

Official Journal of the European Union

L 227



English edition

Legislation

Volume 65

1 September 2022

Contents

II *Non-legislative acts*

INTERNATIONAL AGREEMENTS

- ★ **Voluntary Partnership Agreement between the European Union and the Republic of Honduras on forest law enforcement, governance and trade in timber products to the European Union** 1

REGULATIONS

- ★ **Commission Regulation (EU) 2022/1438 of 31 August 2022 amending Annex II to Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards specific criteria for the approval of active substances that are micro-organisms** ⁽¹⁾ 2
- ★ **Commission Regulation (EU) 2022/1439 of 31 August 2022 amending Regulation (EU) No 283/2013 as regards the information to be submitted for active substances and the specific data requirements for micro-organisms** ⁽¹⁾ 8
- ★ **Commission Regulation (EU) 2022/1440 of 31 August 2022 amending Regulation (EU) No 284/2013 as regards the information to be submitted for plant protection products and the specific data requirements for plant protection products containing micro-organisms** ⁽¹⁾ 38
- ★ **Commission Regulation (EU) 2022/1441 of 31 August 2022 amending Regulation (EU) No 546/2011 as regards specific uniform principles for evaluation and authorisation of plant protection products containing micro-organisms** ⁽¹⁾ 70
- ★ **Commission Implementing Regulation (EU) 2022/1442 of 31 August 2022 amending Implementing Regulation (EU) 2017/1490 as regards the terms of authorisation of manganese chelate of amino acids hydrate as a feed additive for all animal species** ⁽¹⁾ 117

⁽¹⁾ Text with EEA relevance.

EN

Acts whose titles are printed in light type are those relating to day-to-day management of agricultural matters, and are generally valid for a limited period.

The titles of all other acts are printed in bold type and preceded by an asterisk.

★ Commission Implementing Regulation (EU) 2022/1443 of 31 August 2022 concerning the non-approval of calcium propionate as a basic substance 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 ⁽¹⁾	123
★ Commission Implementing Regulation (EU) 2022/1444 of 31 August 2022 concerning the non-approval of black soap E470a as a basic substance 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 ⁽¹⁾	125
★ Commission Implementing Regulation (EU) 2022/1445 of 31 August 2022 amending Implementing Regulation (EU) 2018/1039 as regards the terms of authorisation of copper (II) chelate of amino acids hydrate as a feed additive for all animal species ⁽¹⁾	127

Corrigenda

★ Corrigendum to Directive (EU) 2022/362 of the European Parliament and of the Council of 24 February 2022 amending Directives 1999/62/EC, 1999/37/EC and (EU) 2019/520, as regards the charging of vehicles for the use of certain infrastructures (OJ L 69, 4.3.2022)	133
★ Corrigendum to Council Regulation (EU) 2022/515 of 31 March 2022 amending Regulation (EU) 2022/109 fixing for 2022 the fishing opportunities for certain fish stocks and groups of fish stocks applicable in Union waters and for Union fishing vessels in certain non-Union waters (OJ L 104, 1.4.2022)	134
★ Corrigendum to Regulation (EU) 2021/2115 of the European Parliament and of the Council of 2 December 2021 establishing rules on support for strategic plans to be drawn up by Member States under the common agricultural policy (CAP Strategic Plans) and financed by the European Agricultural Guarantee Fund (EAGF) and by the European Agricultural Fund for Rural Development (EAFRD) and repealing Regulations (EU) No 1305/2013 and (EU) No 1307/2013 (OJ L 435, 6.12.2021)	136

⁽¹⁾ Text with EEA relevance.

II

(Non-legislative acts)

INTERNATIONAL AGREEMENTS

Voluntary Partnership Agreement between the European Union and the Republic of Honduras on forest law enforcement, governance and trade in timber products to the European Union

The Voluntary Partnership Agreement between the European Union and the Republic of Honduras on forest law enforcement, governance and trade in timber products to the European Union, signed in Brussels on 23 February 2021, has pursuant to its Article 31(1), will enter into force on 1 September 2022.

REGULATIONS

COMMISSION REGULATION (EU) 2022/1438

of 31 August 2022

amending Annex II to Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards specific criteria for the approval of active substances that are micro-organisms

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard 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 and repealing Council Directives 79/117/EEC and 91/414/EEC ⁽¹⁾, and in particular Article 22(3) and Article 78(1)(a) thereof,

Whereas:

- (1) Regulation (EC) No 1107/2009 lays down, among others, rules for the procedure and criteria for the approval of active substances, safeners and synergists.
- (2) The Farm to Fork Strategy for a fair, healthy and environmentally friendly food system of the Commission ⁽²⁾ aims at reducing dependency on and use of chemical plant protection products, including through facilitating the placing on the market of biological active substances such as micro-organisms. In order to reach that objective, it is necessary to specify the approval criteria related to micro-organisms taking into account the most up-to-date scientific and technical knowledge, which has evolved significantly.
- (3) The existing procedures and criteria for the approval set out in Annex II to Regulation (EC) No 1107/2009, which are used to assess whether active substances may have harmful effects on human health, animal health, or unacceptable effects on the environment, are referring to the properties of micro-organisms. Since micro-organisms are living organisms, a specific approach is needed compared to chemical substances, in order to also take into account the currently available scientific knowledge that has been gathered on the biology of micro-organisms, such as on their pathogenicity and infectivity, the possible production of metabolite(s) of concern and the capacity to transfer anti-microbial resistance genes to other micro-organisms which are pathogenic and occurring in European environments, potentially affecting the effectiveness of antimicrobials used in human or veterinary medicine.
- (4) The current state of scientific knowledge on micro-organisms allows for a better and more specific approach for their assessment, which is based on the biological and ecological characteristics of the respective species and, where applicable, the respective strains of micro-organisms. As it allows for a more targeted risk assessment, such scientific knowledge should be taken into account when assessing the risks posed by active substances that are micro-organisms and plant protection products containing these substances.
- (5) In order to better reflect the latest scientific developments and the specificities of micro-organisms, while maintaining a high level of protection of human and animal health and of the environment, it is therefore necessary to adapt accordingly the criteria in Annex II to Regulation (EC) No 1107/2009.

⁽¹⁾ OJ L 309, 24.11.2009, p. 1.

⁽²⁾ Communication from the Commission to the European Parliament, the Council, the Economic and Social Committee and the Committee of the Regions A Farm to Fork Strategy for a fair, healthy and environmentally-friendly food system (COM/2020/381 final, <https://eur-lex.europa.eu/legal-content/en/TXT/?qid=1590404602495&uri=CELEX:52020DC0381>).

- (6) Point 3.1(b) of Annex II to Regulation (EC) No 1107/2009 provides for the information to be submitted by the applicant in the dossier in order to reliably predict residues in food and feed. Based on the available scientific knowledge, it is now known that residues for which an assessment is required in the case of micro-organisms are different than those for which an assessment may be required in the case of chemical active substances: the presence of micro-organisms that are non-pathogenic to humans and animals on or in edible parts of treated crops does not constitute *per-se* a hazard and only residues of chemical substances which are relevant for human and animal health may constitute a hazard or risk, i.e. the toxic metabolites possibly produced by the micro-organisms. For the sake of clarity, it is therefore appropriate to provide for this differentiation, so that it is possible to reliably predict relevant residues in relation to micro-organisms.
- (7) Point 3.4 of Annex II to Regulation (EC) No 1107/2009 refers to the composition of active substances, safeners or synergists. However, the current provisions do not apply for micro-organisms due to their different nature compared to chemicals. Indeed, the concepts of isomers and diastereo-isomers mentioned in the current provision are only relevant for chemical substances and not for any living organism, including micro-organisms. Moreover, it is necessary to specify the appropriate information required to define the composition of an active substance that is a micro-organism, such as the taxonomical identification, the deposition of the micro-organism strain at an internationally recognised culture collection including its accession number, and the content of the active substance in units which are used in microbiology. It is therefore appropriate to specify this suitable information for micro-organisms.
- (8) Point 3.5 of Annex II to Regulation (EC) No 1107/2009 refers to methods of analysis of active substances and other components occurring in the manufacturing batch. Currently available scientific knowledge includes knowledge regarding the risk assessment of relevant impurities and contaminating micro-organisms occurring during manufacturing of micro-organisms, and of metabolites produced by them. In addition, due to the different nature of active substances which are micro-organisms compared to chemicals, manufacturing batches and processes are different, and a specific approach is needed for micro-organisms compared to chemicals. Taking into consideration this scientific knowledge and these differences between active substances which are micro-organisms and chemicals, it is therefore appropriate to specify methods of analysis used for micro-organisms.
- (9) Point 3.6 of Annex II to Regulation (EC) No 1107/2009 refers to the assessment of the impact of active substances, safeners and synergists on human health. As regards active substances that are micro-organisms, currently available scientific knowledge includes knowledge regarding the assessment of pathogenicity of micro-organisms to humans, infectivity of viruses and the capacity of bacteria to transfer anti-microbial resistance genes to other micro-organisms, potentially affecting the effectiveness of antimicrobials used in human or veterinary medicine. This scientific knowledge shows that further specification is needed regarding the approval criteria laid down in Article 4 of Regulation (EC) No 1107/2009, implementing the most up-to-date scientific and technical knowledge in the risk assessment of micro-organisms. It is therefore appropriate to specify the approval criteria applying for micro-organisms.
- (10) Specifically on anti-microbial resistance, the current state of scientific knowledge on the capacity of micro-organisms to transfer antimicrobial resistance genes allows for a better and more specific approach for the assessment of which genes encoding for antimicrobial resistance are likely to be transferred to other micro-organisms, and which antimicrobials are those relevant for human or veterinary medicine. In addition, the EU Farm to Fork Strategy has set antimicrobial resistance-related targets. Therefore, further specification is needed on the data requirements to implement the most up-to-date scientific and technical knowledge on transferability of antimicrobial resistance, and to allow an assessment to be made on whether the active substance may have harmful effects on human or animal health, as indicated in the approval criteria laid down in Article 4 of Regulation (EC) No 1107/2009.
- (11) Point 5.2.1 of Annex II to Regulation (EC) No 1107/2009 sets out the criteria for considering active substances that are micro-organisms as low-risk active substances and currently refers to the possible occurrence of multiple resistance to antimicrobials. Without any reference to the possibility of this resistance to be transferred, these criteria refer to the number of treatment options with antimicrobials which are effective against the active substance that is a micro-organism. Indeed, although micro-organisms can only be approved if not pathogenic, not infective under the recommended conditions of use, and not infective to humans under any circumstances if they are viruses,

it is necessary to ensure that several treatment options with effective antimicrobials are available in order to maintain a high level of protection of human health in the unlikely event of an opportunistic infection, especially in vulnerable groups of the population. However, the possible occurrence of multiple resistance to some antimicrobials as currently outlined in point 5.2.1 does not clarify the number of effective treatment options based on antimicrobials which are available. It is therefore appropriate to specify the low-risk criteria applying for micro-organisms other than viruses. For the sake of clarity and legal certainty, it is therefore appropriate to further specify the criteria to consider an active substance that is a micro-organism as low-risk active substance, by referring to the number of antimicrobial agents against which the micro-organism is demonstrated susceptible. In addition, it is appropriate to specify that such criteria apply only for micro-organisms other than viruses, since viruses are usually provided with a narrow host range, and viruses which are infective to humans would be excluded from approval.

- (12) Point 5.2.2 of Annex II to Regulation (EC) No 1107/2009 sets out the criteria to consider baculoviruses as low-risk active substances. However, new applications for approval concerning viruses belonging to species other than the baculovirus species, and used as active substances in plant protection products have been submitted. It is therefore appropriate to include low-risk criteria which are applicable also to other species of viruses. In addition, the currently available scientific knowledge on viruses used as active substances in plant protection products, in particular for those viruses which are non-virulent variants of plant pathogens makes it possible to identify those active substances which may be approved only where, under the proposed conditions of use, the likelihood of reverting to virulent and causing adverse effects in target and non-target plants through mutation is negligible. In light of this concern, it is appropriate to provide that viruses which are non-virulent variants of plant pathogens are not to be considered as low-risk active substances when the likelihood of causing adverse effects in non-target plants could not be entirely excluded. It is therefore appropriate to specify the low-risk criteria applying to viruses which are non-virulent variants of plant pathogens, rather than to baculovirus only.
- (13) As the amended criteria reflect the current state of scientific and technical knowledge and clarify the existing criteria, the new criteria should apply as soon as possible. However, for legal certainty a transitional regime needs to be provided for in this Regulation.
- (14) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

HAS ADOPTED THIS REGULATION:

Article 1

Amendment to Regulation (EC) No 1107/2009

Regulation (EC) No 1107/2009 is amended in accordance with the Annex to this Regulation.

Article 2

Transitional measures

Regulation (EC) No 1107/2009 in the version applicable on 20 November 2022 shall continue to apply in the following cases:

- (a) procedures concerning the approval of an active substance that is a micro-organism or an amendment to the approval of such a substance for which the dossiers provided for in Article 8(1) and (2) of Regulation (EC) No 1107/2009 are submitted before 21 November 2022;

- (b) procedures concerning the renewal of approval of an active substance that is a micro-organism where the application for renewal referred to in Article 5 of Commission Implementing Regulation (EU) 2020/1740 ⁽³⁾ is submitted before 21 November 2022.

Article 3

Entry into force and application

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

It shall apply from 21 November 2022.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 31 August 2022.

For the Commission
The President
Ursula VON DER LEYEN

⁽³⁾ Commission Implementing Regulation (EU) 2020/1740 of 20 November 2020 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council, and repealing Commission Implementing Regulation (EU) No 844/2012 (OJ L 392, 23.11.2020, p. 20).

ANNEX

Annex II to Regulation (EC) No 1107/2009 is amended as follows:

(1) point 3.1(b) is replaced by the following:

‘(b) reliably predict the residues in food and feed, including succeeding crops, on the basis of information provided in accordance with the data requirements for active substances;’;

(2) point 3.4 is replaced by the following:

‘3.4. Composition of the active substance, safener or synergist

3.4.1. For chemical active substances, safeners and synergists, the specification shall define the minimum degree of purity, the identity and maximum content of impurities and, where relevant, of isomers/diastereoisomers and additives, and the content of impurities of toxicological, ecotoxicological or environmental concern within acceptable limits.

3.4.2. For chemical active substances, safeners and synergists, the specification shall be in compliance with the relevant Food and Agriculture Organisation specification as appropriate, where such specification exists. However, where necessary for reasons of protection of human or animal health or the environment, stricter specifications may be adopted.

3.4.3. Active substances that are micro-organisms shall be deposited at an internationally recognised culture collection and shall have an accession number. The species' name of the micro-organisms shall be identified unequivocally, based on the latest scientific information, and the micro-organisms shall be named at the strain level, including any other designation which may be relevant (e.g. isolate level, if relevant for viruses). It shall be indicated whether or not the micro-organisms are wild types, spontaneous or induced mutants, or genetically modified organisms.

3.4.4. For active substances that are micro-organisms, the specification shall define the minimum and maximum content of the micro-organism, the identity and content of relevant contaminating micro-organisms, metabolites of concern and impurities of toxicological, ecotoxicological or environmental concern within acceptable limits.’;

(3) point 3.5 is replaced by the following:

‘3.5. Methods of analysis

3.5.1. The methods of analysis of chemical active substances, safeners or synergists as manufactured and of determination of impurities of toxicological, ecotoxicological or environmental concern or which are present in quantities greater than 1 g/kg in the active substance, safener or synergist as manufactured, shall have been validated and shown to be sufficiently specific, correctly calibrated, accurate and precise.

3.5.2. The methods of residue analysis for chemical active substances and relevant metabolites in plant, animal and environmental matrices and drinking water, as appropriate, shall have been validated and shown to be sufficiently sensitive with respect to the levels of concern.

3.5.3. The evaluation shall have been carried out in accordance with the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6).

3.5.4. For active substances that are micro-organisms, the methods of analysis to identify and quantify them, and relevant contaminating micro-organisms, shall have been validated and shown to be sufficiently specific, correctly calibrated, accurate and precise.

3.5.5. For active substances that are micro-organisms, the methods of analysis of metabolites of concern and relevant impurities shall have been validated and shown to be sufficiently specific, correctly calibrated, accurate and precise.’;

(4) the following point 3.6.6 is added after point 3.6.5:

‘3.6.6. Active substances that are micro-organisms shall only be approved if, on the basis of the assessment carried out on the information provided in accordance with the data requirements, it is concluded that the strain of the micro-organism is not pathogenic to humans.

In addition:

- (a) viruses shall only be approved if, on the basis of the assessment carried out on the information provided in accordance with the data requirements, it is concluded that the isolate of the virus is not infective to humans;
- (b) strains of bacteria shall only be approved if, on the basis of the assessment carried out on the information provided in accordance with the data requirements, it is concluded that they do not have any known, functional and transferable gene coding for resistance to relevant antimicrobial agents as defined in accordance with the data requirements.’;

(5) point 5.2 is replaced by the following:

‘5.2. Micro-organisms

5.2.1. An active substance that is a micro-organism other than a virus may be considered a low-risk active substance unless its susceptibility to at least two classes of antimicrobial agents has not been demonstrated.

5.2.2. An active substance that is a virus may be considered a low-risk active substance unless it is:

- (a) a baculovirus with demonstrated adverse effects on non-target insects; or
 - (b) a non-virulent variant of a plant pathogen with demonstrated adverse effects on non-target plants.’.
-

COMMISSION REGULATION (EU) 2022/1439**of 31 August 2022****amending Regulation (EU) No 283/2013 as regards the information to be submitted for active substances and the specific data requirements for micro-organisms****(Text with EEA relevance)**

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard 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 and repealing Council Directives 79/117/EEC and 91/414/EEC ⁽¹⁾, and in particular Article 78(1)(b) thereof,

Whereas:

- (1) Commission Regulation (EU) No 283/2013 ⁽²⁾ lays down data requirements for active substances. For active substances that are chemicals, these are laid down in Part A of the Annex to that Regulation, and for active substances that are micro-organisms, these are laid down in Part B of that Annex, with common requirements set out in the introductory part of that Annex.
- (2) The Farm to Fork Strategy for a fair, healthy and environmentally-friendly food system ⁽³⁾ aims at reducing dependency on and use of chemical plant protection products, including through facilitating the placing on the market of biological active substances such as micro-organisms. In order to reach those objectives, it is necessary to specify the data requirements related to micro-organisms taking into account the most up-to-date scientific and technical knowledge, which has evolved significantly.
- (3) The currently available scientific knowledge concerning metabolites produced by micro-organisms allows for a better understanding of the role those metabolites play in the mode of action of micro-organisms producing them. Taking into consideration that metabolites produced by micro-organisms are chemical substances, their possible contribution to the mode of action may lead to legal uncertainty on whether applications are to comply with the requirements provided for in Part A of that Annex concerning chemical active substances, or in Part B thereof, concerning micro-organisms. It is therefore appropriate to amend the introduction of the Annex to Regulation (EU) No 283/2013, in order to better specify, based on the properties of the active substances, and in particular of the metabolites produced by micro-organisms, when applications are to comply with the requirements provided for in Part A of that Annex, or in Part B thereof.
- (4) Since micro-organisms are living organisms, a specific approach is needed compared to chemical substances, in order to also take into account the new scientific knowledge that has emerged on the biology of micro-organisms. That scientific knowledge consists in new information on key characteristics of micro-organisms, such as their pathogenicity and infectivity, the possible production of metabolite(s) of concern and the capacity to transfer antimicrobial resistance genes to other micro-organisms which are pathogenic and occurring in European environments, potentially affecting the effectiveness of antimicrobials used in human or veterinary medicine.

⁽¹⁾ OJ L 309, 24.11.2009, p. 1.

⁽²⁾ Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, 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 (OJ L 93, 3.4.2013, p. 1).

⁽³⁾ Communication from the Commission to the European Parliament, the Council, the Economic and Social Committee and the Committee of the Regions A Farm to Fork Strategy for a fair, healthy and environmentally-friendly food system (COM/2020/381 final, <https://eur-lex.europa.eu/legal-content/en/TXT/?qid=1590404602495&uri=CELEX:52020DC0381>).

- (5) The current state of scientific knowledge on micro-organisms allows for a better and more specific approach for their assessment, which is based on their mode of action and the ecological characteristics of the respective species and, where applicable, the respective strains of micro-organisms. As it allows for a more targeted risk assessment, such scientific knowledge should be taken into account when assessing the risks posed by active substances that are micro-organisms.
- (6) In order to better reflect the latest scientific developments and the specific biological properties of micro-organisms, while maintaining a high level of protection of human and animal health and of the environment, it is therefore necessary to adapt the existing data requirements accordingly.
- (7) In general, micro-organisms used for plant protection are active against a specific group of pests, and their specific modes of action may intrinsically not be of relevance as regards effects on human and animal health. They may well produce metabolites that would require specific exposure and risk assessment. Their host range specificity may well limit the risk of persistent effects on non-target organisms, compared to chemical substances, reducing also the relevance of animal testing to establish their pathogenic profile. All these specific characteristics of micro-organisms are important to differentiate the way to conduct the risk assessment for micro-organisms compared to the way it is being done for chemical substances. It is therefore appropriate to amend Part B of the Annex to Regulation (EU) No 283/2013 in order to update the data requirements to the latest scientific developments and adapt them to the specific biological properties of micro-organisms.
- (8) The current title of Part B of the Annex to Regulation (EU) No 283/2013 refers to micro-organisms including viruses. However, Article 3, point (15) of Regulation (EC) No 1107/2009 already defines micro-organisms, and the definition includes viruses. It is therefore appropriate to adapt that title to be consistent with Article 3, point (15) of that Regulation.
- (9) It is appropriate to introduce a definition of 'Microbial Pest Control Agent as manufactured' ('MPCA as manufactured') because certain tests are required to be performed using a sample of the MPCA as manufactured, rather than using the active substance or the other components of the MPCA as manufactured after purification. It is indeed more appropriate to refer, with one unique term, to the micro-organism as manufactured and to those components included in the manufacturing batch which might be of relevance for the risk assessment, such as relevant contaminating micro-organisms and relevant impurities.
- (10) New scientific knowledge has emerged on the capacity of micro-organisms to transfer antimicrobial resistance genes to other micro-organisms which are pathogenic and occurring in European environments, potentially affecting the effectiveness of antimicrobials used in human or veterinary medicine. This new scientific knowledge allows for a better and more specific approach for the assessment of which genes encoding for antimicrobial resistance are likely to be transferred to other micro-organisms, and which antimicrobials are those relevant for human or veterinary medicine. In addition, the EU Farm to Fork Strategy has set antimicrobial resistance-related targets. Therefore, further specification is needed on the data requirements to implement the most up-to-date scientific and technical knowledge on transferability of antimicrobial resistance, and allow for an assessment to be made on whether the active substance may have harmful effects on human or animal health, as indicated in the approval criteria laid down in Article 4 of Regulation (EC) No 1107/2009.
- (11) A reasonable period should be allowed to elapse before the amended data requirements become applicable in order to permit applicants to prepare themselves to meet those requirements.
- (12) In order to permit Member States and interested parties to prepare themselves to fulfil the new requirements, it is appropriate to lay down transitional measures concerning data submitted for applications for the approval, renewal of approval or amendment to the conditions of approval of active substances that are micro-organisms and data submitted for applications for authorisation, renewal of authorisation and amendment to the authorisation of plant protection products containing active substances that are micro-organisms.

