Alternatives to neonicotinoids

Herve Jactel, François Verheggen, Denis Thiery, Abraham J. Escobar-Gutiérrez, Emmanuel Gachet, Nicolas Desneux, . Neonicotinoids Working Group

Environment International 129 (2019) 423–429

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Alternatives to neonicotinoids

Hervé Jactel[a,*], François Verheggen[b], Denis Thiéry[c], Abraham J. Escobar-Gutiérrez[d], Emmanuel Gachet[e], Nicolas Desneux[f], the Neonicotinoids Working Group[1]

[a] INRA (French National Institute for Agricultural Research), UMR 1202 BIOGECO, University of Bordeaux, 33610 Cestas, France
[b] Gembloux Agro-Bio Tech, TERRA, Université de Liège, 5030 Gembloux, Belgium
[c] INRA (French National Institute for Agricultural Research), UMR 1065 Save, BSA, ISVV, UMT Seven, Centre de recherches INRA Nouvelle-Aquitaine-Bordeaux, 33882 Villenave d'Ornon Cedex, France
[d] INRA (French National Institute for Agricultural Research), UR 0004 P3F Unité de Recherche Pluridisciplinaire Prairies et Plantes Fourragères, Centre de recherche Nouvelle-Aquitaine-Poitiers, F-86600 Lusignan, France
[e] ANSES, Plant Health Laboratory, Biological Risk Assessment Unit, 49044 Angers, France
[f] INRA (French National Institute for Agricultural Research), Université Côte D'Azur, CNRS, UMR 1355-7254, Institute Sophia Agrobiotech, 06903 Sophia-Antipolis, France

A R T I C L E I N F O

Handling Editor: Frederic Coulon

A B S T R A C T

The European Food Safety Authority concluded in February 2018 that "*most uses of neonicotinoid insecticides represent a risk to wild bees and honeybees*". In 2016, the French government passed a law banning the use of the five neonicotinoids previously authorized: clothianidin, imidacloprid, thiamethoxam, acetamiprid and thiacloprid. In the framework of an expert assessment conducted by the French Agency for Food, Environmental and Occupational Health and Safety to identify possible derogations, we performed a thorough assessment of the available alternatives to the five banned neonicotinoids. For each pest targeted by neonicotinoids use, we identified the main alternative pest management methods, which we then ranked for (i) efficacy for controlling the target pest, (ii) applicability (whether directly useable by farmers or in need of further research and development), (iii) durability (risk of resistance in targeted pests), and (iv) practicability (ease of implementation by farmers). We identified 152 authorized uses of neonicotinoids in France, encompassing 120 crops and 279 pest insect species (or genera). An effective alternative to neonicotinoids use was available in 96% of the 2968 case studies analyzed from the literature (single combinations of one alternative pest control method or product × one target crop plant × one target pest insect). The most common alternative to neonicotinoids (89% of cases) was the use of another chemical insecticide (mostly pyrethroids). However, in 78% of cases, at least one non-chemical alternative method could replace neonicotinoids (e.g. microorganisms, semiochemicals or surface coating). The relevance of non-chemical alternatives to neonicotinoids depends on pest feeding habits. Leaf and flower feeders are easier to control with non-chemical methods, whereas wood and root feeders are more difficult to manage by such methods. We also found that further field studies were required for many promising non-chemical methods before their introduction into routine use by farmers. Our findings, transmitted to policymakers, indicate that non-chemical alternatives to neonicotinoids do exist. Furthermore, they highlight the need to promote these methods through regulation and funding, with a view to reducing pesticide use in agriculture.

* Corresponding author.
E-mail addresses: herve.jactel@inra.fr (H. Jactel), fverheggen@uliege.be (F. Verheggen), denis.thiery@inra.fr (D. Thiéry), abraham.escobar-gutierrez@inra.fr (A.J. Escobar-Gutiérrez), emmanuel.gachet@anses.fr (E. Gachet), nicolas.desneux@inra.fr (N. Desneux).
[1] Romain Bonafos, romain.bonafos@supagro.fr
Robert Delorme, robert-delorme@club-internet.fr
Brigitte Frérot, Brigitte.frerot@inra.fr
Adrien Jean, adrien.jean@anses.fr
Véronique Mironet, veronique.mironet@anses.fr
Farida Ouadi, farida.ouadi@anses.fr
Franck Radet, franck.radet@anses.fr
Eric Thybaud, eric.thybaud@ineris.fr

https://doi.org/10.1016/j.envint.2019.04.045
Received 21 January 2019; Received in revised form 18 April 2019; Accepted 19 April 2019
Available online 29 May 2019

1. Introduction

Since their discovery and identification as a novel class of insecticides in the 1990s, neonicotinoids have become a mainstay of pest management (Nauen and Denholm, 2005). These agonists of post-synaptic nicotinic acetylcholine receptors protect major crops (e.g. corn, soybean, wheat, sugar beet, grapes and orchards) against the damage caused by an extraordinary large array of phytophagous insects, thanks to their systemic action (Jeschke and Nauen, 2008). Five of these neonicotinoid insecticides have been approved in Europe for use as active substances in plant protection clothianidin, imidacloprid and thiamethoxam for seed dressings, and acetamiprid and thiacloprid for treatments of the aerial parts of the plant.

However, an increasing number of studies reporting adverse effects of neonicotinoids on non-target organisms have been published over the last decade (Desneux et al., 2007; Sánchez-Bayo et al., 2016). Almost 45% of the 3374 articles on neonicotinoids published to date (Web of Science search up to March 2019) addressed the issue of negative interactions of neonicotinoids with bees and other pollinators. Neonicotinoids are now considered at least partly responsible for the occurrence of colony collapse disorder syndrome (CCDS) reported in honeybees since the middle of the first decade of this century, either directly or through complex interactions with bee pathogens (Whitehorn et al., 2012; Di Prisco et al., 2013; Tsvetkov et al., 2017; Tadeï et al., 2019; Thompson et al., 2019). Acute or chronic exposure may also have deleterious effects on the fitness and longevity of wild bees (Rundlöf et al., 2015, Woodcock et al., 2017, Anderson and Harmon-Threatt, 2019) and bumble bees (Baron et al., 2017; Wintermantel et al., 2018). Toxicity to humans has also been mentioned, but this issue remains a matter of debate (Zeng et al., 2013; Cimino et al., 2017).

