Perspective

Received: 19 March 2014 Revised: 8 May 2014 Accepted article published: 15 May 2014 Published online in Wiley Online Library:

(wileyonlinelibrary.com) DOI 10.1002/ps.3829

Biopesticides – towards increased consumer safety in the European Union

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Abstract

The introduction of new food safety regulations in the European Union has resulted in the withdrawal of many synthetic active substances used in plant protection products, in light of their potential or actual harmful effect on human and animal health, as well as on the environment. Alternatives to these compounds are being developed – naturally occurring pesticides, also referred to as biopesticides. The use of biopesticides in crop protection leads to decreased levels of pesticide residues in foods, and as a result to lower risk levels for the consumer. Biologically active agents defined as biopesticides are varied, and therefore application of the same environmental and consumer safety criteria to all of them is impossible. This presents serious complications in the approval of these pesticides as active plant protection products and in their registration. It needs to be stressed that, in the registration procedure of the European Union, biopesticides are subject to the same regulations as synthetic active substances. This situation has resulted in the need to introduce numerous new provisions in the legislation, as well as the preparation of new guidelines facilitating the registration of biopesticides. These activities aim to promote naturally originating pesticides.

Keywords: biopesticides; consumer safety; cut-off criteria; pesticide approval process

1 INTRODUCTION

In recent years, consumers have paid increasing attention to the potential health impact of synthetic chemical substances in food production. Interest in problems related to food safety has resulted in considerable pressure in Europe, exerted not only by consumers but also by various committees and EU organisations, to lower the levels of pesticide residues in food originating from farms where plant protection products are used. Since 2009, new rules have been introduced, tightening the requirements for chemical compounds used as pesticides.[1–4]

The introduction of new regulations in the field of food safety has resulted in the withdrawal of many synthetic active substances from the market, in light of their unacceptable potential or actual harmful effects on the health of humans and animals. Annex II to Regulation (EC) 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 introduced the so-called cut-off criteria, which directly ban numerous substances used as pesticides.[1] This applies, among others, to carcinogenic, mutagenic, toxic (for reproduction), endocrine disruptive and persistent substances. The substances satisfying the above criteria have been named 'candidates for substitution'. Compounds receiving a negative assessment, in accordance with the provisions of the above-mentioned regulation, should be replaced by other substances with safer characteristics. The list of candidates for substitution should be published by the European Commission in as short a time as possible [according to Article 80 (7) of Regulation (EC) 1107/2009 of the European Parliament and the Council].[1] Pesticides replacing the banned chemical compounds should undergo a comparative assessment procedure. The preparation of such a procedure is currently under way.[5]

An additional element driving the search for new pest management tools is the increasing evolution of resistance of pest populations to the pesticides currently used. Another factor supporting the development of the biopesticide market is the increase of demand for so-called ecoproducts.[5]

Alternatives to the withdrawn synthetic pesticides are therefore being developed in the form of natural products, i.e. biopesticides.[6–9]

2 BIOPESTICIDES – CHARACTERISTICS AND ADVANTAGES

The use of biopesticides in crop protection can lead to many positive outcomes, such as decreased pesticide residues in food, thereby reducing the risk to the consumer. Biopesticides are typically specific to pest organisms and low risk to non-target organisms. They generally decompose quickly, and some, such as semiochemicals, are used in very small doses.

Biopesticides constitute a special group of active substances for plant protection that occur naturally or are nature-identical synthetic substances. They also include a number of living organisms (biocontrol organisms).