- (13) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee, on Plants, Animals, Food and Feed,

HAS ADOPTED THIS REGULATION:

Article 1

Amendments to Regulation (EU) No 283/2013

The Annex to Regulation (EU) No 283/2013 is amended as follows:

- (1) the Introduction is replaced by the text set out in Annex I to this Regulation;
- (2) Part B is replaced by the text set out in Annex II to this Regulation.

Article 2

Transitional measures as regards certain procedures concerning active substances that are micro-organisms

1. Applicants may submit data in accordance with Part B of the Annex to Regulation (EU) No 283/2013 as it stood before being amended by this Regulation in the following cases:
 - (a) procedures concerning the approval of an active substance that is a micro-organism or an amendment to the approval of such a substance for which the dossiers provided for in Article 8(1) and (2) of Regulation (EC) No 1107/2009 are submitted before 21 May 2023;
 - (b) procedures concerning the renewal of approval of an active substance that is a micro-organism where the application for renewal referred to in Article 5 of Commission Implementing Regulation (EU) 2020/1740 ⁽⁴⁾ is submitted before 21 May 2023.
2. Where applicants choose to apply the option provided for in paragraph 1, they shall specify that choice in writing when submitting the application concerned. Such choice shall be irrevocable for the procedure concerned.

Article 3

Transitional measures as regards certain procedures concerning plant protection products containing active substances that are micro-organisms

1. For authorisation of plant protection products, within the meaning of Regulation (EC) No 1107/2009, containing one or more active substances that are micro-organisms, where the dossiers have been submitted in accordance with Article 2 of this Regulation or a decision on the renewal of the approval has not been taken in accordance with Article 20 of Regulation (EC) No 1107/2009 on the basis of Part B of the Annex to Regulation (EU) No 283/2013 as amended by this Regulation, applicants:
 - (a) shall submit data in accordance with Part B of the Annex to Regulation (EU) No 283/2013 as it stood before being amended by this Regulation, unless they act in accordance with point (b) of this paragraph;
 - (b) may choose, from 21 November 2022 to submit data in accordance with Part B of the Annex to Regulation (EU) No 283/2013 as amended by this Regulation.
2. Where applicants choose to apply the option provided for in paragraph 1(b), they shall specify that choice in writing when submitting the application concerned. Such choice shall be irrevocable for the procedure concerned.

⁽⁴⁾ Commission Implementing Regulation (EU) 2020/1740 of 20 November 2020 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council, and repealing Commission Implementing Regulation (EU) No 844/2012 (OJ L 392, 23.11.2020, p. 20).

*Article 4***Entry into force and application**

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

It shall apply from 21 November 2022.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 31 August 2022.

For the Commission
The President
Ursula VON DER LEYEN

ANNEX I

INTRODUCTION

Information to be submitted, its generation and its presentation

A dossier shall be submitted in accordance with Part A if the active substance is:

- (a) a chemical substance (including both semiochemicals and extracts from biological material), or
- (b) a metabolite produced by a micro-organism where:
 - the metabolite is purified from the micro-organism; or
 - the metabolite is not purified from a producing micro-organism which is no longer capable of replication or of transferring genetic material.

A dossier shall be submitted in accordance with Part B if the active substance is:

- (a) a micro-organism, either as a single strain or as a qualitatively defined combination of strains as they occur naturally or by manufacture, or
- (b) a micro-organism, either as a single strain or as a qualitatively defined combination of strains as they occur naturally or by manufacture, and one or more metabolites produced by the micro-organism that are claimed to be part of the plant protection action (i.e. when the application of the metabolite(s) purified from the micro-organism would not cause the claimed plant protection action).

1. For the purposes of this Annex, the following definitions apply:

- (1) **'efficacy'** means a measure concerning the overall effect of the application of a plant protection product on the agricultural system in which it is used (i.e. which includes positive effects of treatment in performing the desired plant protection activity and negative effects such as development of resistance, phytotoxicity or reduction of qualitative or quantitative yield);
- (2) **'relevant impurity'** means a chemical impurity that is of concern for human health, animal health or the environment;
- (3) **'effectiveness'** means the capacity of the plant protection product to produce a positive effect regarding the desired plant protection activity;
- (4) **'toxicity'** means the degree of injury or damage in an organism caused by a toxin or a toxic substance;
- (5) **'toxin'** means a substance that is produced within living cells or organisms and is able to injure or cause damage in a living organism.

The information submitted shall meet the requirements set out in points 1.1 to 1.14.

- 1.1. The information shall be sufficient to evaluate the foreseeable risks, whether immediate or delayed, which the active substance may entail for humans, including vulnerable groups, animals and the environment and contain at least the information and results of the studies referred to in this Annex.
- 1.2. Any information including any known data on potentially harmful effects of the active substance, its metabolites and impurities on human and animal health or on their potential presence in groundwater shall be included.
- 1.3. Any information including any known data on potentially unacceptable effects of the active substance, its metabolites and impurities on the environment, plants and plant products shall be included.
- 1.4. The information shall include all relevant data from the scientific peer reviewed open literature on the active substance, relevant metabolites, and where relevant breakdown or reaction products and plant protection products containing the active substance and dealing with side-effects on human and animal health, the environment and non-target species. A summary of that data shall be provided.

- 1.5. The information shall include a full and unbiased report of the studies conducted as well as a full description of them. Such information shall not be required, where a justification is provided showing that:
- (a) it is not necessary owing to the nature of the plant protection product or its proposed uses, or it is not scientifically necessary; or
 - (b) it is technically not possible to supply.
- 1.6. The simultaneous use of the active substance as a biocidal product or in veterinary medicine shall be reported. If the applicant for the application for the approval of the active substance in the plant protection product is identical to the one responsible for the notification of the active substance as a biocidal product or as a veterinary medicine, a summary of all relevant data submitted for approval of the biocidal product or the veterinary medicine shall be submitted. Where relevant, that summary shall include toxicological reference values and MRL proposals, taking into account any possible cumulative exposure due to different uses of the same substance based on scientific methods accepted by the competent authorities of the Union, together with information on residues, toxicology data and use of the plant protection product. If the applicant for the application for the approval of the active substance in the plant protection product is not identical to the one responsible for the notification of the active substance as a biocidal product or in veterinary medicine, a summary of all available data shall be submitted.
- 1.7. Where relevant, the information shall be generated using test methods, which are included in the list referred to in Section 6.
- In the absence of suitable internationally or nationally validated test guidelines, test protocol discussed with and accepted by the competent authorities of the Union shall be used. Any deviations from test guidelines shall be described and justified.
- 1.8. The information shall include a full description of the test methods used.
- 1.9. The information shall include a list of endpoints for the active substance, where relevant.
- 1.10. Where relevant, the information shall be generated in accordance with Directive 2010/63/EU of the European Parliament and of the Council ⁽¹⁾.
- 1.11. The information on the active substance, taken together with the information concerning one or more plant protection products containing the active substance and together, if appropriate, with the information concerning safeners and synergists and other components of the plant protection product, shall be sufficient to:
- (a) permit an assessment of the risks for humans, associated with handling and use of plant protection products containing the active substance;
 - (b) for chemical active substances: permit an assessment of the risks for human and animal health, arising from residues of the active substance and its relevant metabolites, impurities and, where relevant, breakdown and reaction products remaining in water, air, food and feed;
 - (c) for active substances that are micro-organisms: permit an assessment of the risks for human and animal health, arising from residues of the metabolites of concern in water, air, food and feed;
 - (d) for chemical active substances: predict the distribution, fate and behaviour in the environment of the active substance and metabolites, breakdown and reaction products where they are of toxicological, or environmental significance, as well as the time courses involved;
 - (e) permit an assessment of the impact on non-target species (flora and fauna), including the impact on their behaviour, which are likely to be exposed to the active substance, its relevant metabolites and, where relevant, breakdown and reaction products, where they are of toxicological, pathogenic or environmental significance. Impact can result from single, prolonged or repeated exposure and can be direct or, where relevant, indirect, reversible or irreversible;

⁽¹⁾ Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes (OJ L 276, 20.10.2010, p. 33).

- (f) evaluate the impact on biodiversity and the ecosystem;
- (g) identify non-target species and populations for which risks arise because of potential exposure;
- (h) permit an evaluation of short and long-term risks for non-target species - populations, communities and processes;
- (i) classify the chemical active substance as to hazard in accordance with Regulation (EC) No 1272/2008 of the European Parliament and of the Council ⁽²⁾;
- (j) specify the pictograms, the signal words and relevant hazard and precautionary statements for the protection of human and animal health, non-target species and the environment, which are to be used for labelling;
- (k) establish, where relevant, an acceptable daily intake (ADI) level for humans;
- (l) establish, where relevant, acceptable operator exposure levels (AOEL);
- (m) establish, where relevant, an acute reference dose (ARfD) for humans;
- (n) identify relevant first aid measures as well as appropriate diagnostic and therapeutic measures to be followed in the event of poisoning or infection in humans;
- (o) for chemical active substances: establish the isomeric composition and the possible metabolic conversion of the isomers, where relevant;
- (p) establish residues definitions appropriate for risk assessment, where relevant;
- (q) establish residues definitions appropriate for monitoring and enforcement purposes, where relevant;
- (r) permit a risk assessment of consumer exposure, including, where relevant, a cumulative risk assessment deriving from exposure to more than one active substance;
- (s) permit an estimation of the exposure of operators, workers, residents and bystanders including, where relevant, the cumulative exposure to more than one active substance;
- (t) establish, where relevant, maximum residue levels and concentration/dilution factors in accordance with Regulation (EC) No 396/2005 of the European Parliament and of the Council ⁽³⁾;
- (u) permit an evaluation to be made as to the nature and extent of the risks for humans, animals (species normally fed and kept by humans or food-producing animals) and of the risks for other non-target vertebrate species;
- (v) identify measures necessary to mitigate the risks identified for human and animal health, the environment and/or non-target species;
- (w) for chemical active substances: decide whether or not the active substance has to be considered as persistent organic pollutant (POP), persistent, bio accumulative and toxic (PBT) or very persistent and very bio accumulative (vPvB) in accordance with the criteria laid down in Annex II to Regulation (EC) No 1107/2009;
- (x) decide whether or not the active substance is to be approved;
- (y) for chemical active substances: decide whether or not the active substance has to be considered as a candidate for substitution in accordance with the criteria laid down in Annex II to Regulation (EC) No 1107/2009;
- (z) decide whether or not the active substance has to be considered as a low-risk active substance in accordance with the criteria laid down in Annex II to Regulation (EC) No 1107/2009;
- (aa) specify conditions or restrictions to be associated with any approval.

⁽²⁾ Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (OJ L 353, 31.12.2008, p. 1).

⁽³⁾ Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC (OJ L 70, 16.3.2005, p. 1).

- 1.12. Where relevant, tests shall be designed and data analysed using appropriate statistical methods. Details of the statistical analysis shall be reported transparently.
- 1.13. Exposure calculations shall refer to scientific methods accepted by the European Food Safety Authority, where available. Additional methods, when used, shall be justified.
- 1.14. For each section of this Annex, a summary of all data, information and evaluation made shall be submitted. This shall include a detailed and critical assessment in accordance with Article 4 of Regulation (EC) No 1107/2009.
2. The requirements set out in this Annex constitute the minimum set of data to be submitted. Member States may set out additional requirements at national level to address specific circumstances, specific exposure scenarios and specific patterns of use other than those taken into account for approval. The applicant shall pay careful attention to environmental, climatic and agronomic conditions when tests are set up subject to the approval by the Member State where the application has been submitted.

3. **Good laboratory practice (GLP)**

- 3.1. Tests and analyses shall be conducted in accordance with the principles laid down in Directive 2004/10/EC of the European Parliament and of the Council ⁽⁴⁾ where testing is done to obtain data on the properties or safety with respect to human or animal health or the environment.
- 3.2. By way of derogation from point 3.1:
 - (a) for active substances that are micro-organisms, tests and analyses done to obtain data on their properties and safety with respect to other aspects than human health may be conducted by official or officially recognised testing facilities or organisations which satisfy at least the requirements set out in points 3.2 and 3.3 of the Introduction of the Annex to Commission Regulation (EU) No 284/2013 ⁽⁵⁾;
 - (b) for tests and analyses made to obtain data for minor crops required under points 6.3 and 6.5.2 of Part A:
 - the field phase may have been conducted by official or officially recognised testing facilities or organisations which satisfy the requirements as laid down in points 3.2 and 3.3 of the Introduction of the Annex to Regulation (EU) No 284/2013;
 - the analytical phase, if not realised in accordance with the principles of good laboratory practice ('GLP principles'), shall be conducted by laboratories accredited for the relevant method in accordance with the European standard EN ISO/IEC 17025 'General requirements for the competence of testing and calibration laboratories';
 - (c) studies conducted before the application of this Regulation, although not fully compliant with GLP principles or with current test methods, may be integrated into the assessment if carried out in accordance with scientifically validated test guidelines, thereby avoiding repeating animal tests, especially for carcinogenicity and reprotoxicity studies. This derogation from point 3.1 shall apply in particular to studies with vertebrate species.

4. **Test material**

- 4.1. A detailed description (specification) of the test material used shall be provided. Where tests are done using the active substance, the test material used shall comply with the specification that will be used in the manufacture of plant protection products to be authorised, except for radio-labelled chemicals or the purified chemical active substance.

⁽⁴⁾ Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances (OJ L 50, 20.2.2004, p. 44).

⁽⁵⁾ Commission Regulation (EU) No 284/2013 of 1 March 2013 setting out the data requirements for plant protection products, 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 (OJ L 93, 3.4.2013, p. 85).

- 4.2. Where studies are conducted using an active substance manufactured in the laboratory or in a pilot plant production system, the studies shall be repeated using the active substance as manufactured, unless the applicant shows that the test material used is essentially the same, for the purposes of toxicological, pathological, ecotoxicological, environmental and residue testing and assessment. In cases of uncertainty, bridging studies shall be submitted to serve as a basis for a decision as to the possible need for repetition of the studies.
 - 4.3. Where studies are conducted using an active substance of different purity or which contains different impurities or different levels of impurities to the technical specification or where the active substance is a mixture of components, the significance of the differences shall be addressed either by data or scientific case. In cases of uncertainty, appropriate studies using the active substance as manufactured for commercial production shall be submitted to serve as a basis for a decision.
 - 4.4. In the case of studies in which dosing extends over a certain period (for example, repeated dose studies), the same batch of active substance shall be used, if stability permits. Whenever a study implies the use of different doses, the relationship between dose and adverse effect shall be reported.
 - 4.5. For chemical active substances, when tests are conducted using a purified chemical active substance (≥ 980 g/kg) of stated specification, the purity of such test material shall be as high as can be achieved using the best available technology and shall be reported. A justification shall be provided in cases where the degree of purity achieved is less than 980 g/kg. Such justification shall demonstrate that all technically feasible and reasonable possibilities for the production of the purified chemical active substance have been exhausted.
 - 4.6. For chemical active substances, where radio-labelled test material of the chemical active substance is used, radio-labels shall be positioned at sites (one or more as necessary) to facilitate elucidation of metabolic and transformation pathways and to facilitate the investigation of the distribution of the active substance and of its metabolites, reaction and breakdown products.
 5. **Tests on vertebrate animals**
 - 5.1. Tests on vertebrate animals shall be undertaken only where no other validated methods are available. Alternative methods shall include *in vitro* methods or *in silico* methods. Reduction and refinement methods for *in vivo* testing shall also be encouraged to keep the number of animals used in testing to a minimum.
 - 5.2. The principles of replacement, reduction and refinement of the use of vertebrate animals shall be taken into account in the design of the test methods, in particular when appropriate validated methods become available to replace, reduce or refine animal testing.
 - 5.3. Study designs shall be carefully considered from ethical point of view, taking into account the scope for reduction, refinement and replacement of animal tests. For example, by including one or more additional dose groups or time points for blood sampling in one study, it may be possible to avoid the need for another study.
 6. For purposes of information and of harmonisation the list of test methods and guidance documents relevant to the implementation of this Regulation shall be published in the *Official Journal of the European Union*. That list shall be regularly updated.
-

ANNEX II

‘PART B

ACTIVE SUBSTANCES THAT ARE MICRO-ORGANISMS

INTRODUCTION TO PART B

- (i) This Introduction to Part B complements the Introduction to this Annex with points which are specific for active substances that are micro-organisms.
- (ii) For the purpose of Part B, the following definitions apply:
 - (1) **‘strain’** means a genetic variant of an organism in its taxonomic level (species) that is made up of the descendants of a single isolation in pure culture from the original matrix (e.g. the environment) and usually is made up of a succession of cultures ultimately derived from an initial single colony;
 - (2) **‘colony-forming unit’ (‘CFU’)** means a measurement unit used to estimate the number of bacterial or fungal cells in a sample, which have the ability to multiply under controlled growing conditions, with the consequence that one or more cells reproduce and multiply to form a single visible colony;
 - (3) **‘International Unit’ (‘IU’)** means a quantity of a substance that produces a specific effect when tested in accordance with an internationally accepted biological procedure;
 - (4) **‘Microbial Pest Control Agent as manufactured’ (‘MPCA as manufactured’)** means the outcome of the manufacturing process of the micro-organism(s) intended to be used as active substance in plant protection products, consisting of the micro-organism(s) and any additives, metabolites (including metabolites of concern), chemical impurities (including relevant impurities), contaminating micro-organisms (including relevant contaminating micro-organisms) and the spent medium/rest fraction resulting from the manufacturing process or, in case of a continuous manufacturing processes where a strict separation between the manufacturing of the micro-organism(s) and the production process of the plant protection product is not possible, a non-isolated intermediate;
 - (5) **‘additive’** means a component added to the active substance during its manufacturing, to preserve microbial stability and/or facilitate handling;
 - (6) **‘purity’** means the content of the micro-organism present in the MPCA as manufactured expressed in a relevant unit and the maximum content of substances of concern in case they are identified;
 - (7) **‘relevant contaminating micro-organism’** means a pathogenic/infective micro-organism unintentionally present in the MPCA as manufactured;
 - (8) **‘seed stock’** means a microbial strain starter culture used to manufacture the MPCA as manufactured or the final plant protection product;
 - (9) **‘spent medium/rest fraction’** means the fraction of the MPCA as manufactured consisting of remaining or transformed starting materials, and excluding the micro-organism(s) that is the active substance, metabolites of concern, additives, relevant contaminating micro-organisms, and relevant impurities;
 - (10) **‘starting material’** means substances used in the manufacturing process of the MPCA as manufactured as substrate and/or buffering agent;
 - (11) **‘ecological niche’** means an ecological function and actual physical spaces occupied by a particular species within the community or ecosystem;
 - (12) **‘host range’** means the range of different biological host-species that can be infected by a microbial species or strain;
 - (13) **‘infectivity’** means the ability of a micro-organism to cause an infection;

- (14) **'infection'** means the non-opportunistic introduction or entry of a micro-organism into a susceptible host, where the micro-organism is able to reproduce to form new infective units and persist in the host, whether or not the micro-organism causes pathological effects or disease;
- (15) **'pathogenicity'** means the non-opportunistic ability of a micro-organism to inflict injury and damage to the host upon infection;
- (16) **'non-opportunistic'** means a condition under which a micro-organism exerts an infection or inflicts an injury or damage when the host is not weakened by a predisposing factor (e.g. immune system impaired by an unrelated cause);
- (17) **'opportunistic infection'** means an infection occurring in a host weakened by a predisposing factor (e.g. immune system impaired by an unrelated cause);
- (18) **'virulence'** means the degree of pathogenicity that a pathogenic micro-organism is able to exert in the host;
- (19) **'virulence factor'** means a factor that enhance the pathogenicity/virulence of a micro-organism;
- (20) **'metabolite of concern'** means a metabolite produced by the micro-organism under assessment, with known toxicity or known relevant antimicrobial activity, which is present in the MPCA as manufactured at levels that may present a risk to human health, animal health or the environment, and/or for which it cannot be adequately justified that *in-situ* production of the metabolite is not relevant for the risk assessment;
- (21) **'in-situ production'** means the production of a metabolite by the micro-organism after application of the plant protection product containing that micro-organism;
- (22) **'background level of a metabolite'** means a level of a metabolite that is likely to occur in relevant European environments (including also sources different than those of plant protection) and/or in food and feed (e.g. edible plant parts), when the micro-organisms are in conditions to grow, reproduce and to produce such metabolite in presence of a host or availability of carbon and nutrient sources, under consideration of high host densities and nutrients;
- (23) **'antimicrobial resistance' ('AMR')** means the intrinsic or acquired ability of a micro-organism to multiply in the presence of an antimicrobial agent at concentrations which are relevant for therapeutic measures in human or veterinary medicine, making that substance therapeutically ineffective;
- (24) **'antimicrobial agent'** means any antibacterial, antiviral, antifungal, anthelmintic or antiprotozoal agent that is a substance of natural, semi-synthetic, or synthetic origin that at *in vivo* concentrations kills or inhibits the growth of micro-organisms by interacting with a specific target;
- (25) **'acquired antimicrobial resistance'** means a non-intrinsic and acquired novel resistance enabling a micro-organism to survive or multiply in the presence of an antimicrobial agent at concentrations higher than that which inhibits wild type strains of the same species;
- (26) **'intrinsic antimicrobial resistance'** means all inherent properties of a microbial species that limit the action of antimicrobial agents thereby allowing it to survive and multiply in presence of the antimicrobial agents at concentrations that are relevant for their therapeutic uses. Inherent properties of micro-organisms are considered not transferable and can include structural characteristics like lack of drug targets, the impermeability of cellular envelopes, activity of multidrug efflux pumps, or activity of metabolic enzymes. An antimicrobial resistance gene is considered intrinsic if it is located on a chromosome in the absence of mobile genetic element and shared by the majority of wild type strains of the same species;
- (27) **'relevant antimicrobial activity'** means the antimicrobial activity caused by relevant antimicrobial agents;

- (28) **‘relevant antimicrobial agents’** means all antimicrobial agents important for therapeutic use in humans or animals, as described in the latest available versions at the time of submission of the dossier:
- in a list adopted by means of Commission Regulation (EU) 2021/1760 ⁽¹⁾ in accordance with Article 37(5) of Regulation (EU) 2019/6 of the European Parliament and of the Council ⁽²⁾, or
 - by the World Health Organisation ⁽³⁾ in the lists of Critically Important Antimicrobials, Highly Important Antimicrobials and Important Antimicrobials for Human Medicine;
- (29) **‘viroid’** means any of a class of infectious agents consisting of a small strand of RNA not associated with any protein. The RNA does not code for proteins and is not translated; it is replicated by host cell enzymes;
- (30) **‘predicted environmental density’** means a conservative estimation of the population density of the micro-organism in soil or surface water upon application in accordance with the conditions of use, calculated based on the maximum application rate and the maximum number of applications per year of the plant protection product containing the micro-organism.
- (iii) The information from scientific peer-reviewed literature as provided for under point 1.4 of the Introduction shall be provided at the relevant taxonomic level of the micro-organism (e.g. strain, species, genus). An explanation on why the chosen taxonomic level is considered relevant for the addressed data requirement shall be provided.
- (iv) Other available sources of information, such as medical reports, may also be provided and submitted in a summary.
- (v) Where appropriate or specifically indicated in the data requirements, test guidelines as described in Part A shall be used also for this Part, upon adaptation in such a way that they are appropriate for chemical compounds present in the MPCA as manufactured.
- (vi) Where testing is done, a detailed description (specification) of the material used and its impurities, in accordance with point 1.4, shall be provided. Where studies are conducted using micro-organisms produced in the laboratory or in a pilot scale production system, the studies shall be repeated using the MPCA as manufactured, unless it can be demonstrated that the test material used is essentially the same for the purposes of the testing and assessment.
- (vii) If the active substance is a genetically modified micro-organism, a copy of the evaluation of the data concerning the risk assessment, as stated in Article 48 of Regulation (EC) No 1107/2009, shall be submitted.
- (viii) The assessment of pathogenicity and infectivity of micro-organisms shall be based on a weight of evidence approach, taking into account that:
- tests on animals may not always be suitable for extrapolation to humans due to differences between humans and test animals (e.g. immune system, microbiome), and
 - micro-organisms might have narrow host range, as a result of which it cannot always be assumed that a micro-organism that does not cause disease in the animals tested has the same result in humans, and vice-versa.
- (ix) The information on the micro-organism shall be sufficient to permit an evaluation to be made as to the risk concerning to anti-microbial resistance.
- (x) Until validated methods for testing dermal and respiratory sensitisation caused by micro-organisms become available, all micro-organisms shall be considered as potential sensitisers.