In 2018, the European Food Safety Authority published a comprehensive report (EFSA, 2018), including an updated risk assessment for imidacloprid, clothianidin and thiamethoxam. It concluded that there was science-based evidence implicating neonicotinoids in CCDS in bees and in other threats to the environment (Wood and Goulson, 2017; Cressey, 2017). The field use of these three neonicotinoids was therefore banned in the European Union in 2018, although they may still be used in greenhouses.

Two years before this ban came into force, in 2016, the French parliament was the first in the world to ban the use of neonicotinoids for crop protection (Biodiversity Act, 2016), the ban taking effect in September 2018. At the same time, the French Agency for Food, Environmental and Occupational Health and Safety (ANSES) was commissioned by the French Ministry of Agriculture to evaluate the risks and benefits of alternatives (both chemical and non-chemical) to neonicotinoids. For this purpose, a group of independent scientific experts (referred to hereafter as the expert panel) was mandated by the agency to perform a comprehensive analysis of available alternatives to neonicotinoids for pest management. The objective was to identify any technical problems potentially justifying derogation to the ban in specific cases. For each combination of one neonicotinoid use × one target crop plant × one target pest insect, all alternative pest management methods were identified and ranked in terms of (i) efficacy for controlling the target pest, (ii) applicability (directly useable by farmers or requiring further research and development), (iii) durability (risk of resistance in targeted pests), and (iv) practicability (ease of implementation by farmers). We generated a comprehensive database of available pest management methods, including other classes of insecticides, and identified crop plant × pest insect combinations for which there was a risk of missing an alternative to neonicotinoids. We then considered the possible time lag to the actual delivery of effective pest management methods to farmers, according to the progress made in research, and administrative constraints.

2. Materials and methods

We carried out a two-year (2016–2017) comprehensive review and assessment of all possible alternatives to the five neonicotinoids authorized for insect pest control in the European Union. The *Catalog of Phytopharmaceutical Uses*, from the French Ministry of Agriculture (2017) was used to identify all specific authorized uses of neonicotinoids in France. “Uses” correspond here to the uses of the plant protection products listed in the E-Phy database, managed by ANSES (https://ephy.anses.fr). Uses are individually characterized as a combination of target crop, plant organ and pest insect species (or group of species) (see Table S1 for the list of target pest species). Each target pest was assigned to one of five feeding guilds for further analyses: leaf, wood or bark, flower, fruit or seed, root and sap feeders (Table S1).

We considered eight categories of potential alternative methods.

(1) Other synthetic or natural chemical insecticides, including avermectin, benzoylurea, carbamate, copper compounds, cyromazine, diacyl-hydrazine, diamide, diflubenzuron, etofenprox, fenoxycarb, flonicamid, fludioxonil, indoxacarb, organophosphates, phosmet, pymetrozine, pyrethroid, pyrethrin, pyriproxyfen, spinosad, spinosyns, spirotetramat, sulfur, tebufenozide, tetronic and tetramic acid derivatives;
(2) Biological control with macroorganisms, including predators and parasitoids;
(3) Biological control with microorganisms, including entomopathogenic fungi, viruses and bacteria;
(4) Biological control through farming practices, including intercropping, flower strips, grass strips, hedgerows or windbreaks, beetle banks, banker plants, mulching, soil cover, crop rotation, fertilization, irrigation, tillage, mowing, cutting, landscape planning (to favor local natural enemies or disrupt pest insects);
(5) Use of semiochemicals for mass trapping, mating disruption, repulsion, antifeeding effects, push-and-pull or attract-and-kill techniques (including trapping plants);
(6) Physical methods, including uprooting, pruning, cutting of plants, use of mineral or organic oils, application of thermal, electrical, light, or acoustic treatments, passive or food trapping, physical barriers with nets or trenches;
(7) Genetically improved plant varieties, i.e. pest-resistant varieties produced by classical plant breeding or genetic modification techniques;
(8) Plant defense elicitors.

We used four criteria to rank the alternatives to neonicotinoids: efficacy (E), applicability (A), durability (D) and practicability (P). Due to the lack of published quantitative reports, each criterion was attributed a semi-quantitative score [1–3]. Efficacy, E, was attributed a low score (1) if the alternative method yielded a marginal reduction of the pest population and failed to prevent yield loss. It was given an intermediate score (2) if the pest population or damage was decreased but yield losses persisted. E was attributed a high score (3) if the alternative method, used alone, both decreased the pest population or damage and prevented yield loss. Applicability, A, was scored 1 if the method was still at the research and development stage, 2 if already in use somewhere in the world, and 3 if already used in France. An alternative method for which use was not already authorized in France was attributed a score of 1, as the regulatory system takes several years to authorize commercialization. Durability, D, was scored 1, 2 or 3 if there was a high, medium or low risk of selecting resistance in the pests targeted. Practicability, P, was scored 1, 2, or 3 if the method was difficult (technically complex or requiring extra labor), moderately difficult or easy for farmers to implement. No score was awarded if no practical information or scientific data were available.