Biopesticides may be divided into several groups:

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- **Products with pheromones or other semiochemicals as the active ingredient.** These are chemical compounds excreted by animals or plants (or their synthetic analogues) in order to pass information or influence their environment in a certain way, usually for defensive purposes, such as alarms, marking territory or informing partners about sexual readiness. They act either intraspecifically (pheromones, population-regulating autoinhibitors, autotoxins, necromones) or interspecifically (allomones, kairomones, depressors, synomones).[10] An example of this group of pesticides are straight-chained lepidopteran pheromones, which are used in insecticidal traps.
- **Microbial pesticides.** These include fungi, bacteria and viruses. *Beauveria bassiana* strain *GHA*, which is used as an insecticide for the control of sucking insects, insects feeding on greenhouse vegetables and decorative plants, is an example of a fungal crop protection agent. *Bacillus thuringiensis* subsp. *tenebrionis* strain *NB-176*, destroying the larvae of *Leptinotarsa decemlineata* (which feed on potatoes), is an example of a bacterium-based insecticide. *Cydia pomonella* granulovirus, used in the protection of fruit trees from codling moth larvae, a dangerous pest feeding on fruit, is an example of a virus-bearing pesticide. The list of pesticides containing microorganisms is very long. For one genus only – *Bacillus* – several bioactive pesticide ingredients are currently registered in Europe: *B. amyloliquefaciens* MBI 600; *B. amyloliquefaciens* strain FZB24; *B. amyloliquefaciens* subsp. Platarum D747; *B. firmus* I-1582; *B. pumilus* QST 2808; *B. sphaericus*; *B. subtilis* strain QST 713; *B. subtilis* strain IBE 711; *B. thuringiensis aizawai* ABTS-1857; *B. thuringiensis* subsp. *aizawai* strain GC 91; *B. thuringiensis* subsp. *israeliensis* strain AM 6552; *B. thuringiensis* subsp. *kurstaki* strain ABTS 351; *B. thuringiensis* subsp. *kurstaki* strain PB 54; *B. thuringiensis kurstaki* subsp. SA11_SA12_EG2348; *B. thuringiensis tenebrionis* NB-176.
- **Products containing living organisms** – invertebrates (e.g. predatory insects) and nematodes of genus *Heterorhabditis* and *Steinernema*. It must be noted, however, that in the US regulatory scheme these are exempt from biopesticide registration.
- **Plant-extract- and vegetable-oil-based products.** This group is considerably varied both from a chemical and from a functional point of view. Pesticides of this group often include complex mixtures that are chemically difficult to classify (e.g. citronella oil, orange oil, garlic extract, tea tree extract).[11–14] Many of them have been safely used for years.

In certain countries, for example in the United States, biopesticides include genetically modified crops that have transgenes that encode natural plant protectants (e.g. *Bt* toxin). These biopesticides are termed plant incorporated protectants (PIPs) by the USEPA.[6]

Pesticides potentially decreasing the risk for the consumer, apart from the biopesticides mentioned above, include inorganic salts and such compounds as fatty acids. The above-mentioned pesticide groups have various functions in plant protection. They may be used as:

- **Fungicides:** *B. subtilis* (specific strain) is used in the protection of fruits and lettuce from fungal infections; *Coniothyrium minitans* (specific strain) has a strong parasitic character against the endospores of cottony rot (*Sclerotinia sclerotiorum*); laminarin, acquired from *Laminaria digitata*, is used in the protection of cereal crops to elicit crop resistance to plant pathogens.
- **Insecticides:** *B. thuringiensis var. kurstaki*; *C. pomella granulosis*; *Verticillium lecanii*; spinosad, a biologically active substance found in the bacterial species *Saccharopolyspora spionsa*, used in the protection of fruits and vegetables and approved in the European Union (in the United States it is registered as a reduced-risk chemical pesticide, not as a biopesticide); fatty acids.
- **Herbicides:** citronella oil; fatty acids.
- **Others:** *Candida oleophila* strain O, a biological control agent targeting other species of fungi, i.e. grey mould, *Botrytis cinerea*, and blue mould, *Penicillium expansum*; *Peniophora gigantea*, used to protect tree trunks from fungal infections; pepper dust extraction residue (steam-distilled and solvent-extracted black pepper – *Piper nigrum*), used as a cat and dog deterrent; *Zucchini yellow mosaic virus*, weak strain, registered to stimulate defensive mechanisms of vegetable plants; *Verticillium albo-atrum* strain WCS850, a fungus used in injections as a preventive measure for trees, eliciting systemic acquired resistance; sea alga extract, a plant growth regulator; giberellins, plant growth regulators.