⁽¹⁾ Commission Delegated Regulation (EU) 2021/1760 of 26 May 2021 supplementing Regulation (EU) 2019/6 of the European Parliament and of the Council by establishing the criteria for the designation of antimicrobials to be reserved for the treatment of certain infections in humans (OJ L 353, 6.10.2021, p. 1).

⁽²⁾ Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC (OJ L 4, 7. 1.2019, p.43).

⁽³⁾ <https://www.who.int/publications/i/item/97892415115528>.

1. **IDENTITY OF THE APPLICANT, IDENTITY OF THE ACTIVE SUBSTANCE AND MANUFACTURING INFORMATION**

1.1. **Applicant**

The name and address of the applicant shall be provided, as well as the name, address, telephone number and e-mail address of a contact point.

1.2. **Producer**

The following information shall be provided:

- (a) the name and address of the producer of the active substance;
- (b) the name and address of each manufacturing plant in which the active substance is produced or will be produced;
- (c) a contact point (preferably a central contact point), including name, telephone number and e-mail address.

Where, following approval of the micro-organism, there are changes in the address or number of producers, the information required shall again be submitted.

1.3. **Identity, taxonomy and phylogeny of the micro-organism**

The information provided shall allow an unambiguous identification and characterisation of the micro-organism.

- (i) The micro-organism shall be deposited at an internationally recognised culture collection at the time of submission of the dossier. The contact details of the culture collection and accession number shall be submitted.
- (ii) The micro-organism shall be identified as unequivocally belonging to a certain species, based on the latest scientific information, and named at strain level, including any other designation which may be relevant to the micro-organism (e.g. isolate level, if relevant for viruses). Its scientific name and taxonomic grouping shall be stated. This includes traditional Linnean taxonomy (kingdom, phylum, class, order, family, genus, species, and strain) as well as established rank-free phylogenetic taxa in between these Linnean ranks and any other denomination relevant to the micro-organism (e.g. serovar, pathovar, biovar).
- (iii) All known synonymous, alternative, superseded names shall be provided. If code names have been used during development these shall also be provided.
- (iv) A phylogenetic tree including the micro-organism shall be provided. The scale of the phylogenetic tree shall be selected to include relevant strains and species (e.g. in case of use of read-across among related strains or species to address data requirements). Superseded names of included micro-organisms or taxonomic groupings may be indicated in the phylogenetic tree.
- (v) It shall be indicated whether the micro-organism is a wild type, a mutant (either spontaneous or induced) or whether it has been genetically modified. If the micro-organism is a mutant or has been modified, all known differences in properties, including genetic differences, between the modified micro-organism and the parent wild strain shall be provided. The technique used for the modification shall be reported.

1.4. **Specification of the microbial pest control agent as manufactured**

1.4.1. *Content of the active substance*

The minimum and maximum content of the micro-organism in the MPCA as manufactured shall be derived from the analysis of five representative batches as indicated under point 1.4.3 and reported. The content shall be expressed in appropriate microbial unit that most accurately reflects plant protection action, such as number of active units, colony forming units, or international units per volume or weight or any other manner that is relevant to the risk assessment on the micro-organism. A rationale for the relevance of the microbial unit used in the context of the tests to be conducted shall be provided. The use of such unit shall be consistent along studies and literature data provided. In case of provision of literature data with different units, recalculation based on the units used shall be provided.

In case it is claimed that one or more metabolites present in the MPCA as manufactured are part of the plant protection action, the content of these metabolites shall be indicated as provided for in point 1.9 of Part A.

1.4.2. *Identity and quantification of additives, relevant contaminating micro-organisms and relevant impurities*

Data on additives, relevant contaminating micro-organisms, relevant impurities and metabolites of concern, present in the MPCA as manufactured shall be directly derived from the analysis of five representative batches as indicated under point 1.4.3 and reported.

1.4.2.1. Identity and quantification of additives

The identity, minimum and maximum content in g/kg of each additive in the MPCA as manufactured shall be provided.

1.4.2.2. Identity and content of relevant contaminating micro-organisms

The identity and maximum content of relevant contaminating micro-organisms in the MPCA as manufactured, expressed in the appropriate unit, shall be reported.

1.4.2.3. Identity and quantification of relevant impurities

The identity and maximum content of chemical impurities present in the MPCA as manufactured and which are relevant due to undesirable toxicological, ecotoxicological or environmental properties, shall be reported in g/kg, including also metabolites of concern produced by the micro-organism as impurities in the manufacturing batch.

1.4.3. *Analytical profile of batches*

At least five representative batches from recent and current production of the micro-organism shall be analysed. All of the representative batches shall bear a date within the last five years of manufacture. Manufacturing dates of the representative batches and batches size shall be reported.

Where the active substance is produced in different manufacturing plants, the information required under this point shall be provided for each of the plants separately.

Where the information provided relates to a pilot manufacturing plant production system, the information required shall again be provided once industrial scale production methods and procedures have stabilised. Where available, industrial scale data shall be provided before approval under Regulation (EC) No 1107/2009. Where data on industrial scale production are not available, a justification shall be provided.

1.5. **Information on manufacturing process and control measures for the active substance**

1.5.1. *Production and quality control*

Information on how the micro-organism is produced in bulk shall be provided for all the steps of the manufacturing process. Such information shall include relevant descriptions of:

- starting materials,
- culture media sterilisation (e.g. autoclave),
- initial inocula level for the culture media (e.g. number of conidia/g of dry culture media),
- cultures and media conditions (e.g. pH, temperature, water activity (a_w)),
- phase of the growth curve and growth stage of the micro-organism during the production process,
- ratio vegetative cells / (endo)spores,
- fermentation process,
- purification and cellular dehydration,
- other technical parameters (e.g. centrifugation protocols).

The type of manufacturing process (e.g. continuous or batch process) shall be indicated.

Both production method/process and product shall be subject to a continuous quality control, and the quality assurance criteria shall be submitted. In particular, the possible occurrence of spontaneous changes of characteristics of the micro-organism shall be monitored. It shall be indicated where in the process the quality assurance steps are implemented and it shall be described how the samples for quality assurance screening are taken.

The techniques used to ensure a uniform product, and the assay methods for its standardisation, maintenance and purity, to prevent the presence of relevant contaminating micro-organisms and relevant impurities in the MPCA as manufactured shall be described and specified.

Information on possible loss of activity of starting cultures shall be provided along with corresponding methods to assess it. If relevant, any method aiming at preventing the micro-organism from losing its effects on the target organism shall be described.

1.5.2. *Recommended methods and precautions concerning handling, storage, transport or fire*

A safety data sheet pursuant to Article 31 of Regulation (EC) No 1907/2006 ⁽⁴⁾ shall be provided for the MPCA as manufactured.

1.5.3. *Procedures for destruction or decontamination*

Methods to dispose safely of the MPCA as manufactured or, where necessary, to render the micro-organism non-viable prior to disposal of the MPCA as manufactured (e.g. chemical methods or autoclaving) and methods to dispose of contaminated packaging and other materials shall be described.

Information that makes it possible to establish the effectiveness and safety of these methods shall be provided.

2. **BIOLOGICAL PROPERTIES OF THE MICRO-ORGANISM**

2.1. **Origin, occurrence and history of use**

2.1.1. *Origin and isolation source*

The geographical location and environmental compartment (e.g. substrate, host organisms), from which the micro-organism was isolated, shall be stated. The method of isolation and the selection procedure of the micro-organism shall be reported.

2.1.2. *Occurrence*

The geographical distribution of the micro-organism shall be described.

The environmental compartment(s) where the micro-organism is already expected to occur shall be described (e.g. soil, water, rhizosphere, phyllosphere, host organism).

When relevant, food or feed commodities where the micro-organism is already expected to occur shall be described.

The information referred to in this point shall be provided at the most relevant highest taxonomic level (e.g. strain, species, genus) and the choice of the relevant highest taxonomic level shall be justified.

2.1.3. *History of use*

Previous and current known uses of the micro-organism (e.g. research, commercial, uses evaluated for recommending the Qualified Presumption of Safety ⁽⁵⁾ status) shall be described. The description shall include both plant protection and other uses (e.g. uses and/or assessments under other regulatory frameworks, bioremediation, uses in food and feed).

⁽⁴⁾ Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC (OJ L 396, 30.12.2006, p. 1).

⁽⁵⁾ <https://www.efsa.europa.eu/en/topics/topic/qualified-presumption-safety-qps>.

The information referred to in this point shall be provided at the most relevant highest taxonomic level (e.g. strain, species, genus). The choice of the relevant highest taxonomic level shall be justified.

2.2. Ecology and life cycle of the micro-organism

The known life cycle(s) of the micro-organism, its lifestyle(s) (e.g. parasitic, saprophytic, endophytic, pathogenic) and its ecological niche(s) shall be described, along with all forms that may occur and the type of reproduction.

For bacteriophages, information shall be provided on, if applicable, lysogenic and lytic properties.

For fungi and bacteria, information shall be provided, if applicable, on:

- external conditions for resting stages, information on resistance of spores against adverse environmental conditions, survival time of the spores and conditions for germination, and/or
- formation of biofilm.

2.3. Mode of action on the target organism and host range

All available information on modes of action against the target organism(s) shall be provided.

In case of a pathogenic or parasitic mode of action on the target organism, information on the site of infection and mode of entry into the target organism, the infective dose and the susceptible stages of the target organism shall be given. The results of any experimental studies shall be reported.

In case of a mode of action based on a metabolite of concern produced by the micro-organism under assessment and identified as required by point 2.8, information from scientific peer-reviewed literature or any other reliable source on likely mode of action of the metabolite of concern and likely exposure route of the target organism to the metabolite of concern shall be provided.

All known host organisms of the micro-organism shall be listed at the relevant taxonomic level. Available information on possible density of host organisms, supporting the indication on natural occurrence of the micro-organisms, shall be provided.

2.4. Growth requirements

The conditions required for growth and proliferation of the micro-organism shall be described (e.g. host, nutrients, pH, osmotic potential, humidity). The minimum, optimum and maximum temperature required for growth and proliferation shall be reported. The generation time under favourable growth conditions shall be reported.

2.5. Infectivity to the target organism

In case any pathogenic mode(s) of action on the target organism is described under point 2.3, virulence factors and (if applicable) environmental factors affecting them shall be indicated and described. The results of any relevant experimental studies and/or data/information from the existing literature at the relevant taxonomic level shall be reported.

2.6. Relationship to known human pathogens and to pathogens to non-target organisms

Where the micro-organism is closely related to any known pathogens to humans, animals, crops or other non-target species, the applicant shall:

- list the pathogens and the type of known diseases caused,
- describe the known virulence factors belonging to the pathogens,
- describe the known virulence factors belonging to the micro-organism which is the active substance,
- describe the phylogenetic relationship between the micro-organism and the related pathogens identified,
- describe the way or means to distinguish the active micro-organism from pathogenic species.

2.7. Genetic stability and factors affecting it

Where the micro-organism is a non-virulent variant of a plant pathogen virus, the likelihood of regaining virulence through mutation after application under the proposed conditions of use shall be reported, including the information on measures that can be taken to reduce the likelihood of this occurrence and the effectiveness of such measures.

2.8. Information on metabolites of concern

The applicant shall identify and list under this point the metabolites of concern produced by the micro-organism, including a summary of the information submitted under points 5.5.1, 8.8.1, 6.1, 7.2.1 and 7.2.2 used to identify or to exclude metabolites as being of concern, unless the micro-organism is a virus.

Metabolites of concern may be identified based on the scientific literature, or on observation of toxicity, ecotoxicity or antimicrobial activity in studies conducted with the micro-organism or closely related strains. The absence of the gene(s) required for the production of the identified metabolite(s) of potential concern evidenced by employing appropriate genomic methods (e.g. whole genome sequencing), shall be considered to prove the absence of such hazard for that metabolite(s).

All the available information (e.g. scientific literature, experimental studies) on the metabolites and the related identified hazards (e.g. the toxicological characterization) and, where relevant, the exposure to the metabolite shall be submitted under the relevant points (i.e. points 5.5, 6.1, 6.2 and 7.2 if relevant for human and animal health and points 7.2 and 8.8 if relevant for non-target organisms).

2.9. Presence of transferable antimicrobial resistance genes

Where the micro-organism is a bacterium, information on any resistance to relevant antimicrobial agents shall be reported at strain level, and information on whether the antimicrobial resistance genes are acquired, transferable and functional shall be reported. The information provided shall be sufficient to perform an evaluation as to the risks for human and animal health due to a possible transfer of relevant antimicrobial resistance genes.

3. FURTHER INFORMATION**3.1. Function and target organism**

The biological function shall be specified as:

- control of bacteria,
- control of fungi,
- control of viruses,
- control of insects,
- control of mites,
- control of molluscs,
- control of nematodes,
- control of plants,
- other (shall be specified).

3.2. Field of use envisaged

The field(s) of use, existing and proposed, for plant protection product containing the micro-organism shall be specified from among the following:

- field use, such as agriculture, horticulture, forestry and viticulture,
- protected crops (e.g. in greenhouses),
- non-cultivated areas,
- home gardening,

- houseplants,
- stored food/feed items,
- seed treatment,
- other (shall be specified).

3.3. Crops or products protected or treated

Details of existing or intended use in terms of crops, groups of crops, plants or plant products protected shall be provided.

3.4. Information on possible development of resistance in the target organism(s)

Available information from scientific peer-reviewed literature or any other reliable source of information on the possible occurrence of the development of resistance or cross-resistance of the target organism(s) shall be provided. Where possible, appropriate management strategies shall be described.

3.5. Literature data

A summary on the systematic review of the scientific peer-reviewed literature employed to provide the data required under Part B shall be provided, including indication on bibliographic databases employed, criteria for relevance and reliability assessment in relation to the data requirements and search strategies, etc.

The summary shall list the references used for the dossier compilation and for which points the respective references are relevant.

4. ANALYTICAL METHODS

Introduction

Analytical methods shall be used in the context of the analysis of the compliance of manufacturing batches with the agreed specification, where relevant (Section 1) and of the generation of data for the risk assessment on human toxicology or ecotoxicology. Analytical methods shall also support post-approval stages, for instance to monitor residues on crops (Section 6), if applicable. The method used shall be justified.

Descriptions of methods shall be provided and include details of equipment, materials and conditions used. The applicability of any internationally recognised method shall be reported.

Data on specificity, linearity, accuracy and repeatability, as laid down in points 4.1 and 4.2 of Part A, are also required for analytical chemistry methods used to analyse relevant impurities, metabolites of concern and additives included in the MPCA as manufactured.

On request by the rapporteur Member State, the following shall be provided:

- (i) samples of the MPCA as manufactured;
- (ii) if technically possible, analytical standards of metabolites of concern and all other components included in the residue definition (in case of non-provision of such a sample a justification shall be provided);
- (iii) if available, samples of reference substances for the relevant impurities.

4.1. Methods for the analysis of the MPCA as manufactured

The following methods shall be described providing validation data:

- (a) methods for the identification of the micro-organism required in accordance with points 1.3(ii) and 1.3(iv), including the most appropriate molecular analytical or phenotypic methods, based on unique genotypic or phenotypic markers to distinguish the strain from other strains belonging to the same species, with information on appropriate test procedures and criteria used for identification (e.g. morphology, biochemistry, serology and molecular identification);

- (b) methods for the characterisation of the micro-organism, including the most appropriate molecular analytical methods or phenotypic methods, as required by Section 2 with information on appropriate test procedures and criteria used for identification (e.g. morphology, biochemistry, serology and molecular identification);
- (c) methods for providing information on possible variability of seed stock/active micro-organism and its storability (including loss of activity and its assessment), as required by Section 1;
- (d) methods to differentiate a spontaneous or induced mutant of the micro-organism from the parental wild strain, e.g. including the most appropriate molecular analytical methods as required by Section 1;
- (e) methods for the establishment of purity of seed stock from which batches are produced and methods to control that purity, e.g. including the most appropriate molecular analytical methods as required by Section 1;
- (f) methods to determine the content of the micro-organism in the manufacturing batch, and methods to detect and enumerate relevant contaminating micro-organisms, as required in Section 1, to allow verifying the compliance of the material/batch with a maximal threshold of relevant contaminating micro-organism;
- (g) methods for the determination of relevant impurities, metabolites of concern, and additives, where they are present in the manufacturing material as required by Section 1.

4.2. **Methods to determine the density of the micro-organism and quantify residues**

The methods used to determine and quantify:

- the density of the micro-organisms, where relevant, as required in points 5.3, 5.4, 6.1 and 7.1.4 and in Section 8,
- the residues of metabolites of concern, where relevant, as required in points 2.8, 5.5 and 8.8 and Section 6;

on and/or in crops, foodstuffs, feeding stuffs, animal and human body tissues and fluids and in relevant environmental compartments shall be described.

Where relevant, methods for post-approval monitoring shall be described. As far as practicable, the post-approval methods shall be as simple as possible, involve a minimum cost and require commonly available equipment.

5. **EFFECTS ON HUMAN HEALTH**

Introduction

- (i) The information provided, taken together with that provided for one or more plant protection products containing the micro-organism, shall be sufficient to perform an evaluation as to the risks for human and animal (i.e. species normally fed and kept by humans or food-producing animals) health:
 - (a) directly and/or indirectly associated with the handling and use of plant protection products containing the micro-organism;
 - (b) associated with the handling of treated products; and
 - (c) arising from residues or impurities remaining in food and water.

In addition, the information provided shall be sufficient to:

- permit a decision to be made as to whether or not the micro-organism is to be approved,
- specify appropriate conditions or restrictions to be associated with the approval,
- specify risk and safety phrases for the protection of human and animal health and the environment to be included on packaging (containers),

- identify relevant first aid measures as well as appropriate diagnostic and therapeutic measures to be followed in the event of infection or another adverse effect in humans.
- (ii) All adverse effects found during investigations shall be reported. Investigations which may be necessary in order to evaluate the probable mechanism involved, and to assess the significance of these effects shall also be performed.
- (iii) For all studies actual achieved dose of the micro-organisms or of the metabolite of concern in appropriate units per kg body weight (e.g. CFU/kg), or in any other appropriate units shall be reported. Justification for the chosen unit shall be provided.
- (iv) Available information on the identity and biological properties of the micro-organism (Sections 1 and 2) as well as health and medical reports may be sufficient for an assessment of the infectivity and pathogenicity potential of the micro-organism.
- (v) Further studies may be required to complete the evaluation of the effects on human health, and the type of these additional studies shall be decided on a case-by-case approach based on expert judgement, depending on the available information provided in particular as regards the biological properties of the micro-organism. Pending the acceptance of specific guidelines at international level, the information required shall be generated using available test guidelines.
- (vi) Additional studies (see point 5.4) shall be conducted if available information (see point 5.2) or tests under point 5.3 require further investigation or have shown adverse health effects. The type of study to be performed depends on the effects observed.

5.1. Medical data

5.1.1. *Therapeutic and first aid measures*

Therapeutic regimes and first aid measures for use in the event of ingestion, inhalation or eyes and skin contamination shall be described. Available information based on practical experience or on theoretical grounds shall be provided.

Where available and without prejudice to Article 10 of Directive 98/24/EC ⁽⁶⁾, practical data and information relevant to the recognition of the symptoms of infection or pathogenicity and on the effectiveness of therapeutic measures shall be submitted.

For micro-organisms excluding viruses, antimicrobial agents with effectiveness against the micro-organism shall be listed. In case of identification of metabolite(s) of concern, as required in point 2.8, the effectiveness of known antagonists of such metabolite(s) shall be reported.

5.1.2. *Medical surveillance*

Available reports of occupational health surveillance programmes shall be submitted. These reports may refer to the strain under assessment, to closely related strains or to metabolites of concern, and shall be supported with information on the design of the programme, on use of appropriate protective measures including personal protective equipment, on exposure to the micro-organism or the metabolites of concern. These reports shall, where available, include data on effects on individuals exposed to the micro-organism or the metabolites of concern in manufacturing plants or after application of the micro-organism (e.g. agricultural or research workers). These reports shall, where available, also cover data on sensitisation and/or allergenic responses.

In the case of adverse effects, attention shall be paid to whether the individual's susceptibility may have been affected by any pre-disposing conditions, e.g. pre-existing disease, medication, compromised immunity, pregnancy or breast-feeding.

⁽⁶⁾ Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC) (OJ L 131, 5.5.1998, p. 11).

5.1.3. *Information on sensitisation and allergenicity*

Available reports from the peer-reviewed published literature on the micro-organism or closely related members of the taxonomic group and relating to sensitisation in humans shall be submitted. Due to the unavailability of an adequate method to assess sensitisation potential of micro-organisms, they shall be considered as potential sensitisers until a validated test is available and the possible absence of sensitisation potential is demonstrated on a case-by-case basis.

5.1.4. *Direct observation*

Available reports from the peer-reviewed published literature on the micro-organism or closely related members of the taxonomic group and relating to clinical cases of infections in humans shall be submitted together with reports of any follow-up studies undertaken. Such reports shall contain descriptions of the nature and level of exposure, as well as the clinical symptoms observed, first aid and therapeutic measures applied and measurements and other observations made.

In the case of adverse effects, attention shall be paid to whether the individual's susceptibility may have been affected by any pre-disposing conditions, e.g. pre-existing disease, medication, compromised immunity, pregnancy or breast-feeding.

5.2. **Assessment on potential infectivity and pathogenicity of the micro-organism to humans**

Studies to determine the potential infectivity and pathogenicity of the micro-organism shall be performed as set out in points 5.3.1 and 5.4, unless the applicant demonstrates, by following a weight of evidence approach, that no such effects are to be expected. The weight of evidence approach may be based on the information provided under points 2.1, 2.3, 2.4, 2.6 and 5.1, and/or be retrieved from any other reliable sources (e.g. Qualified Presumption of Safety ⁽⁷⁾). A summary shall take into consideration this information to demonstrate absence of infectivity and pathogenicity to humans, in order to justify the non-submission of the studies required in points 5.3.1 and 5.4.

5.3. **Infectivity and pathogenicity studies on the micro-organism**

5.3.1. *Infectivity and pathogenicity*

Unless the applicant can demonstrate absence of infectivity and pathogenicity based on a weight of evidence approach as set out in point 5.2, studies, data and information shall be provided and evaluated as required from points 5.3.1.1 to 5.3.1.3. These shall be sufficient to permit the identification of effects following a single exposure to the micro-organism, and in particular to establish or indicate:

- the infectivity and pathogenicity of the micro-organism,
- the time course and characteristics of the effects with full details of observed changes (clinical and behavioural) and possible gross pathological findings at post-mortem,
- the relative hazards associated with the different routes of exposure, and
- analyses throughout the studies in order to evaluate the clearance of the micro-organism.