For the assessment of each of the eight categories of alternative methods identified above, we assigned two scientists with extensive experience in the specific field concerned. Following the general rules of systematic reviews (Pullin and Stewart, 2006), these scientists thoroughly reviewed the methods for the category concerned, using the same search string and reference databases, including Web of Science®, Scopus®, Google Scholar®, technical and scientific books. The search equations were built by combining keywords corresponding to the names of the target crop and target pest, both common and Latin names, with keywords describing all the methods considered for each of the eight categories of alternatives (as listed above). Only papers published in French or English were retained in the review. For each of the search strings, the experts retrieved the first 50 hits. The search was restricted to the scientific literature (gray literature was not considered). The scientists did not, therefore, assess the susceptibility to bias of the papers retained, based on the assumption that articles published in peer-reviewed journals are reliable (Villemey et al., 2018).

The two reviewers independently scored the methods for the four criteria. They then compared the scores they had awarded for each method, to identify major discrepancies and adjust the scores if necessary. The scores for each criterion were then presented and discussed during working meetings with the expert panel (15 people from independent research institutes, including scientists from INRA and experts from ANSES) and consensus values were determined (see Table S4 for the full dataset).

We considered an alternative pest control method to be directly useable as a replacement (substitutable) for a neonicotinoid use if it had an efficacy score of 2 or 3, and an applicability score of 2 or 3, meaning that it could be used directly and was sufficiently effective to decrease pest damage or populations. We defined the "substitutability" of a category of alternative pest control methods as the number of methods or products from a given category with an efficacy score ≥ 2 and an applicability score ≥ 2 divided by the total number of i methods or products from the category investigated.

We investigated differences in the efficacy, applicability, durability and practicability of alternative control methods between pest feeding guilds, with the aim of identifying general patterns extending beyond the level of the target pest species. The aim was to develop advice concerning methods that could potentially substitute for neonicotinoid use for other pest species, outside the French context. We performed principal component analysis (PCA, based on Pearson's correlations tests) of the mean scores for a given criterion per target pest guild (i.e. 5 variables) for the seven categories of alternative methods (excluding elicitors, i.e. 7 observations). The statistical analyses were performed with XLSTAT (Addinsoft, 2019).

3. Results

In total, we considered 152 specific authorized uses of neonicotinoids in the review (Table S2). These uses concerned 120 targeted crops (Table S3) and 279 pest insect species or genera (Table S1). Overall, 2968 case studies (single combinations of one alternative pest control method or product × one target crop × one target pest) were evaluated for the four criteria described above. For 684 case studies (26.5%), no published information was available for the evaluation of efficacy (E) for a specific alternative method of pest control.

Only six of 152 authorized uses of neonicotinoids (4%) were considered non-substitutable, i.e. with no known alternative methods displaying sufficient efficacy (E) and applicability (A) somewhere in the world (Fig. 1). These six neonicotinoid uses were: 1) protection of corn seeds (*Zea mays* L.) against flies (*Oscinella frit*, *Delia platura*, *Geomyza* sp.), 2) the protection of raspberry (*Rubus idaeus* L.) against flies (*Drosophila* and *Lasioptera* spp.), 3) the protection of turnip (*Brassica rapa* L.) against aphids (*Aphelinus abdominalis*, *Aphidius colemani*, *A. ervi*, *A. matricariae*, *Praon volucre*, *Ephedrus cerasicola*, *Diaeretiella rapae*), 4) the protection of cherry tree (*Prunus avium* L.) against xylophagous insects (*Scolytus rugulosus*, *Anisandrus dispar*, *Cossus cossus*), 5) the protection of forest trees against cockchafers (*Melolontha* sp.), and 6) the protection of trees and shrubs against beetles (e.g. *Otiorhynchus* sp., *Chrysomela* sp.).

For most neonicotinoid uses (71%, $n = 108$), we were able to identify both chemical and non-chemical substitutable alternatives. In 18% of cases ($n = 28$), other chemical insecticides were the only substitutable alternative to neonicotinoids. In seven of these 28 cases, the alternative chemicals were from a single class, and in two other cases only one authorized product was substitutable (a pyrethroid for use in both seed and plant treatments to control aphids on sugar beet). In a small proportion of cases (7%, $n = 10$), only non-chemical substitutable methods were identified (Fig. 1).

The 2968 case studies included 866 authorized chemical insecticides, 848 of which were considered both effective and practical enough to be substitutable alternatives to 138 uses of neonicotinoids (substitutability = 98%) (Fig. 2). By contrast, none of the plant defense elicitors was considered effective enough or sufficiently available in practice (substitutability = 0%).

Substitutability is expressed as a percentage for each category of alternative method and calculated as the number of methods or products from a given category with an efficacy score ≥ 2 and an applicability score ≥ 2 divided by the total number methods or products from the same category investigated.

In terms of these percentages, the most substitutable non-chemical methods were physical methods (substitutability = 65%, relevant to 76 uses of neonicotinoids), followed by biological control methods (41 uses involving microorganisms, 35 based on farming practices and 31 based on macroorganisms), semiochemicals and, finally, resistant plant varieties (Fig. 2).

We compared the mean scores for the four relevance criteria, for the seven different categories of alternatives (plant defense elicitors were excluded because they were never found to be relevant) and the five guilds of pest insects (Fig. 3). The covariation of feeding guild responses to pest management alternatives differed between criteria.

The magnitude of efficacy (Fig. 3a) was represented mostly by PCA axis 1, which clearly separated chemical insecticides (mean efficacy $\bar{E} = 2.99$) from the other categories of pest management methods (ranging from $\bar{E} = 1.91$ for biological control with microorganisms to $\bar{E} = 1.27$ for biological control with macroorganisms). Chemical insecticides were equally effective against all insect guilds. Physical methods and biological control with micro- and macroorganisms were more effective against leaf and sap feeders, whereas biological control with farming practices, semiochemicals and improved resistant varieties were more effective at controlling wood, flower and root feeders (as shown by coordinates along PCA axis 2).