Some of the biopesticides have several applications. For example, garlic extract may be used as an insecticide, nematicide, bird and mammal repellent or fungicide. It also has molluscicidal properties.[13]

Biologically active ingredients classified as biopesticides are extremely varied. Application of the same criteria to assess their safety for the consumer and for the environment is very difficult, which leads to a situation where, in practice, they should be assessed on a case-by-case basis. This results in considerable problems during their assessment in the pesticide approval and registration procedure. On the other hand, new European legislation promotes activities leading to the increased use of biopesticides in plant pest control.[6]

3 LEGAL SITUATION

In order to limit the tests required for the assessment of biopesticides, Regulation (EC) 2229/2004 was amended with article 24b introduced by Regulation (EC) 1095/2007.[15,16] It provides for the possibility of inserting into Annex I to Directive 91/414/EEC [substituted with Implementing Regulation (EU) No. 540/2011][2] active substances for which there are clear indications that they will not be expected to have any harmful effects on human or animal health or on groundwater or any unacceptable influence on the environment, without the need for prior application for a detailed scientific opinion to the European Food Safety Agency (EFSA). Annex IV to Regulation (EC) No. 1095/2007 lists criteria that need to be met by the active substance to be considered a substance of such properties.[16] Many biopesticides meet these requirements.[17] Regulation (EC) No. 1107/2009 of the European Parliament and the Council also includes such terms as low-risk substances and basic substances.[1]

Low-risk pesticides may be defined as products posing minimum risk to the health of humans, animals and the environment without specific testing, based on the ingredients, physical and chemical properties and the area and conditions of application.

Basic substances are substances that, until now, have not been used as pesticides, but that may be useful in this field. They may not exhibit a negative influence on the health of humans and animals or on the environment. Special requirements have been laid down concerning the testing and data of this type of substance for their use in plant protection.[18]

The European Commission has also prepared a draft list of substances that potentially may be used for pest control, and at the same time may be qualified as basic substances.[19] The aim is to facilitate the preparation of applications, as well as to assess them as active substances. Examples of such substances are talc, cinnamon, ferric citrate, potassium chloride, calcium dichloride, carbon dioxide, citric oil and urea.

Annex IV to Regulation (EC) No. 396/2005 of the European Parliament and the Council includes a list of active substances for which maximum residue levels (MRLs) are not required owing to negligent risk to the consumer.[17,20] Guidance Document SANCO/11188/2013 lists criteria that have to be met by active substances to allow their inclusion in the Annex.[21]

These are substances of low toxicological risk profile [in the meaning of point 5 of Annex II to Regulation (EC) No. 1107/2009][1] that do not require the establishment of acceptable daily intake (ADI) and acute reference dose (ARfD). In tests on laboratory animals, these substances do not reveal any negative effect. This group may include microorganisms not producing toxins and not causing infection, as well as substances for which a normal daily dietary intake is higher than from the food after the application of the pesticide containing the same chemical substance (e.g. sulphur, iron phosphate or certain plant extracts). For substances that have nutritional value or are food ingredients, residue levels after application are not a concern. This applies to garlic, certain marine alga extracts, laminarine or mint oil, as well as many other biopesticides from this group.