If these studies are performed, the applicant shall:

- adapt the observation period to the biological properties of the micro-organism administered, in particular its incubation time, rate of clearance and timing for observation of adverse effects,
- estimate, during the infectivity and pathogenicity studies, the micro-organism clearance in the organs which are relevant for microbial examination (e.g. liver, kidneys, spleen, lungs, brain, blood and site of administration),
- take into account the potential differential species susceptibility (i.e. relevance of the chosen test species) to the micro-organism (e.g. based on literature) when the study results and their relevance for humans are evaluated.

⁽⁷⁾ <https://doi.org/10.2903/j.efsa.2021.6377>.

5.3.1.1. Oral infectivity and pathogenicity

The oral infectivity and pathogenicity following a single exposure to the micro-organism shall be reported.

A study in test animals in accordance with relevant guidelines shall be performed, unless the applicant can demonstrate absence of oral infectivity and pathogenicity based on a weight of evidence approach as set out in point 5.2.

5.3.1.2. Intratracheal/ intranasal infectivity and pathogenicity

The intratracheal/ intranasal infectivity and pathogenicity following a single exposure to the micro-organism shall be reported. Expert judgement may support the evaluation on which of the two exposure routes is the most appropriate to be investigated, based on biological properties of the micro-organism and available information described in points 5.1 and 5.2.

A study in test animals in accordance with relevant guidelines shall be performed, unless the applicant can demonstrate absence of intratracheal/ intranasal infectivity and pathogenicity based on a weight of evidence approach as set out in point 5.2.

5.3.1.3. Intravenous, intraperitoneal or subcutaneous single exposure

The intravenous, intraperitoneal or subcutaneous test shall be considered a highly sensitive assay to elicit in particular infectivity. The worst-case scenario – micro-organism bypassing the dermal barrier and entering the body in a high concentration – may be used to assess the results of oral and intratracheal/intranasal testing in case of uncertainties.

The choice on which is the most appropriate exposure route to be investigated shall be based on biological properties of the micro-organism and available information required in points 5.1 and 5.2.

A study in test animals in accordance with the relevant guidelines shall be performed, unless the applicant can demonstrate absence of intravenous, intraperitoneal or subcutaneous infectivity and pathogenicity based on a weight of evidence approach as set out in point 5.2.

5.3.2. *Cell culture study*

This information shall be reported for intracellular replicating micro-organisms, such as viruses, viroids or, where relevant, bacteria and protozoa, unless the information provided in accordance with Sections 1, 2 and 3 clearly demonstrates that the micro-organism does not replicate in homoeothermic (warm-blooded) organisms.

If this information is required, a cell culture study shall be performed in human cell or tissue cultures of different organs. Selection may be based on expected target organs after infection. If human cell or tissue cultures of specific organs are not available, other mammal cell and tissue cultures shall be used. For viruses, particular attention shall be given on the ability to interact with the human genome.

5.4. **Specific infectivity and pathogenicity studies on the micro-organism**

In case, based on expert judgement, available information (see point 5.2) or effects observed in the single dose infectivity and pathogenicity studies (see point 5.3.1) require further investigation, specific infectivity and/or pathogenicity studies shall be carried out, in particular in case of close relatedness to micro-organisms which are pathogenic to humans or animals.

If these studies are required, they shall be designed on an individual basis, in the light of the particular parameters to be investigated and the objectives to be achieved.

5.5. **Information and toxicity studies on metabolites**

5.5.1. *Information on metabolites*

Information (e.g. scientific literature, studies results) on the toxicological characterization of the metabolites and the related identified hazards to human and animal health, collected or generated with the aim to identify the metabolites of concern, or to exclude them as being of concern, shall be submitted.

For those metabolites for which a hazard to human or animal health is identified, an estimation of human exposure shall be provided under points 6.1 and 7.2.1.

5.5.2. *Additional toxicity studies on metabolites of concern*

For metabolite(s) of concern, identified based on information provided on hazard to (see point 5.5.1) and exposure of (see points 6.1, 7.2.1 and 7.2.2) humans or animals and listed under point 2.8, toxicological reference value(s) shall be set based on the available toxicological information for each metabolite of concern. The reference values shall allow risk assessments to be performed for operators, workers, bystanders, residents and consumers, as appropriate, unless a risk assessment can be made by other means (e.g. a qualitative assessment or using the Threshold of Toxicological Concern (TTC) concept).

If reference values cannot be set based on already existing information or if reported effects need further investigation, studies may be required and shall be performed based on a case-by-case approach (for example short-term toxicity studies and genotoxicity studies). If any toxicity studies on metabolites are conducted, the requirements set out in Part A for the specific type of study shall be followed.

For organisms which have not been extensively studied, i.e. where the amount of published information is not sufficient to conclude on the production of metabolites of concern, a repeated-dose toxicity study on relevant fractions of the MPCA as manufactured shall be conducted in accordance with the provisions set out in Part A for the same type of study. The decision to require further studies shall be based on the type of any toxic effects observed during such repeated-dose toxicity study and on expert judgement.

6. **RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED**

Introduction

Data on residues as required in point 6.2 shall be provided, unless:

- based on a weight of evidence approach concerning the information submitted in accordance with Sections 2, 3, 5 and 7, it can be justified that possible metabolites of concern identified (see point 2.8) are not hazardous to humans as a result of the intended use,
- it is possible to conclude, through estimation of consumer exposure to residues of metabolites for which a hazard to human health was identified (see point 5.5.1) that the risk for consumers is acceptable, or
- the micro-organism is a virus.

6.1. **Estimation of consumer exposure to residues**

An estimation of consumer exposure shall be provided for metabolites for which a hazard to human health was identified based on information submitted in accordance with point 5.5.1, considering the intended use.

The estimation shall include, for the metabolites for which a hazard to human health was identified, a calculation of the expected residue levels of these metabolites on edible parts of treated crops using worst-case estimates, taking into account the critical good agricultural practice(s), ecology of the micro-organism, such as its lifestyle (e.g. saprophytic, parasitic, endophytic), host range, life cycle, population growth requirements and the conditions which trigger the production and the properties of the metabolite for which a hazard to human health was identified.

The estimation of exposure to residues of metabolites, for which a hazard to human health was identified may also be supported by direct measurements of the metabolite, e.g. to show the absence of the metabolite on edible parts at time of harvest. When determining the need for direct measurements, the possibility and relevance of exposure to the metabolite produced after application on the edible parts (*in-situ* production) shall be taken into consideration. This may include a comparison between the background level of the metabolite and the elevated level of it due to treatment with the plant protection product containing the active substance. Read across approaches shall be justified.

An estimation of exposure to metabolites, for which a hazard to human health was identified, may be supported by the direct measurements of the density of the micro-organism on edible parts of treated crops, e.g. if it cannot be adequately justified that *in-situ* production of the metabolite is not relevant for the consumers. Such measurements shall be performed under normal conditions of use and in accordance with good agricultural practice.

The estimation shall take into consideration, depending on the case, the whole crop life-cycle (e.g. pre-harvest, and post-harvest), in order to allow a proper assessment of the risk to consumers. A weight of evidence approach shall be employed. Where relevant, adequate justification for read-across shall be provided (e.g. between different substances, members of a species, climatic conditions).

Based on the exposure estimation, an indicative consumer risk assessment shall be performed to demonstrate that the anticipated exposure to metabolites, for which a hazard to human health was identified, does not constitute an unacceptable dietary consumer risk.

6.2. Data generation on residues

For those metabolites of concern identified under point 2.8 and for which it was not adequately demonstrated that the risk to consumers is acceptable based on the information provided under point 6.1, relevant studies of a data package on residues as provided in Section 6 of Part A shall be required. The studies shall be performed with a representative plant protection product aiming at analysing and, if possible, at quantifying the different metabolites of concern identified as described in point 2.8.

If a data package on residues is required:

- half of the supervised residues trials shall be residue decline trials which shall include, unless it can be demonstrated that only non-viable micro-organisms are present at the time of harvest, at least one post-harvest measurement,
- information on levels of the micro-organism and concentrations of the metabolite(s) of concern shall be provided,
- based on the residue trials, a consumer risk assessment shall be performed to demonstrate that the exposure does not constitute an unacceptable consumer risk.

7. ENVIRONMENTAL OCCURRENCE OF THE MICRO-ORGANISM, INCLUDING FATE AND BEHAVIOUR OF METABOLITES OF CONCERN

Introduction

- (i) This Section sets out requirements that make it possible to determine ecological implications of the micro-organism, considering its occurrence in the relevant environmental compartments and to assess the potential exposure of humans and non-target organisms to the active substance, and where relevant to metabolites of concern. Information on the biological properties and ecology of the micro-organism as well as its intended use, i.e. information submitted in accordance with Sections 1 to 6 such as occurrence in European environments, is the main source of information. This may be complemented with literature data, laboratory investigation or field measurements.
- (ii) The information provided for the micro-organism and one or more preparations containing the micro-organism shall be sufficient to permit an assessment of the exposure of non-target organisms to the micro-organism. In addition, sufficient information shall be provided to permit an assessment of metabolites of concern, in case they are identified under point 2.8.
- (iii) The information provided shall be sufficient to identify measures necessary to minimise impact on non-target species and the environment.

7.1. Environmental occurrence of the micro-organism

7.1.1. *Predicted environmental density of the micro-organism*

7.1.1.1. Soil

The predicted environmental density of the micro-organism in soil following treatment with the plant protection product containing that micro-organism under the proposed conditions of use shall be estimated, unless the applicant properly justifies absence of hazard under Section 8.

7.1.1.2. Water

The predicted environmental density of the micro-organism in surface water following treatment with the plant protection product containing that micro-organism under the proposed conditions of use shall be estimated, unless the applicant properly justifies absence of hazard under Section 8.

7.1.2. *Exposure to micro-organisms known to be pathogenic either for plants or for other organisms*

For micro-organisms not occurring in the relevant European environments at the relevant highest taxonomic level and which are known to be pathogenic either for plants or for other organisms (see points 2.2 and 2.3), the host organisms in which proliferation of the micro-organism is expected shall be indicated. If non-target organisms indicated under Section 8 may be exposed to the host organisms colonised by the pathogen, information on the likelihood and, if applicable, level of exposure shall be provided.

Such information may be provided based on the biological properties (see Section 2), literature data and/or studies required under Section 8.

7.1.3. *Qualitative exposure assessment of the micro-organism*

A qualitative assessment of the exposure to the micro-organism shall be carried out if:

- adverse effects are observed on non-target organisms (see Section 8) after exposure to environmentally relevant concentrations, based on the predicted environmental density of the micro-organism calculated as provided for in point 7.1.1, or information is not sufficient to conclude about it, or
- under consideration of the information provided for in point 7.2 a potential risk is identified for humans or non-target organism(s), or information is not sufficient to conclude about it.

If required to provide supporting information for the risk assessment, a qualitative assessment of the exposure to the micro-organism shall be provided employing a weight of evidence approach. Such qualitative assessment shall take into consideration the predicted environmental densities calculated under point 7.1.1, and may be based on the ecology of the micro-organism, such as its lifestyle (e.g. saprophytic, parasitic, endophytic), host range and densities of possible hosts, life cycle, population growth requirements or available monitoring data at the relevant highest taxonomic level. Adequate justification for using read-across shall be provided (e.g., among strains of the same species).

7.1.4. *Experimental exposure data of the micro-organism*

If under consideration of the information provided under points 7.1.1, 7.1.2, 7.1.3 and 7.2 a potential risk is identified for humans or non-target organism(s) or information is not sufficient to conclude about it, the population density of the micro-organism shall be determined in relevant environmental compartment(s) (e.g. soil, water, plant surfaces).

The experimental data shall include population densities measured in a time course including pre-application and immediately post-application, aiming at demonstrating the potential decline of population density.

7.2. Fate and behaviour of metabolite(s) of concern

7.2.1. Predicted environmental concentration

In case metabolites which are hazardous to humans or non-target organisms (see points 5.5.1 and 8.8.1) are present in the MPCA as manufactured, the predicted environmental concentration of the metabolites in the relevant environmental compartment (i.e. soil, surface water, groundwater or air) shall be provided. If it cannot be adequately demonstrated that *in-situ* production of the metabolites is not relevant for the risk assessment, provisions set out in point 7.2.2 shall be followed.

No predicted environmental concentration calculations are needed for metabolites for which a hazard to human health or non-target organisms was identified that are produced *in situ* but are not present in the MPCA as manufactured.

7.2.2. Qualitative exposure assessment

In case of identification of metabolites for which a hazard to human health or non-target organisms was identified (see points 5.5.1 and 8.8.1), a qualitative exposure assessment shall be performed on such metabolites where the information provided under point 7.2.1 is not sufficient to conclude on acceptable risk to non-target organisms or on no-risks to human health.

If required, the assessment may be based on existing knowledge on:

- the micro-organism, such as its ecology, lifestyle, host range, life cycle, population growth requirements, available monitoring data at the relevant highest taxonomic level or the conditions which trigger the production of the metabolite, or
- the metabolite, such as physical and chemical properties or background levels.

A weight of evidence approach shall be employed. Adequate justification for using read-across shall be provided (e.g. between different substances, members of a species, climatic conditions).

7.2.3. Experimental exposure data

Experimental exposure data shall be provided for the metabolites of concern identified under point 2.8 for which the information provided under points 7.2.1 and 7.2.2 is not sufficient to conclude on acceptable risk to non-target organisms, or on no-risks to human health.

In such cases and if technically possible, sufficient information on the concentration of the metabolite of concern in the relevant environmental compartments (e.g. soil, surface water, groundwater, air, flowers, leaves, roots, host organisms) shall be provided to permit an assessment. The study shall be conducted in accordance with the relevant provisions of Part A for the relevant type of study.

8. ECOTOXICOLOGICAL STUDIES

Introduction

(i) This Section sets out requirements for the data to allow:

- for the assessment of potential adverse effects on non-target organisms likely to be exposed to the micro-organism and relevant associated metabolites of concern, and
- for the identification of the relevant tests to be carried out on specific non-target organisms, based on information regarding intrinsic properties, so as to limit testing to what is necessary to conclude the risk assessment.

Special attention shall be paid to microbial species which are not known to occur in the relevant European environments. The information provided shall be sufficient to determine the physiological and ecological host range (in conjunction with the analysis of key biological traits of the micro-organisms) in order to assess impacts on non-target organisms.

- (ii) The information provided at the most relevant highest taxonomic level, taken together with that for one or more preparations containing the micro-organism, shall be sufficient to permit an assessment of the impact on non-target species, likely to be at risk from exposure to the micro-organism. When submitting this information, the applicant shall take into account that the impact on non-target species can result from single, prolonged or repeated exposure and can be reversible or irreversible. The information provided shall be sufficient to:
- decide whether or not the micro-organism can be approved,
 - specify appropriate conditions or restrictions to be associated with any approval,
 - permit an evaluation of short- and long-term risks for non-target species - populations, communities, and processes, as appropriate, and
 - specify any precautions deemed necessary for the protection of non-target species.
- (iii) In general, the duration of experimental studies shall be long enough to permit time for incubation, infection and manifestation of adverse effects in non-target organisms depending on the biological properties of the micro-organism. The provided studies shall take into consideration the maximum recommended application rate or the expected environmental concentration, the exposure that may arise from the intended uses and the potential of the micro-organism to proliferate in the environment or in the host.

In order to distinguish between pathogenicity of the living micro-organism and toxic effects triggered by its metabolites of concern, appropriate controls shall be included in addition to the no-dosed control group, such as inactivated forms of the living micro-organisms, and/or sterile filtrate/supernatant controls.

- (iv) If pathogenicity/infectivity studies are required for any of the non-target organism groups indicated in points 8.1 to 8.6, the choice of the appropriate species of that non-target organisms group shall be based on the biological properties of the micro-organism (including the host range specificity, mode of action and ecology), the proposed use pattern(s) of the plant protection product (e.g. treated crops, frequency, timings, use patterns such as spraying or brushing) and consider relevant guidelines, where available.

Additional studies may be conducted if tests referred to in points 8.1 to 8.6 have shown adverse effects in one or more non-target organisms and may include studies on additional species.

- (v) All known adverse effects on the environment shall be reported. Additional studies may be necessary to investigate the probable mechanisms involved and to assess the significance of these effects.
- (vi) It may be necessary to conduct separate studies for metabolites of concern identified under point 2.8, which constitute a relevant risk to non-target organisms. The study on non-target organisms shall be conducted in accordance with the relevant provision of Part A.
- (vii) In order to facilitate the assessment of the significance of test results obtained, the same species, recorded origin or, where possible, strain of each relevant non-target species shall be used in the various tests performed.

8.1. Effects on terrestrial vertebrates

A summary on potential infectivity and pathogenicity of the micro-organism to terrestrial vertebrates (e.g. mammals, birds, reptiles, and amphibians) shall be provided, based on the information already provided under Sections 1, 2, 3, 5 and 7 and that information which may be retrieved from any other reliable source.

Relevant pathogenicity/infectivity studies shall be performed unless the applicant demonstrates, by following a weight of evidence approach, that pathogenicity/infectivity of the micro-organism to non-target terrestrial vertebrates can be assessed based on the summary provided.

If these studies are required:

- gross necropsy shall be performed and
- for micro-organisms with pathogenic mode of action or viruses (e.g. entomopathogens) that are expected to proliferate significantly in the environment following an application, the oral dose administered in the studies may be justified based on the information submitted under points 7.1.1 and 7.1.2.

8.2. **Effects on aquatic organisms**

8.2.1. *Effects on fish*

A summary on potential infectivity and pathogenicity of the micro-organism to fish shall be provided, based on the information already provided under Sections 1, 2, 3 and 7 and on other information which may be retrieved from any other reliable source.

Relevant pathogenicity/infectivity studies shall be performed unless the applicant demonstrates, by following a weight of evidence approach, that:

- pathogenicity/infectivity of the micro-organism to fish can be assessed based on the summary provided; or
- exposure of fish to the micro-organism is expected to be none based on information provided under Section 7.

Where adverse effects are observed in such studies, further relevant studies (e.g. under representative conditions in accordance with the proposed conditions of use) shall be performed.

8.2.2. *Effects on aquatic invertebrates*

A summary on potential infectivity and pathogenicity of the micro-organism to aquatic invertebrates shall be provided, based on the information already provided under Sections 1, 2, 3 and 7 and on other information which may be retrieved from any other reliable source.

Relevant pathogenicity/infectivity studies shall be performed unless the applicant demonstrates, by following a weight of evidence approach, that:

- pathogenicity/infectivity of the micro-organism to aquatic invertebrates can be assessed based on the summary provided, or
- exposure of aquatic invertebrates to the micro-organism is expected to be none based on information provided under Section 7.

Where adverse effects are observed in such studies, further relevant studies (e.g. under representative conditions in accordance with the proposed conditions of use) shall be performed.

8.2.3. *Effects on algae*

A summary on potential infectivity and pathogenicity of the micro-organism to algae shall be provided, based on the information already provided under Sections 1, 2, 3 and 7 and on other information which may be retrieved from any other reliable source.

Relevant studies on pathogenic/infective effects on algae growth and growth rate shall be performed if the micro-organism is known to have an herbicidal mode of action or to be closely related to a plant pathogen, unless the applicant demonstrates, by following a weight of evidence approach, that:

- pathogenicity/infectivity of the micro-organism to algae can be assessed based on the summary provided, or
- exposure of algae to the micro-organism is expected to be none based on information provided under Section 7.

Where adverse effects are observed in such studies, further relevant studies (e.g. under representative conditions in accordance with the proposed conditions of use) shall be performed.

8.2.4. *Effects on aquatic macrophytes*

A summary on potential infectivity and pathogenicity of the micro-organism to aquatic macrophytes shall be provided, based on the information already provided under Sections 1, 2, 3 and 7 and on other information which may be retrieved from any other reliable source.

Relevant studies on pathogenic/infective effects on aquatic macrophytes shall be performed if the micro-organism is known to have an herbicidal mode of action, or to be closely related to a plant pathogen, unless the applicant demonstrates, by following a weight of evidence approach, that:

- pathogenicity/infectivity of the micro-organism to aquatic macrophytes can be assessed based on the summary provided, or
- exposure of aquatic macrophytes to the micro-organism is expected to be none based on information provided under Section 7.

Where adverse effects are observed in such studies, further relevant studies (e.g. under representative conditions in accordance with the proposed conditions of use) shall be performed.

8.3. **Effects on bees**

A summary on potential infectivity and pathogenicity of the micro-organism to bees shall be provided, based on the information already provided under Sections 1, 2, 3 and 7 and on other information which may be retrieved from any other reliable source.

Relevant pathogenicity/infectivity studies, including adult and larval stages, shall be performed, unless the applicant demonstrates, by following a weight of evidence approach, that:

- pathogenicity/infectivity of the micro-organism to bees can be assessed based on the summary provided, or
- exposure of bees to the micro-organism is expected to be none based on information provided under Section 7.

Where adverse effects are observed in such studies, further relevant studies (e.g. field studies under representative conditions in accordance with the proposed conditions of use) shall be performed.

8.4. **Effects on non-target arthropods other than bees**

A summary on potential infectivity and pathogenicity of the micro-organism to non-target arthropods other than bees shall be provided, based on the information already provided under Sections 1, 2, 3 and 7 and on other information which may be retrieved from any other reliable source.

Relevant pathogenicity/infectivity studies shall be performed unless the applicant demonstrates, by following a weight of evidence approach, that:

- pathogenicity/infectivity of the micro-organism to non-target arthropods other than bees can be assessed based on the summary provided, or
- exposure of non-target arthropods to the micro-organism is expected to be none based on information provided under Section 7.

If studies are required, they shall be performed on two arthropod species other than bees playing a role in biological control and comprising different taxonomic groups (orders), where possible, for which agreed testing protocols are available, and the applicant shall provide a justification for number and taxonomy of the tested species. Moreover, these tests may require conditions affecting growth or viability of the micro-organism.

Where adverse effects are observed in such studies, further relevant studies (e.g. extended laboratory tests or field studies under representative conditions in accordance with the proposed conditions of use) shall be performed.

8.5. **Effects on non-target meso- and macro-organisms in soil**

A summary on potential infectivity and pathogenicity of the micro-organism to non-target soil meso- and macro-organisms shall be provided, based on the information already provided under Sections 1, 2, 3 and 7 and on other information which may be retrieved from any other reliable source.

Relevant pathogenicity/infectivity studies shall be performed unless:

- pathogenicity/infectivity of the micro-organism to non-target soil meso- and macro-organisms can be assessed based on the summary provided, or
- exposure of meso- and macro soil organisms to the micro-organism is expected to be none based on information provided under Section 7.

If studies are required, they shall be performed on two non-target meso- and macro-organisms species chosen based on the biological properties of the micro-organism under evaluation, where possible, for which agreed testing protocols are available.

Where adverse effects are observed in such studies, further relevant studies (e.g. under representative conditions in accordance with the proposed conditions of use) shall be performed.

8.6. **Effects on non-target terrestrial plants**

A summary on potential infectivity and pathogenicity of the micro-organism to non-target terrestrial plants shall be provided, based on the information already provided under Sections 1, 2, 3 and 7 and on other information which may be retrieved from any other reliable source.

Relevant studies on pathogenic/infective effects on non-target terrestrial plants shall be performed if the micro-organism is known to have an herbicidal mode of action or to be closely related to a plant pathogen, unless the applicant demonstrates, by following a weight of evidence approach, that:

- pathogenicity/infectivity of the micro-organism to non-target terrestrial plants can be assessed based on the summary provided, or
- exposure of non-target plants to the micro-organism is expected to be none based on information provided under Section 7.