The first principal component accounted for quantitative variation in applicability (Fig. 3b). Chemical insecticides (mean applicability $\bar{A} = 2.31$), physical methods ($\bar{A} = 2.53$) and microorganisms for biological control ($\bar{A} = 2.31$) were considered more readily applicable, as they were often already available as commercial products, whereas semiochemicals ($\bar{A} = 1.47$), macroorganisms for biological control ($\bar{A} = 1.44$) and improved resistant varieties ($\bar{A} = 1.11$) were mostly still at the research and development stage. Chemical insecticides and farming practices were more applicable for the control of root and sap feeders, whereas biological control with microorganisms and physical methods were mostly applicable against leaf, wood and flower feeders.

Resistant plant varieties and chemical insecticides were considered less durable (mean durability $\overline{D} = 1.58$ and 1.76, respectively) than other alternative control methods (Fig. 3c) due to the documented emergence of pest populations resistant to these two management methods, particularly among sap and root feeders.

Chemical insecticides scored highly for practicability as they are easy to apply by spraying (mean practicability $\overline{P} = 3.00$). The next most practical methods were resistant varieties ($\overline{P} = 2.60$), which require only planting, and microorganisms, which can also be sprayed onto the crop ($\overline{P} = 2.64$) (Fig. 3d). Like the other alternative methods, microorganisms and physical methods were found to be more practical

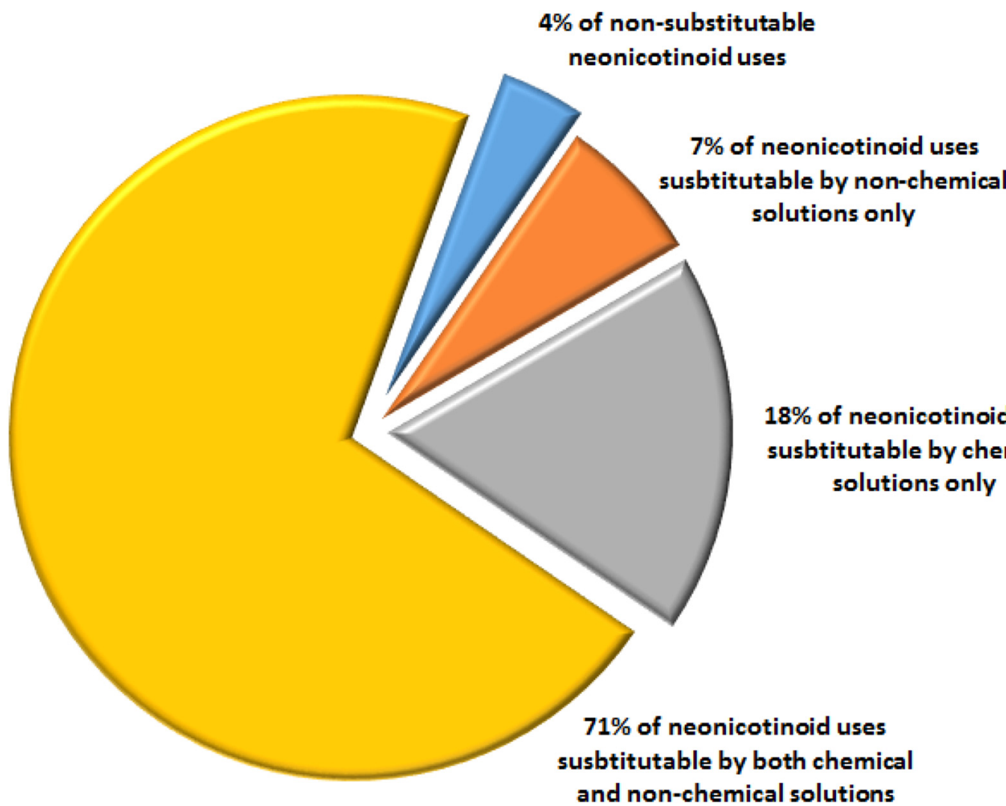

Fig. 1. Percentage of substitutable methods (both sufficiently effective and applicable) for the 152 authorized uses of neonicotinoids in France, as of January 1, 2018.

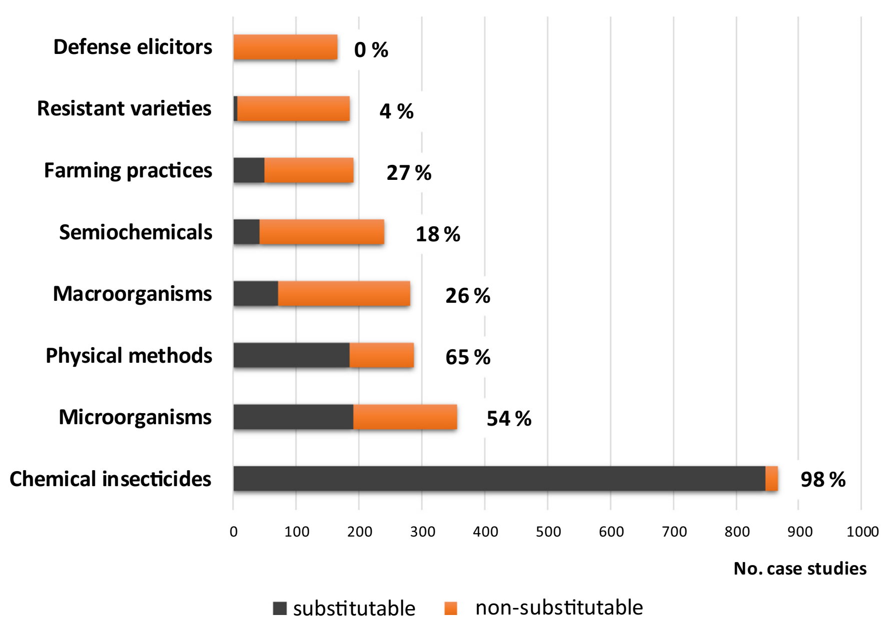

Fig. 2. Number of substitutable and non-substitutable chemical and non-chemical alternatives to neonicotinoids for pest control, for the 2968 case studies considered here (single combinations of one alternative pest control method or product × one target crop × one target pest).

for controlling sap and flower feeders, whereas farming practices were more practical for controlling wood and root feeders.

