chlorantraniliprole	Imazalil	Sodium 5-nitroguaiacolate
Chlormequat	Ipconazole #,\$	Sodium o-nitrophenolate
Chlorotoluron \$	Isoxaben	Sodium p-nitrophenolate
Clethodim	Kresoxim-methyl	Sodium silver thiosulphate
Clodinafop €	Lenacil \$	Spiromesifen
Clofentezine	MCPA	Spirotetramat
Clomazone	MCPB	Spiroxamine
Cycloxydim	Magnesium phosphide	Sulcotrione \$
Cyflufenamid	Malathion €	Sulfuryl fluoride
Cyflumetofen	Mandipropamid	Tebuconazole \$
Cymoxanil	Mecoprop-P	Tebufenozide
Cyprodinil \$,€	Mepanipyrim €	Tebufenpyrad \$
Daminozide	Mepiquat	Tefluthrin
Dazomet	Metaflumizone	Tembotrione \$
Deltamethrin	Metalaxyl \$	Terbuthylazine
Dicamba	Metaldehyde	Tetraconazole
Dichlorprop-P €	Metam £,\$	Thiencarbazone-methyl
Diclofop \$	Metamitron	Tri-allate \$
Difenoconazole \$	Metazachlor	Triclopyr €

Table 5. Cont.

AS		
Diflufenican	Metconazole ^{,\$,€}	Triflusulfuron
Dimethachlor	Metiram	Trinexapac [€]
Dimethomorph	Metobromuron	Triticonazole [€]
Dimoxystrobin ^{,\$,#}	Metrafenone [€]	Tritosulfuron
Dithianon	Metribuzin ^{\$}	Valifenalate
Dodemorph	Metsulfuron-methyl ^{\$}	Zinc phosphide
Dodine	Milbemectin	Ziram ^{€,\$,€}
Esfenvalerate ^{\$}	Napropamide	lambda-Cyhalothrin ^{\$}
Ethephon	Nicosulfuron ^{\$}	tau-Fluvalinate
Etofenprox ^{\$}	Oxamyl ^{,\$,#}	
Fenazaquin	Oxyfluorfen ^{\$}	

* Ongoing proposed renewal, # non-renewal or withdrawal proposed to vote, [€] compromised renewal, ^{\$} candidates for substitution AS, [€] ongoing extension of approval period.

This huge quantity of chemical AS which are rapidly approaching the end of their approval (Tables 4 and 5) are constantly the subject of approval extensions [5] due to the slowness of the AIR programs and the end of the first decade after entry into force of EC Regulation 1107/2009 and Implementing Regulation EC 540/2011. The number of extensions of approval period has already continuously increased up to a maximum of seven times for 20 chemical AS (including ongoing extension of approval period [€] in Table 5) and eight time for 1 chemical AS. Since the duration of period extensions are not limited to 1 year each, the maximum duration of extensions is currently around 10 years, which is the initial duration of an approval. It is worth mentioning that these regulatory excesses are not being reserved only for chemical AS, and that the values are almost as excessive (seven times for a maximum of 9 years) for BCA AS.

In conclusion, the evolution is indeed toward the reduction in chemical substances by the combined effects of a drying up of new chemical AS arrivals and the suppression of existing ones, without the arrival of any new types of active substances compensating for this overall and inexorable decline in chemical AS, especially candidates for substitution AS [22]. This decline in chemical AS is also a major contributor to the decline in total PPP AS. Indeed, the number of replacement candidate AS, especially BCA AS, is not so high (5–6 per year), even though their approval potential is large; the approval potential of chemical AS is very low. It will no doubt take time; however, after seeing BCA AS exceeding 50% of the total AS well before the year 2025, as predicted in 2018 [33], the total number of chemical AS will continue to decline inexorably, accentuated by the fact that no chemical AS has ever had access to a low-risk status (Art. 22), synonymous with sustainability in the PPP AS panel [36]. Be that as it may, according to these negative well-argued forecasts, of the 234 AS studied here, there will be fewer than 230 before the end of the first half of 2023.

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