Where adverse effects are observed in such studies, further relevant studies (e.g. under representative conditions in accordance with the proposed conditions of use) shall be performed.

8.7. **Additional studies on the micro-organism**

Further data may need to be submitted on potential pathogenicity/infectivity of the micro-organism on non-target species different from those species assessed to fulfil the requirements set out in points 8.1 to 8.6.

The data may also consist of a summary including the information already provided under Sections 2, 3, 5 and 7 and those which may be retrieved from any other source, or from additional infectivity and pathogenicity studies.

8.8. **Information and toxicity studies on metabolites**

8.8.1. *Information on metabolites*

Information (e.g. scientific literature, studies results) on the toxicological characterization of the metabolites and the related identified hazards relevant to non-target organisms, collected or generated with the aim to identify the metabolites of concern, or to exclude them as being of concern, shall be submitted.

For those metabolites for which a hazard to non-target organisms is identified, an estimation of exposure of the relevant non-target organisms shall be provided under point 7.2.1.

8.8.2. *Additional toxicity studies on metabolites of concern*

For metabolite(s) of concern, identified based on information provided on hazard to (see point 8.8.1) and exposure of (see points 7.2.1 and 7.2.2) non-target organisms and listed under point 2.8, further information on their toxicity to the non-target organisms which are relevant (e.g. based on exposure and indication of toxicity) among those described in points 8.1 to 8.6, shall be provided. In case it is necessary to generate experimental data, relevant studies on ecotoxicology as provided for in Section 8 of Part A shall be submitted.'

COMMISSION REGULATION (EU) 2022/1440**of 31 August 2022****amending Regulation (EU) No 284/2013 as regards the information to be submitted for plant protection products and the specific data requirements for plant protection products containing micro-organisms****(Text with EEA relevance)**

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard 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 and repealing Council Directives 79/117/EEC and 91/414/EEC ⁽¹⁾, and in particular Article 78(1), point (b), thereof,

Whereas:

- (1) Commission Regulation (EU) No 284/2013 ⁽²⁾ lays down the data requirements for plant protection products containing active substances. For plant protection products containing active substances that are chemicals, these are laid down in Part A of the Annex to that Regulation, and for plant protection products containing active substances that are micro-organisms, these are laid down in Part B of that Annex, with common requirements set out in the introductory part of that Annex.
- (2) The Farm to Fork Strategy for a fair, healthy and environmentally-friendly food system ⁽³⁾ aims at reducing dependency on and use of chemical plant protection products, including through facilitating the placing on the market of biological active substances such as micro-organisms. In order to reach those objectives, it is necessary to specify the data requirements related to plant protection products containing micro-organisms taking into account the most up-to-date scientific and technical knowledge which has evolved significantly.
- (3) Currently available scientific knowledge on plant protection products containing micro-organisms, in particular concerning effectiveness, efficacy, relevance of impurities, and toxicity of certain chemical substances which may be present in these plant protection products, triggers the need to better specify certain definitions which apply for Part B of the Annex to Regulation (EU) No 284/2013. Taking into consideration that these definitions apply also to Part A of that Annex, concerning plant protection products containing chemical active substances, it is appropriate to amend the introduction of the Annex to Regulation (EU) No 284/2013.
- (4) Since micro-organisms are living organisms, a specific approach is needed compared to chemical substances, in order to also take into account the new scientific knowledge that has emerged on the biology of micro-organisms. That scientific knowledge consists in new information on key characteristics of micro-organisms, such as their pathogenicity and infectivity, the possible production of metabolite(s) of concern and the capacity to transfer antimicrobial resistance genes to other micro-organisms which are pathogenic and occurring in European environments, potentially affecting the effectiveness of antimicrobials used in human or veterinary medicine.

⁽¹⁾ OJ L 309, 24.11.2009, p. 1.

⁽²⁾ Commission Regulation (EU) No 284/2013 of 1 March 2013 setting out the data requirements for plant protection products, 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 (OJ L 93, 3.4.2013, p. 85).

⁽³⁾ Communication from the Commission to the European Parliament, the Council, the Economic and Social Committee and the Committee of the Regions – A Farm to Fork Strategy for a fair, healthy and environmentally-friendly food system (COM/2020/381 final, <https://eur-lex.europa.eu/legal-content/en/TXT/?qid=1590404602495&uri=CELEX:52020DC0381>).

- (5) The current state of scientific knowledge on plant protection products containing micro-organisms allows for a better and more specific approach for their assessment, which is based on the mode of action and ecological characteristics of the respective species and, where applicable, the respective strains of micro-organisms. As it allows for a more targeted risk assessment, such scientific knowledge should be taken into account when assessing the risks posed by plant protection products containing micro-organisms.
- (6) In order to better reflect the latest scientific developments and the specific biological properties of plant protection products containing micro-organisms, while maintaining a high level of protection of human and animal health and of the environment, it is therefore necessary to adapt accordingly the existing data requirements.
- (7) It is appropriate to amend Part B of the Annex to Regulation (EU) No 284/2013, in order to update the data requirements to the latest scientific developments and adapt them to the specific biological properties of micro-organisms.
- (8) The current title of Part B of the Annex to Regulation (EU) No 284/2013 refers to plant protection products containing micro-organisms including viruses. However, Article 3, point (15), of Regulation (EC) No 1107/2009 already defines micro-organisms, and the definition includes viruses. It is appropriate to be consistent with Article 3, point (15), of that Regulation, and therefore there is no need to refer to viruses separately.
- (9) It is appropriate to introduce a definition of 'Microbial Pest Control Agent as manufactured' ('MPCA as manufactured') because certain tests are required to be performed using a sample of the MPCA as manufactured, rather than using the active substance or the other components of the MPCA as manufactured after purification. It is indeed more appropriate to refer, with a unique term, to the micro-organism as manufactured and to those components included in the manufacturing batch which might be of relevance for the risk assessment, such as relevant contaminating micro-organisms and relevant impurities.
- (10) New scientific knowledge has emerged on the capacity of micro-organisms to transfer antimicrobial resistance genes to other micro-organisms which are pathogenic and occurring in European environments, potentially affecting the effectiveness of antimicrobials used in human or veterinary medicine. This new scientific knowledge allows for a better and more specific approach for the assessment of which genes encoding for antimicrobial resistance are likely to be transferred to other micro-organisms, and which antimicrobials are those relevant for human or veterinary medicine. In addition, the EU Farm to Fork Strategy has set antimicrobial resistance-related targets. Therefore, further specification is needed on the data requirements to implement the most up-to-date scientific and technical knowledge on transferability of antimicrobial resistance, and allow an assessment to be made on whether the active substance may have harmful effects on human or animal health, as indicated in the approval criteria laid down in Article 4 of Regulation (EC) No 1107/2009.
- (11) A reasonable period should be allowed to elapse before the amended data requirements become applicable in order to permit applicants to prepare themselves to meet those requirements.
- (12) In order to permit Member States and interested parties to prepare themselves to meet the amended requirements, it is appropriate to lay down transitional measures concerning data submitted for applications for authorisation, renewal of authorisation and amendment to the authorisation of plant protection products containing active substances that are micro-organisms, and concerning data on the representative uses of plant protection products submitted in the context of applications for the approval, renewal of approval or amendment to the conditions of approval of active substances that are micro-organisms.
- (13) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

HAS ADOPTED THIS REGULATION:

Article 1

Amendments to Regulation (EU) No 284/2013

The Annex to Regulation (EU) No 284/2013 is amended as follows:

- (a) the Introduction is replaced by the text set out in Annex I to this Regulation;
- (b) Part B is replaced by the text set out in Annex II to this Regulation.

Article 2

Transitional measures as regards certain procedures concerning plant protection products containing active substances that are micro-organisms

1. Applicants shall submit data, in the context of applications for authorisation of plant protection products within the meaning of Regulation (EC) No 1107/2009 containing one or more active substances that are micro-organisms, in accordance with Part B of the Annex to Regulation (EU) No 284/2013 as it stood before being amended by this Regulation in either of the following cases:

- (a) the application for authorisation is submitted by 21 November 2024;
- (b) the dossiers for all the active substances contained in the plant protection product concerned have been submitted in accordance with Commission Regulation (EU) No 283/2013 ⁽⁴⁾ as it stood before being amended by Commission Regulation (EU) 2022/1441 ⁽⁵⁾.

2. As a derogation from paragraph 1, applicants may choose, from 21 November 2022 to submit data in accordance with Part B of the Annex to Regulation (EU) No 284/2013 as amended by this Regulation.

3. Where applicants choose to apply the option provided for in paragraph 2, they shall specify that choice in writing when submitting the application concerned. Such choice shall be irrevocable for the procedure concerned.

Article 3

Transitional measures as regards certain procedures concerning active substances that are micro-organisms and are contained in plant protection products

Regulation (EU) No 284/2013 as it stood before being amended by this Regulation shall continue to apply as regards data required on one or more representative uses of a plant protection product, submitted before 21 May 2023 to fulfil the requirements of one of the following provisions:

- (a) Article 8(1), point (a), of Regulation (EC) No 1107/2009;

⁽⁴⁾ Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, 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 (OJ L 93, 3.4.2013, p. 1).

⁽⁵⁾ Commission Regulation (EU) 2022/1441 of 31 August 2022 amending Regulation (EU) No 546/2011 as regards specific uniform principles for evaluation and authorisation of plant protection products containing micro-organisms (see page 70 of this Official Journal).

- (b) Article 7(1), point (c), of Commission Implementing Regulation (EU) No 844/2012 ⁽⁶⁾;
- (c) Article 6(2), point (c), of Commission Implementing Regulation (EU) 2020/1740 ⁽⁷⁾.

Article 4

Entry into force and application

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

It shall apply from 21 November 2022.

This Regulation shall be binding in its entirety and directly applicable in the Member States in accordance with the Treaties.

Done at Brussels, 31 August 2022.

For the Commission
The President
Ursula VON DER LEYEN

⁽⁶⁾ Commission Implementing Regulation (EU) No 844/2012 of 18 September 2012 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market (OJ L 252, 19.9.2012, p. 26).

⁽⁷⁾ Commission Implementing Regulation (EU) 2020/1740 of 20 November 2020 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council, and repealing Commission Implementing Regulation (EU) No 844/2012 (OJ L 392, 23.11.2020, p. 20).

ANNEX I

‘INTRODUCTION

Information to be submitted, its generation and its presentation

1. For the purposes of this Annex, the following definitions apply:
 - (1) **“storage stability”** means the capacity of a plant protection product to maintain the initial properties and the specified content during the storage period under established storage conditions;
 - (2) **“effectiveness”** means the capacity of the plant protection product to produce a positive effect regarding the desired plant protection activity;
 - (3) **“efficacy”** means a measure concerning the overall effect of the application of a plant protection product on the agricultural system in which it is used (i.e. which includes positive effects of treatment in performing the desired plant protection activity and negative effects such as development of resistance, phytotoxicity or reduction of qualitative or quantitative yield);
 - (4) **“relevant impurity”** means a chemical impurity that is of concern for human health, animal health or the environment;
 - (5) **“toxicity”** means the degree of injury or damage in an organism caused by a toxin or a toxic substance;
 - (6) **“toxin”** means a substance that is produced within living cells or organisms and is able to injure or cause damage in a living organism.

The information submitted shall meet the requirements set out in points 1.1 to 1.15.

- 1.1. The information shall be sufficient to evaluate efficacy and the foreseeable risks, whether immediate or delayed, which the plant protection product may entail for humans, including vulnerable groups, animals and the environment and contain at least the information and results of the studies referred to in this Annex.
- 1.2. Any information including any known data on potentially harmful effects of the plant protection product on human and animal health or on groundwater shall be included as well as known and expected cumulative and synergistic effects.
- 1.3. Any information including any known data on potentially unacceptable effects of the plant protection product on the environment, plants and plant products shall be included as well as known and expected cumulative and synergistic effects.
- 1.4. The information shall include all relevant data from the scientific peer reviewed open literature on the active substance, relevant metabolites, and where relevant breakdown or reaction products, and plant protection products containing the active substance and dealing with side-effects on human and animal health, the environment and non-target species. A summary of that data shall be provided.
- 1.5. The information shall include a full and unbiased report of the studies conducted as well as a full description of them. Such information shall not be required, where a justification is provided showing that:
 - (a) it is not necessary owing to the nature of the plant protection product or its proposed uses, or it is not scientifically necessary; or
 - (b) it is technically not possible to supply.
- 1.6. Where relevant, the information shall be generated using test methods, which are included in the list referred to in point 6.

In the absence of suitable internationally or nationally validated test guidelines, test guidelines accepted by the competent authority shall be used. Any deviations from test guidelines shall be described and justified.
- 1.7. The information shall include a full description of the test methods used.

- 1.8. Where relevant, the information shall be generated in accordance with Directive 2010/63/EU of the European Parliament and of the Council ⁽¹⁾.
- 1.9. The information shall include a list of endpoints for the plant protection product where relevant.
- 1.10. The information shall include the proposed classification and labelling of the plant protection product in accordance with Regulation (EC) No 1272/2008 of the European Parliament and of the Council ⁽²⁾, where relevant.
- 1.11. Information as provided for in Commission Regulation (EU) No 283/2013 ⁽³⁾ may be required by the competent authorities on co-formulants. Before requiring additional studies to be performed, the competent authorities shall assess all available information provided in accordance with other Union legislation.
- 1.12. The information provided for the plant protection product and that provided for the active substance, shall be sufficient to:
- (a) decide whether or not the plant protection product is to be authorised;
 - (b) specify conditions or restrictions to be associated with any authorisation;
 - (c) permit an evaluation of short and long-term risks for non-target species - populations, communities and processes;
 - (d) identify relevant first aid measures as well as appropriate diagnostic and therapeutic measures to be followed in the event of poisoning in humans;
 - (e) permit a risk assessment of acute and chronic consumer exposure, including, where relevant, a cumulative risk assessment deriving from exposure to more than one active substance;
 - (f) permit an estimation of acute and chronic exposure of operators, workers, residents and bystanders including, where relevant, the cumulative exposure to more than one active substance;
 - (g) permit an evaluation to be made as to the nature and extent of the risks for humans, animals (species normally fed and kept by humans or food-producing animals) and of the risks for other non-target vertebrate species;
 - (h) predict the distribution, fate and behaviour in the environment, as well as the time courses involved;
 - (i) identify non-target species and populations for which risks arise because of potential exposure;
 - (j) permit an assessment of the impact of the plant protection product on non-target species;
 - (k) identify measures necessary to minimise contamination of the environment and impact on non-target species;
 - (l) classify the plant protection product as to hazard in accordance with Regulation (EC) No 1272/2008;
 - (m) specify the pictograms, the signal words, and relevant hazard and precautionary statements for the protection of human health, non-target species and the environment, which are to be used for labelling purposes.
- 1.13. Where relevant, tests shall be designed and data analysed using appropriate statistical methods. Details of the statistical analysis shall be reported transparently.

⁽¹⁾ Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes (OJ L 276, 20.10.2010, p. 33).

⁽²⁾ Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (OJ L 353, 31.12.2008, p. 1).

⁽³⁾ Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, 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 (OJ L 93, 3.4.2013, p. 1).

- 1.14. Exposure calculations shall refer to scientific methods accepted by the European Food Safety Authority, when available. The use of additional methods shall be justified.
- 1.15. For each section of this Annex, a summary of all data, information and evaluation made shall be submitted. This shall include a detailed and critical assessment in accordance with Article 4 of Regulation (EC) No 1107/2009.
2. The requirements set out in this Annex constitute the minimum set of data to be submitted. Member States may set out additional requirements at national level to address specific circumstances, specific exposure scenarios and specific patterns of use other than those taken into account for approval. The applicant shall pay careful attention to environmental, climatic and agronomic conditions when tests are set up subject to the approval by the Member State where the application has been submitted.
3. **Good laboratory practice (GLP)**
- 3.1. Tests and analyses shall be conducted in accordance with the principles laid down in Directive 2004/10/EC of the European Parliament and of the Council (*) where testing is done to obtain data on the properties or safety with respect to human or animal health or the environment.
- 3.2. By way of derogation from point 3.1, tests and analyses, required under Section 6 of Part A and Section 6 of Part B, may be conducted by official or officially recognised testing facilities or organisations, which satisfy at least the following requirements:
- (a) they have at their disposal sufficient scientific and technical staff having the necessary education, training, technical knowledge and experience for their assigned functions;
 - (b) they have at their disposal suitable equipment required for correct performance of the tests and measurements which they claim to be competent to carry out; that equipment is properly maintained and calibrated, where appropriate, before being put into service and thereafter in accordance with an established programme;
 - (c) they have at their disposal appropriate experimental fields and, where necessary, greenhouses, growth cabinets or storage rooms; they ensure that environment in which the tests are undertaken does not invalidate their results or adversely affect the required accuracy of measurement;
 - (d) they make available to all relevant personnel operating procedures and protocols used for the trials;
 - (e) they make available, where requested by the competent authority, prior to the commencement of a test, information on its location and on the tested plant protection products;
 - (f) they ensure that the quality of the work performed is appropriate to its type, range, volume and intended purpose;
 - (g) they maintain records of all observations, calculations and derived data and calibrations records and final test report as long as the plant protection product concerned is authorised in a Member State.
- 3.3. Officially recognised testing facilities and organisations, and, where requested by the competent authorities, official facilities and organisations shall:
- (a) report to the relevant national authority all information necessary to demonstrate that they can satisfy the requirements set out in point 3.2,
 - (b) permit at any time the inspections, which each Member State shall regularly organise on its territory in order to verify the compliance with point 3.2.

(*) Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances (OJ L 50, 20.2.2004, p. 44).

3.4. By way of derogation from point 3.1:

- (a) For active substances that are micro-organisms, tests and analyses performed to obtain data on their properties and safety with respect to other aspects than human health, may be conducted by official or officially recognised testing facilities or organisations which satisfy at least the requirements specified in points 3.2 and 3.3.
- (b) Studies conducted before the application of this Regulation, although not fully compliant with GLP principles or with current test methods, shall be considered for the assessment if carried out in accordance with the recognised international test guidelines in place at the time of conduction of the studies and/or scientifically valid, thereby avoiding repeating animal tests, especially for carcinogenicity and reprotoxicity studies. This derogation shall apply in particular to studies with vertebrate species.

4. **Test material**

- 4.1. Due to the influence that impurities and other components can have on toxicological and ecotoxicological behaviour, a detailed description (specification) of the test material used shall be provided for each study submitted. Studies shall be conducted using the plant protection product to be authorised or bridging principles may be applied, for example, by using a study on a plant protection product with a comparable/equivalent composition. A detailed description of the composition used shall be provided.
- 4.2. Where radio-labelled test material is used, radio-labels shall be positioned at sites (one or more as necessary), to facilitate elucidation of metabolic and transformation pathways and to facilitate investigation of the distribution of the active substance and of its metabolites, breakdown and reaction products.
- 4.3. Whenever a study implies the use of different doses, the relationship between the dose and the adverse effect shall be reported.

5. **Tests on vertebrate animals**

- 5.1. Tests on vertebrate animals shall be undertaken only where no other validated methods are available. Alternative methods shall include *in vitro* methods or *in silico* methods. Reduction and refinement methods for *in vivo* testing shall also be encouraged to keep the number of animals used in testing to a minimum.
 - 5.2. The principles of replacement, reduction and refinement of the use of vertebrate animals shall be taken into account in the design of the test methods, in particular when appropriate validated methods become available to replace, reduce or refine animal testing.
 - 5.3. Study designs shall be carefully considered from an ethical point of view, taking into account the scope for reduction, refinement and replacement of animal tests. For example, by including one or more additional dose groups or time points for blood sampling in one study, it may be possible to avoid the need for another study.
 - 6. For purposes of information and harmonisation, the list of test methods and guidance documents referred to in this Annex shall be published in the *Official Journal of the European Union*. That list shall be regularly updated.
-

ANNEX II

PART B

PLANT PROTECTION PRODUCTS CONTAINING AN ACTIVE SUBSTANCE THAT IS A MICRO-ORGANISM

INTRODUCTION TO PART B

- (i) This Introduction to Part B complements the Introduction to this Annex with points which are specific for plant protection products containing an active substance that is a micro-organism.
- (ii) For the purposes of Part B, the following definitions apply:
 - (1) “**strain**” means a genetic variant of an organism in its taxonomic level (species) that is made up of the descendants of a single isolation in pure culture from the original matrix (e.g. the environment) and usually is made up of a succession of cultures ultimately derived from an initial single colony;
 - (2) “**colony-forming unit**” (“**CFU**”) means a measurement unit used to estimate the number of bacterial or fungal cells in a sample, which have the ability to multiply under controlled growing conditions, with the consequence that one or more cells reproduce and multiply to form a single visible colony;
 - (3) “**Microbial Pest Control Agent as manufactured**” (“**MPCA as manufactured**”) means the outcome of the manufacturing process of the micro-organism(s) intended to be used as active substance in plant protection products, consisting of the micro-organism(s) and any additives, metabolites (including metabolites of concern), chemical impurities (including relevant impurities), contaminating micro-organisms (including relevant contaminating micro-organisms) and the spent medium/rest fraction resulting from the manufacturing process or, in case of a continuous manufacturing processes where a strict separation between the manufacturing of the micro-organism(s) and the production process of the plant protection product is not possible, a non-isolated intermediate;
 - (4) “**additive**” means a component added to the active substance during its manufacturing, to preserve microbial stability and/or facilitate handling;
 - (5) “**purity**” means the content of the micro-organism present in the MPCA as manufactured expressed in a relevant unit and the maximum content of substances of concern in case they are identified;
 - (6) “**relevant contaminating micro-organism**” means a pathogenic/infective micro-organism unintentionally present in the MPCA as manufactured;
 - (7) “**seed stock**” means a microbial strain starter culture used to manufacture the MPCA as manufactured or the final plant protection product;
 - (8) “**spent medium/rest fraction**” means the fraction of the MPCA as manufactured consisting of remaining or transformed starting materials, and excluding the micro-organism(s) that is the active substance, metabolites of concern, additives, relevant contaminating micro-organisms, and relevant impurities;
 - (9) “**starting material**” means substances used in the manufacturing process of the MPCA as manufactured as substrate and/or buffering agent;
 - (10) “**infectivity**” means the ability of a micro-organism to cause an infection;
 - (11) “**infection**” means the non-opportunistic introduction or entry of micro-organism into a susceptible host, where the micro-organism is able to reproduce to form new infective units and persist in the host, whether or not the micro-organism causes pathological effects or disease;
 - (12) “**pathogenicity**” means the non-opportunistic ability of a micro-organism to inflict injury and damage to the host upon infection;
 - (13) “**non-opportunistic**” means a condition under which a micro-organism exerts an infection or inflicts an injury or damage when the host is not weakened by a predisposing factor (e.g. immune system impaired by an unrelated cause);

- (14) “**opportunistic infection**” means an infection occurring in a host weakened by a predisposing factor (e.g. immune system impaired by an unrelated cause);
- (15) “**metabolite of concern**” means a metabolite produced by the micro-organism under assessment, with known toxicity or known relevant antimicrobial activity, which is present in the MPCA as manufactured at levels that may present a risk to human health, animal health or the environment, and/or for which it cannot be adequately justified that *in-situ* production of the metabolite is not relevant for the risk assessment;
- (16) “**in situ production**” means the production of a metabolite by the micro-organism after application of the plant protection product containing that micro-organism;
- (17) “**relevant antimicrobial activity**” means the antimicrobial activity caused by relevant antimicrobial agents;
- (18) “**antimicrobial agent**” means any antibacterial, antiviral, antifungal, anthelmintic or antiprotozoal agent that is a substance of natural, semi-synthetic, or synthetic origin that at *in vivo* concentrations kills or inhibits the growth of micro-organisms by interacting with a specific target;
- (19) “**relevant antimicrobial agents**” means all antimicrobial agents important for therapeutic use in humans or animals, as described in the latest available versions at the time of submission of the dossier:
- in a list adopted by means of Commission Regulation (EU) 2021/1760 ⁽¹⁾ in accordance with Article 37(5) of Regulation (EU) 2019/6 of the European Parliament and of the Council ⁽²⁾, or
 - by the World Health Organisation ⁽³⁾ in the lists of Critically Important Antimicrobials, Highly Important Antimicrobials and Important Antimicrobials for Human Medicine.
- (iii) The information from scientific peer-reviewed literature as mentioned under the Introduction to this Annex, point 1.4, shall be provided at the relevant taxonomic level. An explanation on why the chosen taxonomic level is considered relevant for the addressed data requirement shall be provided.
- (iv) Other available sources of information, such as medical reports, may also be provided and submitted in a summary.
- (v) Where appropriate or specifically indicated in the data requirements, test guidelines as described in Part A shall be used also for this Part, upon adaptation in such a way that they are appropriate for chemical compounds present in the plant protection product containing an active substance that is a micro-organism.
- (vi) Where testing is done, a detailed description (specification) of the material used and its impurities, in accordance with point 1.4, shall be provided.
- (vii) In cases where a new plant protection product containing an active substance that is a micro-organism is to be dealt with, data extrapolation from Part B of the Annex to Regulation (EU) No 283/2013, may be acceptable, provided that all the possible toxic effects of the co-formulants and other components, are sufficiently characterized and evaluated as of no concern.
- (viii) Alternative methods to test toxicity of plant protection products containing an active substance that is a micro-organism on vertebrates, may also be included in a weight of evidence approach.