4. Discussion

Following the recent EU decision to ban the outdoor use of three neonicotinoids (European Commission, 2018), the need to promote and support the development of alternative pest management methods, to champion eco-friendly European agriculture, is greater than ever. Indeed, substantial restrictions on the use of neonicotinoids should be favorable to both non-target and beneficial organisms, such as pollinators, currently threatened by the use of this class of insecticide (Woodcock et al., 2017). However, these benefits will only operate if the alternative methods replacing neonicotinoids are less harmful to the environment. Since 2007, the French government has been trying to reduce insecticide use, investing half a billion Euros in ambitious plans

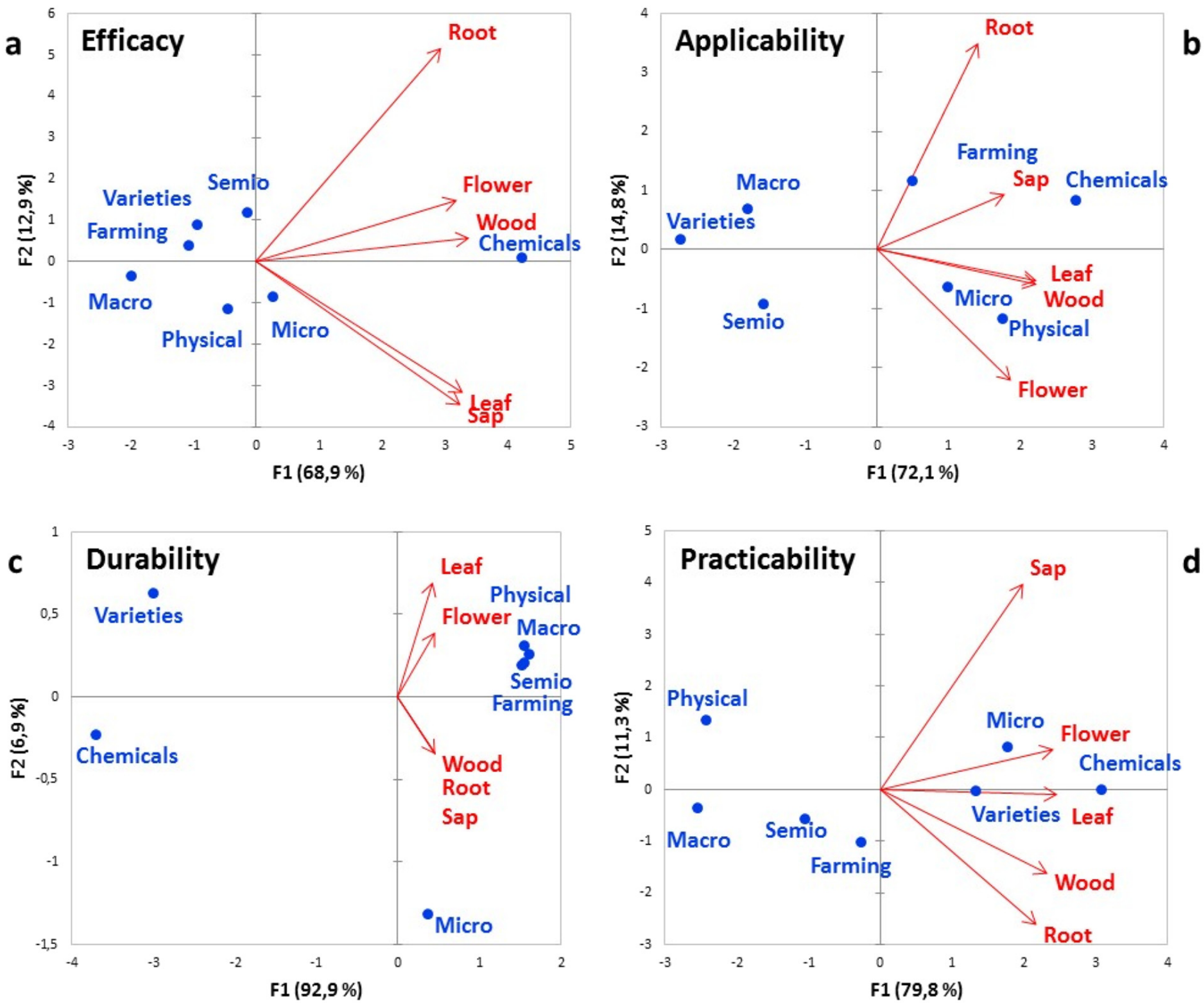

Fig. 3. Projection of the scores for the four criteria (efficacy (a), applicability (b), durability (c), practicability(d)), for the seven categories of pest management alternatives to neonicotinoids (blue dots) on the plane defined by PCA axes 1 and 2, constructed with the mean criterion scores for five guilds of pest insects (red arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

(Ecophyto 1 and 2, Stokstad, 2018). The recent ban on neonicotinoids in France was another step forward in the steady decrease in overall insecticide use in France. However, this decrease requires the identification of sustainable alternative methods and an understanding of their potential drawbacks. Our thorough analysis of alternatives to all specific authorized uses of neonicotinoids in France demonstrates that it is possible to replace neonicotinoids by effective alternative methods, techniques and/or products in most cases (96% of cases). However, the alternative methods may not always match neonicotinoids in terms of efficacy, applicability, durability, and/or practicability, at least as things stand. Furthermore, they may not necessarily be safer for the environment.