Annex IV may also include substances that do not leave any residue in the protected foods. These include, for example, carbon dioxide used as insecticide and acaricide, or pheromones used in plant protection [straight-chain lepidopteran pheromones (SCLPs)]. Pheromones used as insecticides include as many as 30 chemical compounds.[22] Other substances from this group are currently under assessment.[23]

In order to approve a substance for inclusion in Annex IV, it is necessary to answer the following questions:[21]

1 Can the assessed substance be qualified as food?
2 Does it cause any toxicological concern?
3 Does it occur naturally in the human environment, or is it approved for use in other food-related fields, e.g. as a food additive? If so, is the exposure to this substance after the application of a plant protection product lower in comparison with exposure from other sources (also naturally occurring in the environment or resulting from other uses in foods)? For substances occurring naturally that are not food ingredients, it is necessary to answer the question as to whether there is a possibility of consumer exposure as a result of using them as active substances.

Examples of biologically active ingredients with multidirectional exposure are carbon dioxide or gibberellins. As carbon dioxide is found naturally in the environment, being a product of biological and chemical processes, there is no need to indicate its residue after using it as a bioactive pesticide. There is also no possibility of differentiating between such exposure and the natural background.[24] In case of gibberellins, which are natural plant hormones, there is no way of distinguishing between exogenic and endogenic sources.[25]

The majority of biopesticides may be counted among basic or low-risk substances of a minimum risk level, for which the setting of MRLs is unnecessary. Many of them are used in concentrations similar to their natural occurrence. Low-risk substances decompose very quickly (except for basic substances), and so leave little or no residue in the environment or in food able to affect living organisms.

Microorganisms approved for use in the European Union comply with the requirements necessary for qualification as low-risk, biologically active agents. Still, when assessing microorganisms, a thorough check has to be made to determine whether they interact with other organisms living in the environment, and to pay attention to metabolites produced by them that may have a negative effect. Other problems that arise in the assessment of microorganisms are the hitherto insufficiently researched issues of interspecific transfer of genetic material and its expression. Such doubts were expressed, for example, during the assessment of *B. thuringiensis* subsp. *tenebrionis* strain NB-176.[26] In the assessment of plant extracts, problems may also arise during identification of a mix of many active agents.[27,28]

The majority of biopesticides comply with the criteria listed for low-risk active substances, or they belong to basic substances. In accordance with Annex VI of Regulation (EC) No. 1095/2007,[16] they may be described as not having any harmful effects on human or animal health or on groundwater, or any unacceptable influence on the environment. They are also included in Annex IV of Regulation (CE) 396/2005 of the European Parliament and the Council as active substances, for which MRLs are not required owing to negligent risk to the consumer.[20] Biopesticides may then be an alternative to pesticides that have been banned from use.

4 CONCLUSIONS

The increased use of biopesticides will make it possible to limit the exposure of the consumer to synthetic pesticide residues and to reduce the associated risk. The toxicological risk of biopesticides is lower than that of most synthetic pesticides. Moreover, many of them have a high selectivity/specificity, as they do not have a negative impact on organisms that are not targeted. They could also play an invaluable role in tackling the increasing problem of resistance to synthetic pesticides.

Nevertheless, the positive properties of biopesticides, described above, do not release anyone from the obligation of thorough assessment before any approval for use in pest control, as not all naturally occurring substances are safe for humans and for the environment.

It needs to be stressed that biopesticides in the registration procedure of the European Union are subject to the same regulations as synthetic active substances. In spite of the introduction of many elements aimed at facilitating the procedure of assessment of bioactive agents, described above, manufacturers are reluctant to register this type of pesticide owing to problems related to their approval (assessment) and registration that result from the fairly vague criteria of assessment, and above all from the considerable freedom of interpretation of these criteria by the experts carrying out the registration process for the pesticides.[29]

Still, the implementation of such pesticides on a larger scale in plant protection will be led by their economic value. In this case, the economic calculation will take into account the cost of application of a biopesticide in relation to the profit acquired from the crop, put against the same calculation made for a 'conventional pesticide'. The above calculation should also account for social and environmental costs resulting from exposure of people and the environment to synthetic pesticides, as well as the cost of monitoring food and environmental pesticide residues in the EU. For this reason, the European Commission, which has influence on the very important field of plant protection, is taking an active part in the promotion of biopesticides.

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