⁽¹⁾ Commission Delegated Regulation (EU) 2021/1760 of 26 May 2021 supplementing Regulation (EU) 2019/6 of the European Parliament and of the Council by establishing the criteria for the designation of antimicrobials to be reserved for the treatment of certain infections in humans (OJ L 353, 6.10.2021, p. 1).

⁽²⁾ Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC (OJ L 4, 7.1.2019, p. 43).

⁽³⁾ <https://www.who.int/publications/i/item/9789241515528>.

1. IDENTITY OF THE APPLICANT, IDENTITY OF THE PLANT PROTECTION PRODUCT AND MANUFACTURING INFORMATION

The information provided, taken together with that provided for the active substance that is a micro-organism, shall be sufficient to precisely identify and define plant protection products. The information provided, shall be sufficient to identify if any factor could alter the properties of the active substance that is a micro-organism as a plant protection product, in comparison to the active substance as such, which is treated in Part B of the Annex to Regulation (EU) No 283/2013. The information and data referred to, unless otherwise specified, are required for all plant protection products.

1.1. Applicant

The name and address of the applicant shall be provided as well as the name, address, telephone number and email address of the contact point.

1.2. Producer of the preparation and the micro-organism(s)

The name and address of the producer of the preparation and of each active substance that is a micro-organism in the preparation shall be provided, as well as the name and address of each manufacturing plant in which the preparation and active substance that is a micro-organism are manufactured. If the producer contracts a third party for the manufacturing process, same information shall be provided for such third party.

A contact point (preferable a central contact point, to include name, telephone number, email address and fax number) shall be provided for each producer.

If the active substance that is a micro-organism is manufactured by a producer whose data have not been submitted in accordance with Regulation (EU) No 283/2013, data to address the relevant requirements laid down in Regulation (EU) No 283/2013 shall be provided.

1.3. Trade name or proposed trade name, and producer's development code number of the preparation if appropriate

All former and current trade names and proposed trade names and development code numbers of the preparation referred to in the dossier as well as the current names and numbers shall be provided. Full detail of any differences shall be provided. The proposed trade name shall not give rise to confusion with the trade name of already authorised plant protection products.

1.4. Detailed quantitative and qualitative information on the composition of the preparation

(i) Each micro-organism that is subject to the application shall be identified as unequivocally belonging to a certain species, based on the latest scientific information, and named at the strain level, including any other designation which may be relevant to the micro-organism (e.g. isolate level, if relevant for viruses), as required by point 1.3 of Part B of the Annex to Regulation (EU) No 283/2013. The micro-organism shall be deposited at an internationally recognised culture collection and given an accession number. The scientific name shall be stated, as well as the group assignment (bacteria, virus, etc.) and any other denomination relevant to the micro-organism (e.g. strain, serotype). In addition, the development phase of the micro-organism (e.g. spores, mycelium) in the marketed plant protection product shall be stated.

(ii) For preparations, the following information shall be reported:

- the minimum and maximum content of the active substance that is a micro-organism in the plant protection product, as required in point 1.4.1 of Part B of the Annex to Regulation (EU) No 283/2013,
- the minimum and maximum content of the MPCA as manufactured in the plant protection product,
- in case of presence of relevant contaminating micro-organisms, the identity and the maximum content of relevant contaminating micro-organisms expressed in appropriate microbial unit,

- in case of presence of chemical impurities that are relevant for human and animal health and/or the environment, including metabolites of concern (identified in accordance with point 2.8 of Part B of the Annex to Regulation (EU) No 283/2013) produced by the micro-organism as relevant impurities in the manufacturing batch, the identity and maximum content, expressed in appropriate units, shall be provided,
 - the content of co-formulants, safeners and synergists in the plant protection product.
- (iii) Co-formulants, safeners and synergists shall, where possible, be identified either by their International Chemical Identification as given in Annex VI to Regulation (EC) No 1272/2008, or, if not included in that Regulation, in accordance with both IUPAC and CA nomenclature. Their structure or structural formula shall be provided. For each component of the co-formulants safeners and synergists the relevant EC (EINECS or ELINCS) number and CAS number, where they exist, shall be provided. Where the information provided does not lead to an identification, an appropriate specification shall be provided. The trade name of co-formulants, safeners and synergists, shall also be provided.
- (iv) For co-formulants, the function shall be given as:
- adhesive (sticker),
 - antifoaming agent,
 - antifreeze,
 - antioxidant,
 - binder,
 - buffer,
 - carrier,
 - deodorant,
 - dispersing agent,
 - dye,
 - emetic,
 - emulsifier,
 - fertilising product,
 - odorant,
 - osmoprotectant,
 - perfume,
 - preservative,
 - propellant,
 - repellent,
 - safener,
 - solar protectant,
 - solvent,
 - stabiliser,
 - thickener,
 - wetting agent,
 - miscellaneous (shall be specified).
- (v) Relevant contaminating micro-organisms shall be identified as provided for under point 1.4.2.2 of Part B of the Annex to Regulation (EU) No 283/2013.

Chemicals (inert components, by-products, etc.) shall be identified as provided for under point 1.10 of Part A of the Annex to Regulation (EU) No 283/2013. Where the information provided does not fully identify a component (such as condensate, culture medium), detailed information on the composition shall be provided for each such component.

1.5. Physical state and nature of the preparation

The type and code of preparation shall be designated in accordance with relevant guidance documents. Where a particular preparation is not defined precisely in relevant guidance documents, a full description of the physical nature and state of the preparation shall be provided, together with a proposal for a suitable description of the type of preparation and a proposal for its definition.

1.6. Method of production of the preparation and quality control

Full information on how the plant protection product is produced in bulk shall be provided for all the steps of the manufacturing process. The type of manufacturing process (e.g. continuous or batch process) shall be indicated.

1.7. Packaging and compatibility of the preparation with proposed packaging materials

- (i) Packaging to be used shall be described and specified in terms of the materials used, manner of construction (e.g. extruded, welded), size and capacity, size of opening, type of closure and seals.
- (ii) The suitability of the packaging, including closures, in terms of its strength, leakproofness and resistance to normal transport, storage and handling conditions, shall be determined and reported.
- (iii) The resistance of the packaging material to its content shall be reported.

2. PHYSICAL, CHEMICAL AND TECHNICAL PROPERTIES OF THE PLANT PROTECTION PRODUCT

2.1. Appearance (colour and odour)

A description of the colour and the odour, if any, and the physical state of the preparation shall be provided.

2.2. Explosivity and oxidising properties

Explosivity and oxidising properties shall be reported as provided for under point 2.2 of Part A, unless it can be justified that it is technically or scientifically not necessary to perform such studies.

2.3. Flash point and other indications of flammability or spontaneous ignition

Flash point and flammability shall be reported, as provided for under point 2.3 of Part A, unless it can be justified that it is technically or scientifically not necessary to perform such studies.

2.4. Acidity, alkalinity and if necessary pH value

Acidity, alkalinity and pH (before and after storage at the recommended conditions) shall be reported, as provided for under point 2.4 of Part A, unless it can be justified that it is technically or scientifically not necessary to perform such studies.

2.5. Viscosity and surface tension

Viscosity and surface tension shall be reported, as provided for under point 2.5 of Part A, unless it can be justified that it is technically or scientifically not necessary to perform such studies.

2.6. Storage stability and shelf life

2.6.1. Use concentration

The appropriate minimum and maximum use concentrations of the plant protection product, justifying the volume of the commercial packaging used in line with a reasonable storage period, shall be indicated, as well as the nature of the packaging material in line with the recommended storage conditions.

2.6.2. *Effects of temperature and packaging*

The optimal temperature and packaging to ensure the storage stability of the plant protection product in line with the recommended maximal shelf life shall also be stated. Where shelf life is less than two years, the shelf life in months, shall be reported.

At these conditions, information shall be provided on:

- the physical stability of the preparation during and after storage at the recommended storage temperature and, in case of liquid preparation, at low temperatures, evaluated by performing tests in the original packaging,
- the content of the active substance that is a micro-organism, which shall be in accordance with the minimum and maximum certified content declared by the applicant before and after storage at the recommended storage temperature and, if applicable, at low temperatures,
- growth of possible relevant contaminating micro-organisms, before and after storage at the recommended storage temperature, described in appropriate terms for micro-organisms (such as number of active units per volume or weight, colony forming units (CFU) or international units per volume or weight, or any other manner that is relevant to the micro-organism),
- presence of metabolites of concern identified in accordance with point 2.8 of Part B of the Annex to Regulation (EU) No 283/2013, before and after storage.

2.6.3. *Other factors affecting stability*

Effect of exposure to air, light, etc., on the plant protection product's stability shall be reported.

The optimal moisture conditions to ensure the storage stability of the plant protection product shall be stated. For dry preparations also the effects of contaminating water on viability of the micro-organism shall be described. This information may be provided by direct measurement of moisture content before and after storage or by describing packaging integrity and viability of the micro-organism before and after storage.

2.7. **Technical characteristics of the plant protection product**

The technical characteristics of plant protection products shall be determined and reported at appropriate concentrations.

2.7.1. *Wettability*

The wettability of solid plant protection products which are diluted for use (e.g. wettable powders and water dispersible granules), shall be determined and reported.

2.7.2. *Persistent foaming*

The persistence of foaming of plant protection products to be diluted with water shall be determined and reported.

2.7.3. *Suspensibility, spontaneity of dispersion and dispersion stability*

The suspensibility of water dispersible plant protection products (e.g. wettable powders, water dispersible granules, suspension concentrates) shall be determined and reported.

The spontaneity of dispersion of water dispersible plant protection products (e.g. suspension concentrates and water dispersible granules) shall be determined and reported.

The dispersion stability of plant protection products such as aqueous suspo-emulsions (SE), oil-based suspension concentrates (OD) or emulsifiable granules (EG) shall be determined and reported.

2.7.4. *Dry sieve test and wet sieve test*

In order to ensure that dustable powders have a suitable particle size distribution for ease of application, a dry sieve test shall be conducted and reported. In the case of water dispersible plant protection products, a wet sieve test shall be conducted and reported.

The nominal size range of granules shall be determined and reported.

2.7.5. *Particle size distribution (dustable and wettable powders, granules), content of dust/fines (granules), attrition and friability (granules)*

- (i) The size distribution of particles in the case of powders shall be determined and reported. The nominal size range of granules for direct application shall be determined and reported.
- (ii) The dust content of granular plant protection products shall be determined and reported. If results show > 1 % w/w dust then the particle size of the dust generated shall be determined and reported. If relevant for operator exposure the particle size of dust shall be determined and reported.
- (iii) The friability and attrition characteristics of granules and tablets, which are loose packed, shall be determined and reported.
- (iv) The hardness and integrity of tablets shall be determined and reported.

2.7.6. *Emulsifiability, re-emulsifiability and emulsion stability*

- (i) The emulsifiability, emulsion stability and re-emulsifiability of plant protection products which form emulsions, shall be determined and reported.
- (ii) The stability of dilute emulsions and of plant protection products which are emulsions, shall be determined and reported.

2.7.7. *Flowability, pourability (rinsability) and dustability*

- (i) The flowability of granular plant protection products shall be determined.
- (ii) The pourability (including rinsed residue) of suspension plant protection products (e.g. suspension concentrates, suspo-emulsions) shall be determined and reported.
- (iii) The dustability of dustable powders shall be determined and reported.

2.8. **Physical and chemical compatibility with other plant protection products including plant protection products with which its use is to be authorised**

2.8.1. *Physical compatibility*

If in the label claim a use in a mixture with other plant protection products or adjuvants is indicated, the physical compatibility of the plant protection product with different plant protection products and adjuvants, which are indicated in the label claim, to be used in the same recommended tank mixes shall be determined and reported.

2.8.2. *Chemical compatibility*

If in the label claim a use in a mixture with other plant protection products or adjuvants is indicated, the chemical compatibility of the plant protection product with different plant protection products or adjuvants in the same recommended tank mixes shall be determined and reported, except where after examination of the individual properties of the plant protection product it is established that there is no possibility of reaction taking place. In such cases, it is sufficient to provide that information as justification for not practically determining the chemical compatibility.

2.9. **Adherence and distribution to seeds**

In the case of plant protection products for seed treatment, distribution and adhesion of the plant protection product to the seeds shall be investigated and reported.

3. **DATA ON APPLICATION**

3.1. **Field of use envisaged**

The field(s) of use, existing and proposed, for plant protection product containing the micro-organism shall be specified as:

- field use, such as agriculture, horticulture, forestry and viticulture,
- protected crops (e.g. in greenhouses),
- non-cultivated areas,

- home gardening,
- houseplants,
- stored food/feed items,
- other (shall be specified).

3.2. **Mode of action on the target organism**

The information required in accordance with point 2.3 of Part B of the Annex to Regulation (EU) No 283/2013 shall be provided for the plant protection product. Additional information on the mode of action on the target organism shall be provided in case the chemical components (e.g. co-formulants) may have a relevant effect on efficacy, human and animal health or the environment.

3.3. **Function, target organisms and plants or plants products to be protected and possible risk mitigation measures**

The biological function shall be given as one of the following:

- control of bacteria,
- control of fungi,
- control of insects,
- control of mites,
- control of molluscs,
- control of nematodes,
- control of plants,
- other (shall be specified).

Details of the target organisms and plants or plant products to be protected shall be provided.

3.4. **Application rate**

For each method of application and each use, the rate of application per unit treated, in terms of g, kg, ml or l for the plant protection product and in terms of appropriate units for the micro-organism (e.g. number of active units, colony forming units (CFU) or international units per volume or weight) shall be provided. For protected crops and home gardening use rates shall be expressed in g or kg/100 m², or g or kg/m³, ml or l/100 m², or ml or l/m³.

3.5. **Content of micro-organism in material used (e.g. in the diluted spray, baits or treated seed)**

The content of micro-organism shall be reported, as appropriate, such as number of active unit per volume or weight, colony forming units (CFU) or international units per volume or weight, or any other manner that is relevant to the micro-organism.

3.6. **Method of application**

The method of application proposed shall be described, indicating the type of equipment to be used, if any, as well as the type and volume of diluent to be used per unit of area of application, or volume of plant protection product.

3.7. **Number and timing of applications on the same crop, duration of protection and waiting period(s)**

The maximum number of applications to be used on the same crop and their timing shall be reported.

Where relevant, the growth stages of the crops to be protected and the development stages of the target organisms shall be indicated. Where applicable, the interval between applications, in days, shall be stated. The duration of protection afforded both by each application and by the maximum number of applications to be used shall be indicated.

3.8. **Proposed instructions for use**

The proposed instructions for use of the plant protection product to be printed on labels and leaflets shall be provided. Details on the risk mitigation measures (if relevant) shall be provided.

3.9. **Safety intervals and other precautions to protect human health, animal health and the environment**

The information provided shall follow from and be supported by the data provided for the micro-organism(s) and that provided under Sections 7 to 10.

- (i) Where relevant, pre-harvest intervals, re-entry periods or withholding periods necessary to minimise the presence of residues in or on crops, plants and plant products, or in treated areas or spaces, with a view to protecting human and animal health, shall be specified, e.g.:
 - pre-harvest interval (in days) for each relevant crop,
 - re-entry period (in days) for livestock, to areas to be grazed,
 - re-entry period (in hours or days) for humans to crops, buildings or spaces treated,
 - withholding period (in days) for animal feeding stuffs and for post-harvest uses,
 - waiting period (in days) between application and handling treated products.
- (ii) Where necessary, in the light of the test results, information on any specific agricultural, plant health or environmental conditions under which the plant protection product may or may not be used shall be provided.

4. **FURTHER INFORMATION ON THE PLANT PROTECTION PRODUCT**

4.1. **Procedures for cleaning and decontaminating of application equipment**

Cleaning and decontaminating procedures for application equipment and protective clothing shall be described.

Such procedures shall aim at inactivating or destroying the active substance that is a micro-organism and at removing residues of the plant protection product (including metabolites of concern, if any were identified in accordance with point 2.8 of Part B of the Annex to Regulation (EU) No 283/2013).

Sufficient data shall be submitted to demonstrate the effectiveness of the cleaning and decontaminating procedures.

4.2. **Recommended methods and precautions concerning: handling, storage, transport, fire or use**

The recommended methods and precautions concerning (detailed) handling procedures for the storage, at both warehouse and user level of plant protection products, for their transport and in the event of fire shall be provided. Where relevant, information on combustion products shall be provided. The hazards likely to arise and the methods and procedures to minimise the risks shall be specified. Procedures to preclude or minimize the generation of waste or leftovers shall be provided.

Where relevant, an assessment of the procedures shall be provided.

The nature and characteristics of protective clothing and equipment proposed shall be provided. The data provided shall be sufficient to evaluate obtainability, suitability and effectiveness under realistic conditions of use (e.g. field or greenhouse circumstances), resistance and compatibility with the plant protection product.

4.3. **Measures in case of accident**

Whether arising during transport, storage or use, detailed procedures to be followed in the event of an accident shall be provided and include:

- containment of spillages,
- decontamination of areas, vehicles and buildings,

- disposal of damaged packaging, adsorbents and other materials,
- protection of emergency workers and residents, including bystanders,
- first-aid measures.

4.4. Procedures for destruction or decontamination of the plant protection product and its packaging

Procedures for destruction and decontamination shall be developed and described for both small quantities (e.g. user level) and large quantities (e.g. warehouse level). The procedures shall be consistent with provisions in place relating to the disposal of waste and of toxic waste. The means of disposal proposed shall be without unacceptable effects on the environment and be the most cost effective and practical means of disposal feasible.

4.4.1. Controlled incineration

The applicant shall provide detailed instructions for safe disposal, taking into consideration that, in many cases, the preferred or sole means to safely dispose of plant protection products and in particular the co-formulants contained in it, contaminated materials, or contaminated packaging, is through controlled incineration in a licensed incinerator.

4.4.2. Others

Other methods for destruction or decontamination of plant protection products, packaging and contaminated materials, where proposed, shall be described. Data shall be provided for such methods.

5. ANALYTICAL METHODS

Introduction

Both production and the resulting plant protection product shall be subject to a continuous quality control by the applicant. The quality criteria for the plant protection product shall be submitted.

Descriptions of methods shall be provided and include details of equipment, materials and conditions used. The applicability of internationally recognised methods shall be reported.

On request of competent authorities, the following samples shall be provided:

- (i) samples of the preparation;
- (ii) samples of the MPCA as manufactured;
- (iii) sample of the seed stock;
- (iv) if technically possible, analytical standards of metabolites of concern (see point 2.8 of Part B of the Annex to Regulation (EU) No 283/2013) and all other components included in the residue definition;
- (v) if technically possible and needed, analytical standards of relevant impurities.

As far as practicable, the post-authorisation methods shall employ the simplest approach, involve the minimum cost and require commonly available equipment.

5.1. Methods for the analysis of the preparation

The following methods shall be described:

- for identification and quantification of each micro-organism in the plant protection product, of which the active substance consists, including methods on how to distinguish between different micro-organisms, when the plant protection product includes more than one, and the most appropriate molecular analytical or phenotypic methods as described in point 4.1 of Part B of the Annex to Regulation (EC) No 283/2013,
- to establish microbiological purity of the plant protection product,

- to detect and enumerate relevant contaminating micro-organisms in the plant protection product,
- used to determine the storage stability and shelf life of the plant protection product.

5.2. **Methods to determine and quantify residues**

Analytical methods for the determination of densities of the micro-organism and residues, as provided for under point 4.2 of Part B of the Annex to Regulation (EU) No 283/2013, shall be submitted, unless the information already submitted in accordance with the requirements of point 4.2 of Part B of the Annex to Regulation (EU) No 283/2013 is sufficient.

6. **EFFICACY DATA**

Introduction

The data supplied shall be sufficient to permit an evaluation of the plant protection product to be made. In particular, it shall be possible to evaluate the nature and extent of benefits that accrue following use of the plant protection product, in comparison to suitable reference products where they exist, and/or an untreated control, damage thresholds, and to define its conditions of use.

The design, analysis, conduct and reporting of trials shall be in accordance with the relevant standards, where available. Deviations from available relevant standards may only be acceptable if the trials design meets the minimum requirements of the relevant standards and it is described and justified. The report shall include a detailed and critical assessment of the data.

The number of trials to be conducted and reported shall depend on factors such as the extent to which the properties of the active substance that is a micro-organism in the plant protection product are known. This number may depend also on the variability of conditions that arise in the trials (e.g. variability of plant health or climatic conditions), on the range of agricultural practices, the uniformity of the crops, the mode of application, the type of target organism, the climatic region and the type of plant protection product.

Data submitted shall be sufficient to be representative for the regions and the range of conditions of use encountered in practice concerning the uses of the plant protection product. If properly justified and relevant based on case-by-case approach and expert judgement, the applicant may read-across data to support the application, including data generated on other relevant uses, crops, European environments or other relevant conditions.

If read-across cannot be applied in order to assess seasonal differences, if any, sufficient data shall be generated and submitted to confirm the efficacy of the plant protection product in each agronomically and climatically different region for each particular crop (or commodity)/target organism combination. Trials on efficacy or phytotoxicity, where relevant, in at least two growing seasons shall be reported.

Any effects, positive or negative, on any non-target organism, which are observed in the tests performed in accordance with the requirements of this Section, shall be reported.

6.1. **Preliminary tests**

When requested by the competent authority, summary reports of preliminary tests shall be submitted, including laboratory, greenhouse and field studies, used to assess the biological activity, mode of action and dose-range finding of the plant protection product and the active substance(s) it contains. These reports shall provide justification on the combination of several active substances, safeners and/or synergists, if applicable, and they shall provide additional information for the competent authority when it evaluates the plant protection product. Where this information is not submitted, a justification, which is acceptable to the competent authority, shall be provided.