The most common alternative to neonicotinoids (89% of cases), of high efficacy, immediate applicability and practicality, is the use of other chemical insecticides, particularly those belonging to previous generations of substances, such as pyrethroids. The underlying mechanisms of action and resistance are often common to different classes of insecticides, so the use of newly developed neonicotinoids or substances with similar modes of action (e.g., sulfoxaflor, flupyradifurone) is not a viable option for replacing former neonicotinoids, as they are likely to have the same adverse effects on the environment (Furlan et al., 2018). A large increase in pest populations resistant to the remaining insecticides available is a major issue here, given that 40% of former neonicotinoid uses are likely to be replaced by a single class of chemical substance (21%), a single substance (17%) or even a single commercial product (2%) to control a specific group of pest species. Following the ban on neonicotinoids, crop productivity would be threatened by a decrease in effective insecticide availability, at least in the short term. Furthermore, chemical treatment for curative purposes would require accurate pest monitoring coupled with repeated applications to hit successive pest generations. Finally, integrated pest management (IPM) systems are still lacking for some crops, for which the neonicotinoids introduced in the 1990s immediately superseded other insecticides (Alyokhin et al., 2015; Biddinger and Rajotte, 2015).

Tools facilitating the development of new cropping systems based on the use of fewer chemical insecticides are already available (see Fig. 1), and, in 78% of cases, at least one non-chemical alternative to neonicotinoids was identified. However, the incorporation of non-chemical methods into IPM packages is largely underdeveloped (Hokkanen, 2015), despite EU directives requiring the implementation of IPM (EU, 2009). The most promising substitutable methods involve the use of microorganisms (e.g. granulosis virus or bacteria, such as *Bacillus thuringiensis*) for biological control. Physical (e.g. coating the fruit with paraffin oil or clay; Vincent et al., 2003) and semiochemical methods (mating disruption with sex pheromones) have also proved quite effective (Witzgall et al., 2010) and are often available as commercial products. In addition, farming practices designed to conserve biological control (Heimpel and Mills 2017; Gardarin et al., 2018) have considerable potential for this purpose over and above their other benefits (Wratten et al., 2012; Kleijn et al., 2018). Last, but not least, most of these environment-friendly methods can be combined (Barzman et al., 2015).

The relevance of non-chemical alternatives to neonicotinoids depended largely on the feeding guild of the pest targeted. Leaf and flower feeders are more easily managed with non-chemical methods than other pest guilds, such as wood, bark and root feeders. These latter groups were easily controlled by the systemic mode of action of neonicotinoids. The key difficulty is actually reaching the wood and root feeders, which are endophagous or live below the ground.

This rating of alternatives to neonicotinoids has two main limitations. First, it does not take into account the relative toxicities of the pest management methods compared. Many studies have shown that chemical insecticides are toxic to the environment and the user if applied without sufficient caution (Devine and Furlong, 2007). Much less is known about the toxicity of non-chemical pest management methods. For example, very few scientific studies (Goulson et al., 2000) have evaluated the harm to pollinators of biological control (e.g. granulosis virus). Second, economic performance was not included among the evaluation criteria. This criterion was not evaluated here mostly due to the complexity of cost measurement and allocation, which should take into account not only direct costs, such as product price and the depreciation of application equipment or labor, but also compensatory benefits, such as the added value of specific goods (e.g. organic farming produce) or subsidies. Cost-benefit analyses of this type can be performed only at the level of the agricultural sector level and must be holistic, and such an analysis was therefore beyond the scope of this simple scoring exercise.

A number of alternatives to neonicotinoids were considered to be not fully substitutable due to poor current applicability. A number of promising methods are still at the research and development stage and are hardly implemented in fields at the moment. For example, most plant defense elicitors (Bektas and Eulgem, 2015), multiple plant-based semiochemicals (Murali-Baskaran et al., 2018), gene editing for the development of resistant crop varieties (Lombardo et al., 2016) and conservation biological control methods (Crowder et al., 2010) are very promising new methods for pest management. However, they all require further development, testing in the field and fine-tuning to farmers' needs before release onto the market. This may be one of the reasons for which Ecophyto plan 1 actually failed to reduce insecticide use in France over the last decade (Stokstad, 2018). This plan led to the generation of a large number of major scientific results, but few have spilled over into agricultural extension, as specialists in this area often carry out their own practical research without building on novel and challenging scientific paradigms. Strengthening scientific research and shifting it toward the needs of farmers will be a key challenge in the new neonicotinoid-free area that will require not only biotechnology, but also input from the social sciences to address technology transfer, as participatory and citizen sciences methods are of particular relevance for improving the adoption of new biocontrol techniques through joint development with farmers (Wyckhuys et al., 2018).

The French government will also have to meet two other challenges. First, plant protection products are covered by specific European regulations (EC - No 1107/2009), resulting in a substantial delay between the submission for authorization of any new active substance and the availability on the market of products containing the substance concerned. The transition from decades of pesticide use to more environmentally friendly pest management methods will require farmers to have rapid access to effective non-chemical products. The registration and authorization processes must therefore be accelerated. Alternatively, substitutable methods not based on products, such as changes in farming practices, should be promoted as a priority (Muneret et al., 2018). Second, both companies producing new-generation plant protection products, and farmers willing to use them will face economic issues. Plant protection products can be very costly for farmers and not business-efficient for companies if produced at too small a scale (the case for most new products). Government subsidies could help to support the transition from neonicotinoids to more environmentally sound management methods. In addition, economic insurance initiatives could compensate farmers for shortfalls in bad years (Furlan et al., 2018) as alternative methods may be less reliable and more susceptible to various factors (e.g. environmental conditions lowering the efficacy of natural enemies of pests).

Pest management should effectively be based on the multifaceted methods of IPM. In our view, the prophylactic use of systemic insecticides for seed treatment is unacceptable in such a system. The EU is committed to continuing agricultural production while reducing the use of chemical insecticides by making the application of integrated pest management practices mandatory, to protect the ecosystem services that support agricultural productivity (EU, 2009). In a provocative, but intellectually stimulating scientific article, Jensen (2015) suggested that we should "*ban first, ask questions later*" as far as neonicotinoids are concerned, which is essentially the approach adopted by France in 2016. Our results confirm that this was a wise decision, retrospectively justified by the existence of a wide range of effective alternatives. However, the same reflection should now apply to other classes of insecticides. As argued by Jansen, environmental protection agencies should not leave an insecticide on the market until scientists demonstrate that it is toxic, and they should not authorize new insecticides until phytosanitary product manufacturers have shown them to be harmless, to avoid "*unreasonable risk to both the environment and the economy*".

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.04.045.

Acknowledgements

We thank the French Agency for Food, Environmental and Occupational Health and Safety that funded this research.

References

Addinsoft, 2019. XLSTAT Statistical and Data Analysis Solution. Long Island, NY, USA. .

Alyokhin, A., Mota-Sanchez, D., Baker, M., Snyder, W.E., Menasha, S., Whalon, M., Dively, G., Moarsi, W.F., 2015. The Red Queen in a potato field: integrated pest management versus chemical dependency in Colorado potato beetle control. Pest Manag. Sci. 71 (3), 343–356.

Anderson, N.L., Harmon-Threatt, A.N., 2019. Chronic contact with realistic soil concentrations of imidacloprid affects the mass, immature development speed, and adult longevity of solitary bees. Sci. Rep. 9, 3724.

Baron, G.L., Raine, N.E., Brown, M.J., 2017. General and species-specific impacts of a neonicotinoid insecticide on the ovary development and feeding of wild bumblebee queens. Proc. R. Soc. B Biol. Sci. 284 (1854), 20170123.

Barzman, M., Bàrberi, P., Birch, A.N.E., Boonekamp, P., Dachbrodt-Saaydeh, S., Graf, B., Hommel, B., Jensen, J.E., Kiss, J., Kudsk, P., Lamichhane, J.R., Messéan, A., Moonen, A.C., Ratnadass, A., Ricci, P., Sarah, J.L., Sattin, M., 2015. Eight principles of integrated pest management. Agronomy for sustainable development. 35 (4), 1199–1215.

Bektas, Y., Eulgem, T., 2015. Synthetic plant defense elicitors. Front. Plant Sci. 5, 1–9.

Biddinger, D.J., Rajotte, E.G., 2015. Integrated pest and pollinator management—adding a new dimension to an accepted paradigm. Current Opinion in Insect Science 10, 204–209.

Biodiversity Act, 2016. Loi n° 2016-1087 du 8 août 2016 pour la reconquête de la biodiversité, de la nature et des paysages. https://www.legifrance.gouv.fr/eli/loi/2016/8/8/2016-1087/jo/texte.

Cimino, A.M., Boyles, A.L., Thayer, K.A., Perry, M.J., 2017. Effects of neonicotinoid pesticideinsecticide exposure on human health: a systematic review. Environ. Health Perspect. 125 (2), 155–162.

Cressey, D., 2017. The bitter battle over the world's most popular insecticides. Nature News 551 (7679), 156.

Crowder, D.W., Northfield, T.D., Strand, M.R., Snyder, W.E., 2010. Organic agriculture promotes evenness and natural pest control. Nature 466 (7302), 109–112.

Desneux, N., Decourtye, A., Delpuech, J., 2007. The sublethal effects of pesticides on beneficial arthropods. Annu. Rev. Entomol. 52, 81–106.

Devine, G.J., Furlong, M.J., 2007. Insecticide use: contexts and ecological consequences. Agric. Hum. Values 24 (3), 281–306.

Di Prisco, G., Cavaliere, V., Annoscia, D., Varricchio, P., Caprio, E., Nazzi, F., Gargiulo, G., Pennacchio, F., 2013. Neonicotinoid clothianidin adversely affects insect immunity and promotes replication of a viral pathogen in honey bees. Proc. Natl. Acad. Sci. U. S. A. 110 (46), 18466–18471 5.

EU, 2009. Directive 2009/128/EC of the European Parliament and of the council of 21 October 2009 establishing a framework for community action to achieve the