6.2. Minimum effective dose

The minimum effective dose shall be reported, or a range of minimum doses, necessary to achieve with sufficient efficacy the claimed plant protection action, across the broad range of situations in which that plant protection product is to be applied.

6.3. Testing effectiveness

The tests shall provide sufficient data to permit an evaluation of the level, duration and consistency of intended effects of the plant protection product. Also, possible beneficial effects on treated crops shall be reported. Tests shall include an untreated control. In case of availability of suitable reference products, a comparison shall be performed between the plant protection product subject of the application and the reference product. Trials shall be designed to investigate specified issues, to minimise the effects of random variation between different parts of each testing site and to enable statistical analysis to be applied to results amenable to such analysis. The design, analysis and reporting of trials shall be in accordance with relevant standards or with guidelines satisfying at least the requirements of the corresponding relevant standards. The report shall include a detailed and critical assessment of the data. A statistical analysis of results amenable to such analysis shall be carried out. Where necessary, the test guideline used shall be adapted to enable such analysis.

6.4. Information on possible development of resistance in target organisms

Data on the occurrence and development of resistance or cross-resistance in populations of target organisms to the active substance that is a micro-organism shall be provided, unless the applicant shows that the data and information already submitted for the active substance under point 3.4 of Part B of the Annex to Regulation (EU) No 283/2013 are sufficient to permit an assessment to be performed.

If provision of data is required, such data may be generated in experimental studies (either in laboratories or under field condition) or retrieved from available scientific literature.

If provision of data is required and information is available for uses not directly relevant to the uses for which authorisation is sought or to be renewed, including information on different species of target organism or different crops, this information shall also be provided. Where there is evidence or information to suggest that, in commercial use, the development of resistance is likely, evidence shall be generated and submitted as to the sensitivity of the population of the target organism concerned to the plant protection product. In such cases, a management strategy designed to minimise the likelihood of resistance or cross-resistance developing in target species shall be provided.

6.5. Adverse effects on treated crops

6.5.1. Phytotoxicity to target plants (including different cultivars) or to target plant products

For herbicides and for other plant protection products for which adverse effects, however transitory, are seen during the trials, the margins of selectivity on target crops shall be established, using twice the recommended rate of application. In this case, tests shall be performed to provide sufficient data to permit an evaluation of the possible occurrence of phytotoxicity after treatment with the plant protection product. Where serious phytotoxic effects are seen, an intermediate application rate shall also be investigated. Where adverse effects occur, but are claimed to be unimportant in comparison with the benefits of use or transient, evidence to support that claim is required. If necessary, yield measurement shall be submitted.

If testing is required, the safety of the plant protection product to the main cultivars of the main crops for which it is recommended shall be demonstrated, including effects of crop growth stage, vigour and other factors, which may influence susceptibility to damage or injury.

The extent of investigation necessary on other crops shall depend on their degree of similarity to the main crops already tested, the quantity and quality of data available on those main crops and how far the manner of use of the plant protection product, if relevant, is similar. The test may be performed with the main preparation type to be authorised.

Where proposed label claims include recommendations for the use of the plant protection product with other plant protection product(s), the provisions laid down in this point shall apply for the mixture.

Where phytotoxic effects are seen, they shall be accurately assessed and recorded in accordance with the relevant EPPO standards or, when a Member State requires so and when the test is carried out on the territory of that Member State, with guidelines satisfying at least the requirements of the relevant EPPO guideline.

6.5.2. *Effects on the yield of treated plants or plant products*

Tests shall be performed to provide sufficient data to permit an evaluation of the efficacy of the plant protection product and of possible occurrence of yield reduction or loss in storage of treated plants or plant products.

The effects of plant protection products on the yield or yield components of treated plant products shall be determined, unless the applicant can properly justify that such data is not relevant. When treated plants or plant products are likely to be stored, possible effects on the yield after storage, including data on storage life, shall be reported.

6.5.3. *Effects on the quality of plants or plant products*

Appropriate observations of quality parameters may be required for individual crops (for example, cereal grain quality and sugar content). Such information may be gathered from appropriate assessments in trials described under points 6.3 and 6.5.1.

Where relevant, taint testing shall be conducted.

6.5.4. *Effects on transformation processes*

The tests shall provide sufficient data to permit an evaluation of the possible occurrence of adverse effects after treatment with the plant protection product on transformation processes or on the quality of their products, and they are required when all of the following circumstances apply:

- the treated plants or plant products are normally intended for use in transformation process (e.g. wine making, brewing or bread making),
- at harvest, significant residues are present (see Section 8), and
- at least one of the following two also apply:
 - there are indications that the use of the plant protection product could have an influence on the processes involved (e.g., in the case of active substance that is a micro-organism with fungicidal function, when used close to the harvest), or
 - other plant protection products based on the same or a closely similar active ingredient have been shown to have an adverse influence on these processes or their products.

When the test is required, it may be performed with the main preparation type to be authorised. The possibility of the occurrence of adverse effects on transformation processes shall be investigated and reported. The tests shall provide sufficient data to permit an evaluation of the possible occurrence of adverse effects after treatment with the plant protection product on transformation processes or on the quality of their products.

6.5.5. *Impact on treated plants or plant propagating material*

Sufficient data shall be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on plants or plant products to be used for propagation, except where the proposed uses preclude use on crops intended for production of seeds, cuttings, runners or tubers for planting, as appropriate.

Observations shall be submitted for:

- (i) seeds – viability, germination and vigour;
- (ii) cuttings – rooting and growth rates;
- (iii) runners – establishment and growth rates;
- (iv) tubers – sprouting and normal growth.

Seeds testing shall be done in accordance with the relevant standards or with guidelines satisfying at least their requirements.

6.6. **Observations on undesirable or unintended side-effects on succeeding crops and other plants**

6.6.1. *Impact on succeeding crops*

The provision laid down in this point shall apply only for:

- plant-pathogenic micro-organisms, or
- metabolites of concern for which a hazard to plants was identified, and for which data provided in accordance with Section 9 shows that significant amounts of these metabolites of concern remain in soil or in plant materials, such as straw or organics material up to sowing or planting time of possible succeeding crops.

Sufficient data shall be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on succeeding crops. Minimum waiting periods between the last application and sowing or planting of succeeding crops shall be stated. Limitations on choice of succeeding crops, if any, shall be stated. The duration of protection brought both by each application and by the maximum number of applications to be used shall be indicated.

6.6.2. *Impact on other plants, including adjacent crops*

Sufficient data shall be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on other plants, including adjacent crops.

Observations shall be submitted on adverse effects on other plants, including the normal range of adjacent crops, when there are indications that the plant protection product could affect these plants via drift.

6.7. **Compatibility in plant protection programmes**

Where the proposed label claim includes requirements for the use conditions with other plant protection products in tank mix, spray sequences or other relevant types of applications, potential effects (e.g. antagonism, fungicidal effects) on the activity of the micro-organism after mixing, spraying in sequence, or employing other relevant types of applications with other plant protection products shall be investigated. Appropriate information shall be provided.

A general precautionary statement shall be proposed on the label, alerting the user about possible loss of efficacy of the micro-organism due to interaction in tank mix, spray sequences or other relevant types of applications with plant protection products other than those indicated in the label. Known biological incompatibilities with other plant protection products shall be reported on the label.

Appropriate recommendations (e.g. intervals between application of the plant protection product and other products) shall be specified, where necessary to avoid potential negative effects on the activity of the micro-organism. Appropriate information supporting the recommendations shall be provided.

If relevant, potential adverse effects of the plant protection product on natural enemies (e.g. released biological control agents) or other practices (e.g. conservation biological control) under the expected condition of use of the plant protection product shall be reported. The assessment of those potential adverse effects shall be based on information provided on one or more of the following:

- host range of the micro-organism (point 2.3 of Part B of the Annex to Regulation (EU) No 283/2013),
- effects on bees (point 8.3 of Part B of the Annex to Regulation (EU) No 283/2013 and point 10.3 of Part B of the Annex to Regulation (EU) No 284/2013),
- effects on non-target arthropods other than bees (point 8.4 of Part B of the Annex to Regulation (EU) No 283/2013 and point 10.4 of Part B of the Annex to Regulation (EU) No 284/2013) or
- any other relevant information.

7. EFFECT ON HUMAN HEALTH

Introduction

For proper evaluation of risks for human and animal (i.e. species normally fed and kept by humans or food-producing animals) health linked to the use of a plant protection product containing an active substance that is a micro-organism, the infectivity and pathogenicity of the micro-organism have been already assessed in accordance with Section 5 of Part B of the Annex to Regulation (EU) No 283/2013. This assessment includes the micro-organism and any metabolite(s) of concern for human and animal health identified in accordance with point 2.8 of Part B of the Annex to that Regulation.

This Section identifies the relevant additional tests to be carried out to determine the classification and labelling of the plant protection product and the acceptability of the risks related to its use. In some cases, already existing information on toxicity of co-formulants and other non-active ingredients of the plant protection product may be sufficient to conclude on the toxicity of the plant protection product.

In view of determining the classification and labelling of the plant protection product, as well as the risks associated with its use, information on intrinsic toxicological properties of the co-formulants, safeners and synergists, shall be provided. Possible adverse synergistic effects and/or interaction among chemical substances present in the plant protection product (e.g. co-formulants, other active substance(s) and its/their impurities present in the same plant protection product) shall also be investigated. Available data concerning any possible adverse effect on human health shall be reported.

The information provided shall be sufficient to allow an evaluation of the risks to human health associated with the use of the plant protection products (e.g. operators, workers, bystanders, residents and consumers), the risks for human health handling treated crops, as well as the risk for human health and animals arising from residual traces remaining in food, feed and water. In addition, the information provided shall be sufficient to:

- permit a decision to be made as to whether, or not, the plant protection product may be authorised,
- specify appropriate conditions or restrictions to be associated with any authorisation,
- specify hazard and precautionary statements for the protection of human health, animal health and the environment to be included on packaging (containers),
- identify relevant first aid measures as well as appropriate diagnostic and therapeutic measures to be followed in the event of infection or another adverse effect in humans.

In the context of the possible contribution that relevant impurities and other components can have on the toxicological profile of the plant protection product, for each study submitted, a detailed description of the material used shall be provided. Tests shall be conducted using the plant protection product to be authorised. In particular, the information provided shall demonstrate that the micro-organism used in the plant protection product and the conditions of culturing it are the same for which information and data are submitted in accordance with Part B of the Annex to Regulation (EU) No 283/2013. While performing toxicology studies, all signs of adverse effects shall be reported.

Based on the information submitted, proposals for the classification and labelling of the plant protection product, using CLP calculation rules in accordance with Regulation (EC) No 1272/2008, where applicable, shall be submitted and justified, including:

- pictograms,
- signal words,
- hazard statements, and
- precautionary statements.

Where the information available is considered not to be robust enough to exclude possible adverse synergistic effects of substances present in the plant protection product (e.g. co-formulants, other active substance(s) and its/their impurities present in the same plant protection product), toxicological studies on possible adverse synergistic effects shall be required by the competent authority, as described under points 7.4 and 7.7.

7.1. Medical data

Any available information on possible adverse effect on human health shall be reported, including sensitisation and allergenic response of humans exposed to the plant protection product. In the case of adverse effects, special attention shall be paid to whether the individual's susceptibility may have been affected by e.g. pre-existing disease, medication, compromised immunity, pregnancy or breast-feeding. The information provided shall include details of level and duration of exposure, symptoms observed and other relevant clinical observation.

7.2. Assessment of potential toxicity of the plant protection product

Possible human health hazards related to pathogenic events linked to the use of the plant protection product are addressed through data on infectivity, pathogenicity, and clearance of the active substance that is a micro-organism in accordance with Section 5 of Part B of the Annex to Regulation (EU) No 283/2013.

Studies to determine the potential toxicity of the plant protection product shall be performed as required in point 7.3, unless the applicant demonstrates by following a weight of evidence approach, based on the information provided under Sections 2, 3, 4 and point 7.1 or retrieved from any other reliable sources (e.g. Integrated Approach to Testing and Assessment – IATA, CLP calculation rules in accordance with Regulation (EC) No 1272/2008 or read-across data from similar preparations) that no such effects are to be expected. An assessment of the potential toxicity of the plant protection product shall be submitted, taking into consideration information on the intrinsic properties of co-formulants, metabolites of concern identified in accordance with point 2.8 of Part B of the Annex to Regulation (EU) No 283/2013, relevant impurities, with consideration for possible adverse synergistic effects and/or interaction between them and with the proposal for classification and labelling. With this assessment, the applicant shall demonstrate whether or not sufficient information is available to classify the plant protection product in accordance with Regulation (EC) No 1272/2008 with regard to toxicity to humans and whether or not acute toxicity studies on animals as described in points 7.3.1 to 7.3.6 are needed.

7.3. Acute toxicity

Unless information can be provided to allow an assessment to be conducted on the possible human toxicity of the plant protection product as set out in point 7.2, the applicant shall define which of the tests described in points 7.3.1 to 7.3.6 is relevant for the plant protection product and perform the test(s) identified in accordance with the instruction provided in each respective relevant point. The studies indicated in points 7.3.1 to 7.3.6, data and information to be provided and evaluated shall be sufficient to permit the identification of effects following a single exposure to the plant protection product and in particular to establish or indicate:

- the acute toxicity of the plant protection product,
- the time course and characteristics of the adverse effect with full details of behavioural changes and possible gross toxicological findings at post-mortem in animal studies,
- where possible, the mode of toxic action, and
- the relative hazard associated with the different routes of exposure.

The information generated shall also permit the plant protection product to be classified in accordance with Regulation (EC) No 1272/2008.

7.3.1. Acute oral toxicity

Unless information can be provided to allow an assessment to be conducted on the possible acute oral toxicity of the plant protection product as set out in point 7.2, a test for acute oral toxicity shall be carried out in accordance with the most appropriate guidelines.

7.3.2. *Acute dermal toxicity*

Unless information can be provided to allow an assessment to be conducted on the possible dermal toxicity of the plant protection product as set out in point 7.2, a test for dermal toxicity shall be carried out in accordance with the most appropriate guidelines.

7.3.3. *Acute inhalation toxicity*

Unless information can be provided to allow an assessment to be conducted on the possible inhalation toxicity of the plant protection product as set out in point 7.2, a test for acute inhalation toxicity shall be carried out if the plant protection product:

- is used with fogging equipment,
- is used as a smoke generating formulation,
- is used as a vapour releasing preparation,
- is to be applied from aircraft in cases where inhalation exposure is relevant (broadcast air-assisted sprayer),
- is an aerosol,
- is a powder containing a significant proportion of particles of diameter < 50 micrometre (> 1 % on a weight basis),
- is to be applied in a manner which generates a significant proportion of particles or droplets of diameter < 50 micrometre (> 1 % on a weight basis), or
- contains a volatile component at greater than 10 %.

7.3.4. *Skin irritation*

Unless information can be provided to allow an assessment to be conducted on the skin irritation potential of the plant protection product from the available information regarding its components, including the active substance, co-formulants, safeners, synergists, and relevant impurities as set out in point 7.2, a test for skin irritation shall be carried out in accordance with the most appropriate guidelines.

The test shall provide the potential of skin irritancy of the plant protection product including the potential reversibility of the effects observed.

7.3.5. *Eye irritation*

A test for eye irritation shall be carried out in accordance with the most appropriate guidelines, unless:

- information can be provided to allow an assessment to be conducted on the eye irritating potential of the plant protection product as set out in point 7.2, or
- the micro-organism is an already known eye irritant or it is likely, as indicated in the test guideline, that severe effects on the eyes may be produced.

The test shall provide the potential for eye irritation of the plant protection product, including the potential reversibility of the effects observed.

7.3.6. *Skin sensitisation*

Unless information can be provided to allow an assessment to be conducted on the skin sensitisation properties of the plant protection product from the available information regarding its chemical components (i.e. co-formulants, metabolites of concern and relevant impurities) as set out in point 7.2, a test for skin sensitisation when available, shall be carried out in accordance with the most appropriate guidelines.

7.4. **Additional toxicity information**

If, based on results of the studies required in point 7.3, one or more substances of concern is present in the plant protection product (e.g. metabolites of concern and/or co-formulants) for which the risk is for human and animal health is considered not acceptable based on those studies already performed, relevant additional information on toxicity may be necessary for the plant protection product. The need to perform supplementary studies on the plant protection product shall be based on expert judgement case-by-case, in the light of the particular parameters to be investigated and the objectives to be achieved, for example, if concern on the toxicity of the plant protection products has arisen from studies described in points 7.3.1 to 7.3.6 or a conclusion on toxicity could not be reached.

7.5. **Data on exposure**

If, based on data provided in Section 5 of Part B of the Annex to Regulation (EU) No 283/2013 and this Section, effects on human health cannot be excluded, sufficient information and data shall be generated and reported to permit an assessment of the extent of exposure to the plant protection product likely to occur under the proposed conditions of use. Study design shall take into account biological, physical, chemical and toxicological properties of the plant protection product as well as the type of the product (undiluted/diluted), preparation type, and the route, the degree and duration of exposure.

In the case where there is a particular concern for a possibility of dermal absorption of a toxic component of the plant protection product based on information provided in this Section, dermal absorption data shall be provided as provided for under point 7.3 of Part A.

Results from exposure monitoring during production and use of the plant protection product shall be submitted.

The information and data referred to in this point shall provide the basis for the selection of appropriate protective measures including personal protective equipment (see point 4.2) to be used by operators and workers and other appropriate risk mitigation measures (e.g. for bystanders and residents) and to be specified on the label.

7.6. **Available toxicological data relating to non-active substances**

Where relevant, the following information shall be submitted for each co-formulants, safeners and synergists:

- (a) the registration number as referred to in Article 20(3) of Regulation (EC) No 1907/2006 of the European Parliament and of the Council ⁽⁴⁾;
- (b) the study summaries included in the technical dossier; and
- (c) the safety data sheet as referred to in Article 31 of Regulation (EC) No 1907/2006.

All other available information shall be submitted.

7.7. **Supplementary studies for combinations of plant protection products**

Where the plant protection product label indicates the use of the plant protection product with other plant protection products and/or with adjuvants as a tank mix, the studies as referred to under points 7.3.1 to 7.3.6 shall be carried out for the relevant combination of plant protection products. Decisions as to the need for supplementary studies shall be made on a case-by-case basis, taking into account the results of the acute toxicity studies of the individual plant protection products, the possibility for exposure to the combination of the plant protection products concerned and available information or practical experience with the plant protection products concerned or similar plant protection products.

⁽⁴⁾ Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC (OJ L 396, 30.12.2006, p. 1).

The need to perform supplementary studies on the plant protection product shall be based on expert judgement case-by-case, in the light of the particular parameters to be investigated and the objectives to be achieved (for example, for plant protection products containing active substances or other components suspected to have synergistic or additive toxicological effects).

8. RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED

Data and information on residues in or on treated products, food and feed in accordance with Section 6 of Part B of the Annex to Regulation (EU) No 283/2013 shall be submitted, unless the applicant shows that the data and information already submitted for the active substance are sufficient to permit a risk assessment to be performed on the plant protection product.

9. FATE AND BEHAVIOUR IN THE ENVIRONMENT

Data and information in accordance with Section 7 of Part B of the Annex to Regulation (EU) No 283/2013 shall be submitted on the fate and behaviour of the plant protection product in the environment, unless the applicant shows that the data and information already submitted for the active substance are sufficient to permit a risk assessment to be performed on the plant protection product.

10. EFFECTS ON NON-TARGET ORGANISMS

Introduction

- (i) The information provided, taken together with that for the active substance that is a micro-organism provided in accordance with Part B of the Annex to Regulation (EU) No 283/2013 (including possible metabolite(s) of concern as identified in accordance with point 2.8 of Part B of the Annex to Regulation (EU) No 283/2013) shall be sufficient to permit an assessment of the potential impact on non-target species of the plant protection product, when used as proposed. When submitting this information, the applicant shall take into account that the impact on non-target species can result from single, prolonged or repeated exposure and can be reversible or irreversible.
- (ii) Where exposure data are necessary to decide whether a study shall be performed, the data obtained in accordance with Section 9 shall be used. For the estimation of exposure of organisms all relevant information on the plant protection product and on the micro-organism shall be taken into account. Where relevant, the data provided for under this Section shall be used. Where it appears from available data that the plant protection product has a stronger effect than the active substance that is a micro-organism, the data on effects on non-target organisms of the plant protection product shall be used for the calculation of relevant effect/exposure ratios.
- (iii) Unless it can be justified that an assessment of effects on non-target organisms can be performed with the information already available, experimental data may be required. The duration of experimental studies shall be long enough to permit time for incubation, infection and manifestation of adverse effects in non-target organisms, but in line with the expected exposure under the proposed use. In order to distinguish between pathogenic and toxic effects, appropriate controls shall be used in addition to the no-dosed control group, such as inactivated controls and/or sterile filtrate/supernatant controls. Special attention shall be required when the plant protection product contains a micro-organism which is pathogenic to non-target organisms other than mammals and that was not isolated from a relevant European environment. The information provided shall be sufficient to assess environmental impacts.
- (iv) The relevance of non-target organism species used for testing environmental effects shall be based on a weight of evidence approach, taking into consideration, for instance:
 - information on the micro-organism (particularly on biological properties) as required in Part B of the Annex to Regulation (EU) No 283/2013,

- information concerning the co-formulants, safeners and synergists, as required in Sections 1 to 9, and
- proposed use patterns of the plant protection product (e.g. foliar or soil application).

In order to facilitate the assessment of the significance of test results obtained, where possible, the same strain of each relevant species of non-target organisms shall be used in the various specified tests for effects on non-target organisms.

- (v) All the adverse effects observed in tests and trials performed with the plant protection product shall be reported, and additional studies, which may be necessary to investigate the mechanisms involved and assess the significance of these effects, shall be undertaken and reported.
- (vi) Where adverse toxic effects are indicated in the studies considered for the risk assessment and risk identified may be considered not acceptable, additional toxicity studies under field conditions and in accordance with the proposed recommendations for use shall be conducted, if applicable.

The type of study to be performed depends on the effects and the affected non-target organism(s) observed in the studies required in points 10.1 to 10.7 and during efficacy testing and may have to include also further studies on additional non-target species (i.e. different than those initially tested). Special attention shall be given to possible effects on non-target organisms occurring in the relevant European environment and deliberately released organisms for biological control purposes.

- (vii) The information provided for the plant protection product, together with other relevant information, and that provided for the micro-organism (including possible metabolites of concern as identified in point 2.8 of Part B of the Annex to Regulation (EU) No 283/2013) shall be sufficient to:
 - specify the hazard symbols, the indications of danger and relevant risk and safety phrases or the pictograms, signal words, relevant hazard and precautionary statements for the protection of the environment to be mentioned on packaging (containers),
 - permit an evaluation of the short- and long-term risks for non-target species – populations, communities, and processes as appropriate,
 - permit an evaluation whether special precautions are necessary for the protection of non-target species.

10.1. Effects on terrestrial vertebrates

The same information submitted on the micro-organism (and/or on a plant protection product containing that active substance with respect to a representative use), as detailed in points 8.1, 8.7 and 8.8 of Part B of the Annex to Regulation (EU) No 283/2013 shall be provided for the plant protection product subject of the application, unless the applicant can:

- justify the applicability and relevance of the outcome of the assessment made on the same data submitted for the micro-organism approval (and/or for a plant protection product containing that active substance with respect to a representative use),
- predict the effects of the plant protection product on the basis of the data available for the co-formulants (e.g. qualitative and quantitative composition), as well as for the micro-organism and possible metabolites of concern (based on data submitted in accordance with Section 8 of Part B of the Annex to Regulation (EU) No 283/2013 for the approval of the micro-organism(s) in the plant protection product), or
- justify that the non-target terrestrial vertebrates (e.g. mammals, birds, reptiles, and amphibians) will not be exposed to the plant protection product (based on data submitted in accordance with Section 9).