sustainable use of pesticideinsecticides. OJ EU L309, 71–86 24.11.2009.
European Commission, 2018. Neonicotinoids. https://ec.europa.eu/food/plant/pesticideinsecticides/approval_active_substances/approval_renewal/neonicotinoids_en (2018).
European Food Safety Authority, 2018. Neonicotinoids: risks to bees confirmed. February 28. https://www.efsa.europa.eu/en/press/news/180228 (2018).
Furlan, L., Pozzebon, A., Duso, C., Simon-Delso, N., Sánchez-Bayo, F., Marchand, P.A., Codato, F., Bijleveld van Lexmond, M., Bonmatin, J., 2018. An update of the worldwide integrated assessment (WIA) on systemic insecticides. Part 3: alternatives to systemic insecticides. Environ. Sci. Pollut. Res. 1–23.
Gardarin, A., Plantegenest, M., Bischoff, A., Valantin-Morison, M., 2018. Understanding plant–arthropod interactions in multitrophic communities to improve conservation biological control: useful traits and metrics. J. Pest. Sci. 91 (3), 943–955.
Goulson, D., Martınez, A.M., Hughes, W.O., Williams, T., 2000. Effects of optical brighteners used in biopesticide formulations on the behavior of pollinators. Biol. Control 19 (3), 232–236.
Heimpel, G.E., Mills, N.J, 2017. Biological control. Cambridge University Press.
Hokkanen, H.M.T., 2015. Integrated pest management at the crossroads: science, politics, or business (as usual)? Arthropod Plant Interact. 9, 543–545.
Jensen, E., 2015. Banning neonicotinoids: ban first, ask questions later. Seattle J. Envtl. L. 5, i.
Jeschke, P., Nauen, R., 2008. Neonicotinoids—from zero to hero in insecticide chemistry. Pest Manag. Sci. 64 (11), 1084–1098.
Kleijn, D., Bommarco, R., Fijen, T.P., Garibaldi, L.A., Potts, S.G., van der Putten, W.H., 2018. Ecological intensification: bridging the gap between science and practice. Trends Ecol. Evol. 34 (2), 154–166.
Lombardo, L., Coppola, G., Zelasco, S., 2016. New technologies for insect-resistant and herbicide-tolerant plants. Trends Biotechnol. 34 (1), 49–57.
Ministry of Agriculture. Catalogue of Phytopharmaceutical Uses, from the French Ministry of Agriculture (http://daaf.reunion.agriculture.gouv.fr/Catalogue-national-des-usages,653) (2017).
Muneret, L., Mitchell, M., Seufert, V., Aviron, S., Djoudi, E.A., Pétillon, J., Plantegenest, M., Thiéry, D., Rusch, A., 2018. Evidence that organic farming promotes pest control. Nature sustainability 1, 361–368.
Murali-Baskaran, R.K., Sharma, K.C., Kaushal, P., Kumar, J., Parthiban, P., Senthil-Nathan, S., Mankin, R.W., 2018. Role of kairomone in biological control of crop pests-a review. Physiol. Mol. Plant Pathol. 101, 3–15.
Nauen, R., Denholm, I., 2005. Resistance of insect pests to neonicotinoid insecticides: current status and future prospects. Arch. Insect Biochem. Physiol. 58 (4), 200–215.
Pullin, A.S., Stewart, G.B., 2006. Guidelines for systematic review in conservation and environmental management. Conserv. Biol. 20, 1647–1656.
Regulation (EC), 2009. No 1107/2009 of the European Parliament and of the Council of 21 October 2009 Concerning the Placing of Plant Protection Products on the Market and Repealing Council Directives 79/117/EEC and 91/414/EEC.
Rundlöf, M., Andersson, G.K., Bommarco, R., Fries, I., Hederström, V., Herbertsson, L., Jonsson, O., Klatt, B.K., Pedersen, T.R., Yourstone, J., Smith, H.G., 2015. Seed coating with a neonicotinoid insecticide negatively affects wild bees. Nature 521 (7550), 77.
Sánchez-Bayo, F., Goulson, D., Pennacchio, F., Nazzi, F., Goka, K., Desneux, N., 2016. Are bee diseases linked to pesticideinsecticides?—a brief review. Environ. Int. 89, 7–11.
Stokstad, E., 2018. France's decade-old effort to slash pesticideinsecticide use failed. Will a new attempt succeed? Science. https://doi.org/10.1126/science.aav6762.
Tadeï, R., Domingues, C.E., Malaquias, J.B., Camilo, E.V., Malaspina, O., Silva-Zacarin, E.C., 2019. Late effect of larval co-exposure to the insecticide clothianidin and fungicide pyraclostrobin in Africanized Apis mellifera. Sci. Rep. 9, 3277.
Thompson, H., Overmyer, J., Feken, M., Ruddle, N., Vaughan, S., Scorgie, E., Bocksch, S., Hill, M., 2019. Thiamethoxam: Long-term effects following honey bee colony-level exposure and implications for risk assessment. Sci. Total Environ. 654, 60–71.
Tsvetkov, N., Samson-Robert, O., Sood, K., Patel, H.S., Malena, D.A., Gajiwala, P.H., Maciukiewicz, P., Fournier, V., Zayed, A., 2017. Chronic exposure to neonicotinoids reduces honey bee health near corn crops. Science 356 (6345), 1395–1397.
Villemey, A., Jeusset, A., Vargac, M., Bertheau, Y., Coulon, A., Touroult, J., ... Deniaud, N., 2018. Can linear transportation infrastructure verges constitute a habitat and/or a corridor for insects in temperate landscapes? A systematic review. Environmental Evidence 7 (1), 5.
Vincent, C., Hallman, G., Panneton, B., Fleurat-Lessard, F., 2003. Management of agricultural insects with physical control methods. Annu. Rev. Entomol. 48 (1), 261–281.
Whitehorn, P.R., O'Connor, S., Wackers, F.L., Goulson, D., 2012. Neonicotinoid pesticideinsecticide reduces bumble bee colony growth and queen production. Science 336 (6079), 351–352.
Wintermantel, D., Locke, B., Andersson, G.K., Semberg, E., Forsgren, E., Osterman, J., Pedersen, T.P., Bommarco, R., Smith, H.G., Rundlöf, M., de Miranda, J.R., 2018. Field-level clothianidin exposure affects bumblebees but generally not their pathogens. Nat. Commun. 9 (1), 5446.
Witzgall, P., Kirsch, P., Cork, A., 2010. Sex pheromones and their impact on pest management. J. Chem. Ecol. 36 (1), 80–100.
Wood, T.J., Goulson, D., 2017. The environmental risks of neonicotinoid pesticideinsecticides: a review of the evidence post 2013. Environ. Sci. Pollut. Res. 24 (21), 17285–17325.
Woodcock, B.A., Bullock, J.M., Shore, R.F., Heard, M.S., Pereira, M.G., Redhead, J., ... Peyton, J., 2017. Country-specific effects of neonicotinoid pesticideinsecticides on honey bees and wild bees. Science 356 (6345), 1393–1395.
Wratten, S.D., Gillespie, M., Decourtye, A., Mader, E., Desneux, N., 2012. Pollinator habitat enhancement: benefits to other ecosystem services. Agric. Ecosyst. Environ. 159, 112–122.
Wyckhuys, K.A., Bentley, J.W., Lie, R., Fredrix, M., 2018. Maximizing farm-level uptake and diffusion of biological control innovations in today's digital era. BioControl 63 (1), 133–148.
Zeng, G., Chen, M., Zeng, Z., 2013. Risks of neonicotinoid pesticideinsecticides. Science 340 (6139), 1403.