If generation of data is required based on the provisions laid down under this point, relevant studies shall be performed and they shall provide LD₅₀ values and include gross pathological findings. The studies may be conducted on the species used in the studies referred to in point 8.1 of Part B of the Annex to Regulation (EU) No 283/2013.

10.2. Effects on aquatic organisms

10.2.1. *Effects on fish*

The same information submitted on the micro-organism (and/or on a plant protection product containing that active substance with respect to a representative use) as detailed in points 8.2.1, 8.7 and 8.8 of Part B of the Annex to Regulation (EU) No 283/2013 shall be provided for the plant protection product subject of the application, unless the applicant can:

- justify the applicability and relevance of the outcome of the assessment made on the same data submitted for the micro-organism approval (and/or on a plant protection product containing that active substance with respect to a representative use),
- predict the effects of the plant protection product on the basis of the data available for the co-formulants (e.g. qualitative and quantitative composition), as well as for the micro-organism and possible metabolites of concern (based on data submitted in accordance with Section 8 of Part B of the Annex to Regulation (EU) No 283/2013 for the approval of the active substance(s) in the plant protection product), or
- justify that fish will not be exposed to the components of the plant protection product (based on data submitted in accordance with Section 9).

If generation of data is required based on the provisions laid down under this point, relevant studies shall be performed and they shall provide LD₅₀ values, and shall include gross pathological findings. The studies may be conducted on the species used in the studies referred to in point 8.2.1 of Part B of the Annex to Regulation (EU) No 283/2013.

10.2.2. *Effects on aquatic invertebrates*

The same information submitted on the micro-organism (and/or on a plant protection product containing that active substance with respect to a representative use) as detailed in points 8.2.2, 8.7 and 8.8 of Part B of the Annex to Regulation (EU) No 283/2013 shall be provided for the plant protection product subject of the application, unless the applicant can:

- justify the applicability and relevance of the outcome of the assessment made on the same data submitted for the micro-organism approval (and/or on a plant protection product containing that active substance with respect to a representative use),
- predict the effects of the plant protection product on the basis of the data available for the co-formulants (e.g. qualitative and quantitative composition), as well as for the micro-organism and possible metabolites of concern (based on data submitted in accordance with Section 8 of Part B of the Annex to Regulation (EU) No 283/2013 for the approval of the active substance(s) in the plant protection product), or
- justify that the aquatic invertebrates will not be exposed to the components of the plant protection product (based on data submitted in accordance with Section 9).

If generation of data is required based on the provisions laid down under this point, relevant studies shall be performed.

10.2.3. *Effects on algae*

The same information submitted on the micro-organism (and/or on a plant protection product containing that active substance with respect to a representative use) as detailed in points 8.2.3, 8.7 and 8.8 of Part B of the Annex to Regulation (EU) No 283/2013 shall be provided for the plant protection product subject of the application, unless the applicant can:

- justify the applicability and relevance of the outcome of the assessment made on the same data submitted for the micro-organism approval (and/or on a plant protection product containing that active substance with respect to a representative use),

- predict the effects of the plant protection product on the basis of the data available for the co-formulants (e.g. qualitative and quantitative composition), as well as for the micro-organism and possible metabolites of concern (based on data submitted in accordance with Section 8 of Part B of the Annex to Regulation (EU) No 283/2013 for the approval of the micro-organism(s) in the plant protection product), or
- justify that algae will not be exposed to the components of the plant protection product (based on data submitted in accordance with Section 9).

If generation of data is required based on the provisions laid down under this point, relevant studies shall be performed.

10.2.4. *Effects on aquatic macrophytes*

The same information submitted on the micro-organism (and/or on a plant protection product containing that active substance with respect to a representative use) as detailed in points 8.2.4, 8.7 and 8.8 of Part B of the Annex to Regulation (EU) No 283/2013 shall be provided for the plant protection product subject of the application, unless the applicant can:

- justify the applicability and relevance of the outcome of the assessment made on the same data submitted for the micro-organism approval (and/or on a plant protection product containing that active substance with respect to a representative use),
- predict the effects of the plant protection product on the basis of the data available for the co-formulants (e.g. qualitative and quantitative composition), as well as for the micro-organism and possible metabolites of concern (based on data submitted in accordance with Section 8 of Part B of the Annex to Regulation (EU) No 283/2013 for the approval of the micro-organism(s) in the plant protection product), or
- justify that aquatic macrophytes will not be exposed to the components of the plant protection product (based on data submitted in accordance with Section 9).

If generation of data is required based on the provisions laid down under this point, relevant studies shall be performed.

10.3. **Effects on bees**

The same information submitted on the micro-organism (and/or on a plant protection product containing that active substance with respect to a representative use) as detailed in points 8.3, 8.7 and 8.8 of Part B of the Annex to Regulation (EU) No 283/2013 shall be provided for the plant protection product subject of the application, unless the applicant can:

- justify the applicability and relevance of the outcome of the assessment made on the same data submitted for the micro-organism approval (and/or on a plant protection product containing that active substance with respect to a representative use),
- predict the effects of the plant protection product on the basis of the data available for the co-formulants (e.g. qualitative and quantitative composition), as well as for the micro-organism and possible metabolites of concern (based on data submitted in accordance with Section 8 of Part B of the Annex to Regulation (EU) No 283/2013 for the approval of the micro-organism(s) in the plant protection product), or
- justify that bees will not be exposed to the components of the plant protection product (based on data submitted in accordance with Section 9).

If generation of data is required based on the provisions laid down under this point, relevant studies shall be performed.

10.4. Effects on non-target arthropods other than bees

The same information submitted on the micro-organism (and/or on a plant protection product containing that active substance with respect to a representative use) as detailed in points 8.4, 8.7 and 8.8 of Part B of the Annex to Regulation (EU) No 283/2013 shall be provided for the plant protection product subject of the application, unless the applicant can:

- justify the applicability and relevance of the outcome of the assessment made on the same data submitted for the micro-organism approval (and/or on a plant protection product containing that active substance with respect to a representative use),
- predict the effects of the plant protection product on the basis of the data available for the co-formulants (e.g. qualitative and quantitative composition), as well as for the micro-organism and possible metabolites of concern (based on data submitted in accordance with Section 8 of Part B of the Annex to Regulation (EU) No 283/2013 for the approval of the micro-organism(s) in the plant protection product), or
- justify that the non-target arthropods other than bees will not be exposed to the components of the plant protection product (based on data submitted in accordance with Section 9).

If generation of data is required based on the provisions laid down under this point, relevant studies shall be performed. Analyses might include further studies on additional species, or higher tier studies such as studies on selected non-target organisms using the formulated plant protection product. The choice of non-target arthropods test species playing an important role in integrated pest management may be based on several factors, such as biological properties of the micro-organism and the intended use (e.g. crop type).

10.5. Effects on non-target meso- and macroorganisms in soil

The same information submitted on the micro-organism (and/or on a plant protection product containing that active substance with respect to a representative use) as detailed in points 8.5, 8.7 and 8.8 of Part B of the Annex to Regulation (EU) No 283/2013 shall be provided for the plant protection product subject of the application, unless the applicant can:

- justify the applicability and relevance of the outcome of the assessment made on the same data submitted for the micro-organism approval (and/or on a plant protection product containing that active substance with respect to a representative use),
- predict the effects of the plant protection product on the basis of the data available for the co-formulants (e.g. qualitative and quantitative composition), as well as for the micro-organism and possible metabolites of concern (based on data submitted in accordance with Section 8 of Part B of the Annex to Regulation (EU) No 283/2013 for the approval of the micro-organism(s) in the plant protection product), or
- justify that the non-target meso- and macroorganisms in soil will not be exposed to the components of the plant protection product (based on data submitted in accordance with Section 9).

If generation of data is required based on the provisions laid down under this point, relevant studies shall be performed.

10.6. Effects on non-target terrestrial plants

The same information submitted on the micro-organism (and/or on a plant protection product containing that active substance with respect to a representative use) as detailed in points 8.6, 8.7 and 8.8 of Part B of the Annex to Regulation (EU) No 283/2013 shall be provided for the plant protection product subject of the application, unless the applicant can:

- justify the applicability and relevance of the outcome of the assessment made on the same data submitted for the micro-organism approval (and/or on a plant protection product containing that active substance with respect to a representative use),

- predict the effects of the plant protection product on the basis of the data available for the co-formulants (e.g. qualitative and quantitative composition), as well as for the micro-organism and possible metabolites of concern (based on data submitted in accordance with Section 8 of Part B of the Annex to Regulation (EU) No 283/2013 for the approval of the micro-organism(s) in the plant protection product), or
- justify that the non-target terrestrial plants will not be exposed to the components of the plant protection product (based on data submitted in accordance with Section 9).

If generation of data is required based on the provisions laid down under this point, relevant studies shall be performed.

10.7. Additional toxicity studies

Further data may be submitted or additional toxicity studies performed, if tests required in points 10.1 to 10.6 have shown adverse effects in one or more non-target organisms and the risk is considered not acceptable. The type of study to be performed shall be chosen based on the effects and the affected non-target organism(s) observed in the studies required in points 10.1 to 10.6 and during efficacy testing, and may have to include also further studies on additional non-target species.'

COMMISSION REGULATION (EU) 2022/1441**of 31 August 2022****amending Regulation (EU) No 546/2011 as regards specific uniform principles for evaluation and authorisation of plant protection products containing micro-organisms****(Text with EEA relevance)**

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard 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 and repealing Council Directives 79/117/EEC and 91/414/EEC ⁽¹⁾, and in particular Article 29(6) and Article 78(1)(c) thereof,

Whereas:

- (1) Commission Regulation (EU) No 546/2011 ⁽²⁾ provides for uniform principles for evaluation and authorisation of plant protection products. Part I and Part II of the Annex to Regulation (EU) No 546/2011 lay down, for plant protection products containing chemical substances and micro-organisms respectively, the existing uniform principles for assessing whether the plant protection products may have harmful effects on human health, animal health or unacceptable effects on the environment in view of their authorisation.
- (2) The Farm to Fork Strategy for a fair, healthy and environmentally friendly food system of the Commission ⁽³⁾ aims at reducing dependency on and use of chemical plant protection products, including through facilitating the placing on the market of biological active substances such as micro-organisms. In order to reach these objectives, it is necessary to specify the uniform principles related to plant protection products containing micro-organisms taking into account the most up-to-date scientific and technical knowledge, which has evolved significantly.
- (3) Since micro-organisms are living organisms, a specific approach is needed compared to chemical substances, in order to also take into account the current state of Science regarding the biology of micro-organisms. That scientific knowledge consists of information on key characteristics of micro-organisms, such as their pathogenicity and infectivity, the possible production of metabolite(s) of concern and the capacity to transfer antimicrobial resistance genes to other micro-organisms which are pathogenic and occurring in European environments, potentially affecting the effectiveness of antimicrobials used in human or veterinary medicine.
- (4) The currently available scientific knowledge on plant protection products containing micro-organisms allows for a better and more specific approach for their assessment, which is based on the mode of action and the ecological characteristics of the respective species and, where applicable, the respective strains of micro-organisms. As it allows a more targeted risk assessment, such scientific knowledge should be taken into account when assessing the risks posed by plant protection products containing micro-organisms.
- (5) In order to better reflect the latest scientific developments and the specificities of micro-organisms, while maintaining a high level of protection of human and animal health and of the environment, it is therefore necessary to adapt the existing uniform principles accordingly.

⁽¹⁾ OJ L 309, 24.11.2009, p. 1.

⁽²⁾ Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products (OJ L 155, 11.6.2011, p. 127).

⁽³⁾ Communication from the Commission to the European Parliament, the Council, the Economic and Social Committee and the Committee of the Regions A Farm to Fork Strategy for a fair, healthy and environmentally-friendly food system (COM/2020/381 final, <https://eur-lex.europa.eu/legal-content/en/TXT/?qid=1590404602495&uri=CELEX:52020DC0381>).

- (6) Currently available scientific knowledge about the capacity of micro-organisms to transfer antimicrobial resistance genes to other micro-organisms which are pathogenic and occurring in European environments, hence potentially affecting the effectiveness of antimicrobials used in human or veterinary medicine allows for a better and more specific approach for the assessment of which genes encoding for antimicrobial resistance are likely to be transferred to other micro-organisms, and which antimicrobials are those relevant for human or veterinary medicine. In addition, the EU Farm to Fork Strategy has set antimicrobial resistance-related targets. Therefore, further specification is needed on the data requirements to implement the most updated scientific and technical knowledge on transferability of antimicrobial resistance, and ensure for an assessment to be made on whether the active substance may have harmful effects on human or animal health, as indicated in the approval criteria laid down in Article 4 of Regulation (EC) No 1107/2009.
- (7) For the sake of clarity of the uniform principles, various points that currently appear in sections A, B and C of both Part I and Part II of the Annex should be consolidated in a general introduction.
- (8) The current Annex to Regulation (EU) No 546/2011 contains references to Commission Regulations (EU) No 544/2011 ⁽⁴⁾ and (EU) No 545/2011 ⁽⁵⁾, which are no longer in force. It is therefore appropriate to update these references and refer to Commission Regulation (EU) No 283/2013 ⁽⁶⁾ and Commission Regulation (EU) No 284/2013 ⁽⁷⁾, respectively, which replaced Regulations (EU) No 544/2011 and (EU) No 545/2011.
- (9) The uniform principles for evaluation and authorisation of plant protection products aim to ensure that evaluations and decisions with regard to authorisation of plant protection products by Member States result in a high level of protection of human and animal health and the environment as required by Regulation (EC) No 1107/2009. The uniform principles also give some explanations on how the Member States are to assess data submitted by applicants in accordance with the data requirements as set out in the relevant legislation. Considering that the legislation setting out the data requirements is being amended by Commission Regulation (EU) 2022/1441 ⁽⁸⁾ it is necessary to ensure consistency in the application of new rules, so that new applications are submitted according to the amended data requirements.
- (10) Part A of the Annexes to Regulation (EU) No 283/2013 and Regulation (EU) No 284/2013 sets out the requirements for the data to be assessed in accordance with the uniform principles, and refers to chemical active substances and plant protection products containing them, respectively. For the sake of legal certainty, clarity and consistency with Regulation (EU) No 283/2013 and Regulation (EU) No 284/2013, Part I of the Annex to Regulation (EU) No 546/2011 should be renamed as 'Part A'.
- (11) Part B of the Annexes to Regulation (EU) No 283/2013 and Regulation (EU) No 284/2013 sets out the requirements for the data to be assessed in accordance with the uniform principles, and refers to active substances that are micro-organisms and plant protection products containing them, respectively. For the sake of legal certainty, clarity and consistency with Regulation (EU) No 283/2013 and Regulation (EU) No 284/2013, Part II of the Annex to Regulation (EU) No 546/2011 should be renamed as 'Part B'.

⁽⁴⁾ Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances (OJ L 155, 11.6.2011, p. 1).

⁽⁵⁾ Commission Regulation (EU) No 545/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for plant protection products (OJ L 155, 11.6.2011, p. 67).

⁽⁶⁾ Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, 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 (OJ L 93, 3.4.2013, p. 1).

⁽⁷⁾ Commission Regulation (EU) No 284/2013 of 1 March 2013 setting out the data requirements for plant protection products, 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 (OJ L 93, 3.4.2013, p. 85).

⁽⁸⁾ Commission Regulation (EU) 2022/1441 of 31 August 2022 amending Regulation (EU) No 284/2013 as regards the information to be submitted for plant protection products and the specific data requirements for plant protection products containing micro-organisms (see page 70 of this Official Journal).

- (12) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

HAS ADOPTED THIS REGULATION:

Article 1

The Annex to Regulation (EU) No 546/2011 is replaced by the text set out in the Annex to this Regulation.

Article 2

Regulation (EU) No 546/2011 as it stood prior to being amended by this Regulation shall continue to apply to applications for authorisation of plant protection products, within the meaning of Regulation (EC) No 1107/2009, for which data is submitted in accordance with Commission Regulation (EU) No 284/2013 in the version applicable before 21 November 2022.

Article 3

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

It shall apply from 21 November 2022.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 31 August 2022.

For the Commission
The President
Ursula VON DER LEYEN

ANNEX

'ANNEX

GENERAL INTRODUCTION

1. GENERAL PRINCIPLES

1.1. The objective of the principles developed in this Annex is to ensure a high level of protection of human and animal (species normally fed and kept by humans or food-producing animals) health and the environment in evaluations and decisions by Member States with regard to authorisation of plant protection products, implementing the requirements of Article 29(1)(e) in conjunction with Article 4(3) and Article 29(1)(f), (g) and (h) of Regulation (EC) No 1107/2009. For the purpose of this Annex, the following definitions apply:

- (1) **'efficacy'** means a measure concerning the overall effect of the application of a plant protection product on the agricultural system in which it is used (i.e. which includes positive effects of treatment in performing the desired plant protection activity and negative effects such as development of resistance, phytotoxicity or reduction of qualitative or quantitative yield);
- (2) **'relevant impurity'** means a chemical impurity that is of concern for human health, animal health or the environment;
- (3) **'storage stability'** means the capacity of a plant protection product to maintain the initial properties and the specified content during the storage period under established storage conditions.

1.2. In evaluating applications for granting authorisations Member States shall:

- (a)
 - ensure that dossiers supplied are in accordance with the requirements of the Annex to Commission Regulation (EU) No 284/2013 ⁽¹⁾, at the latest at the time of finalisation of the evaluation for the purpose of decision-making, without prejudice, where relevant, to Articles 33, 34 and 59 of Regulation (EC) No 1107/2009,
 - ensure that the data submitted by the applicant are acceptable in terms of quantity, quality, consistency and reliability and sufficient to permit a proper evaluation of the dossier,
 - evaluate, where relevant, justifications submitted by the applicant for not supplying certain data;
- (b) take into account the data concerning the active substance in the plant protection product of the Annex to Commission Regulation (EU) No 283/2013 ⁽²⁾, submitted for the purpose of approval of the active substance under Regulation (EC) No 1107/2009, and the results of the evaluation of those data, without prejudice, where relevant, to the provisions of Article 33(3) and of Articles 34 and 59 of Regulation (EC) No 1107/2009;
- (c) take into consideration other relevant technical or scientific information with regard to the efficacy of the plant protection product or to the potentially adverse effects of the plant protection product its components or its residues, where relevant.

1.3. Where, in the specific principles on evaluation, reference is made to the data of the Annex to Regulation (EU) No 283/2013 this shall be understood as being the data referred to in point 1.2(b) of this Annex.

⁽¹⁾ Commission Regulation (EU) No 284/2013 of 1 March 2013 setting out the data requirements for plant protection products, 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 (OJ L 93, 3.4.2013, p. 85).

⁽²⁾ Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, 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 (OJ L 93, 3.4.2013, p. 1).

- 1.4. Where the data and information provided are sufficient to permit completion of the evaluation for one of the proposed uses, Member States shall evaluate applications and make a decision for the proposed use.

Taking account of justifications provided and with the benefit of any subsequent clarifications, Member States shall reject applications for granting authorisations for which the data gaps are such that it is not possible to finalise the evaluation and to make a reliable decision for at least one of the proposed uses.

- 1.5. During the process of evaluation and decision-making, Member States shall cooperate with the applicants in order to resolve any questions on the dossier quickly or to identify at an early stage any additional studies necessary for a technically complete dossier that allows for a proper evaluation, or to amend any proposed conditions for the use of the plant protection product or to modify its nature or its composition in order to ensure full compliance with the requirements of this Annex and more generally with the provisions of Regulation (EC) No 1107/2009.
- 1.6. During the process of evaluation and decision-making, Member States shall base their assessment on scientific principles, preferably recognised at international level, and this process shall be made with the benefit of expert advice.
- 1.7. Member States shall take into account those guidance documents applicable at the date of the submission of the application for the authorisation.

2. EVALUATION, GENERAL PRINCIPLES

- 2.1. Having regard to current scientific and technical knowledge, Member States shall evaluate the information referred to in point 1.2, and in particular:
- (a) identify the risks arising, assess their significance and the expected exposure, and make a judgement as to the likely risks to humans, animals or the environment;
 - (b) assess efficacy in terms of effectiveness (including possible development of resistance or cross-resistance of the target organism(s)) and adverse effects (including phytotoxicity/pathogenicity) on crops (including treated crops, succeeding crops and adjacent crops) of the plant protection product for each use for which authorisation is sought.
- 2.2. Member States shall evaluate the quality and the methodology of tests, especially where there are no standardised test methods, as well as the following characteristics of the methods described, when available:
- relevance; representativeness; sensitivity; specificity; reproducibility.
- 2.3. In interpreting the results of evaluations, Member States shall take into consideration and report possible elements of uncertainty in the information obtained during the evaluation, in order to ensure that the chances of failing to detect adverse effects or of underestimating their importance are reduced to a minimum. The decision-making process shall be examined to identify critical decision points or items of data for which uncertainties could lead to a false classification of risk.
- 2.4. In accordance with Article 29 of Regulation (EC) No 1107/2009, Member States shall ensure that evaluations carried out have regard to the proposed practical conditions of use and, in particular, to the purpose of use, the application dose, the application method, frequency and timing of applications, and the nature and composition of the plant protection product.
- In accordance with the requirements for proper use as set out in Article 55 of Regulation (EC) No 1107/2009, Member States shall take into account the provisions of Directive 2009/128/EC of the European Parliament and of the Council ^(*) and, in particular, the principles of integrated pest management.
- 2.5. In the evaluation, Member States shall consider the agricultural, plant health or environmental (including climatic) conditions in the areas of use.

(*) 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 pesticides (OJ L 309, 24.11.2009, p. 71).

- 2.6. Where specific principles in Section 1 of Part A or Section 1 of Part B (as applicable) provide for the use of calculation models in the evaluation of a plant protection product, those models shall:
- (a) make a best possible estimation in an appropriate way of all relevant processes involved taking into account realistic parameters and assumptions;
 - (b) be submitted to an evaluation as referred to in point 2.3;
 - (c) be reliably validated with measurements carried out under circumstances relevant for the use of the model;
 - (d) be relevant to the conditions in the area of use;
 - (e) in cases the models have not been validated, be supported with details indicating how the model calculates estimates provided, and explanations of all the inputs to the model and details of how they have been derived.
- 2.7. Where metabolites are referred to in the specific principles, only those that are relevant for the proposed criterion shall be taken into consideration. For Part A this concerns also degradation or reaction products. For Part B this concerns what is defined as “metabolites of concern”.
3. **DECISION-MAKING, GENERAL PRINCIPLES**
- 3.1. Where appropriate, Member States shall impose conditions or restrictions on the authorisations they grant. The nature and severity of these conditions or restrictions shall be selected on the basis of, and be appropriate to, the nature and extent of the expected advantages and the risks likely to arise.
- 3.2. Member States shall ensure that decisions taken to grant authorisations take account of the agricultural, plant health or environmental (including climatic) conditions in the areas of envisaged use. Such considerations may result in specific conditions and restrictions on use, and in authorisation being granted for some but not other areas within the Member State in question.
- 3.3. Member States shall ensure that the authorised application rates and number of applications, are the minimum necessary to achieve the desired effect even where higher rates would not result in unacceptable risks to human or animal health or to the environment. The authorised rates shall be differentiated in accordance with, and be appropriate to, the agricultural, plant health or environmental (including climatic) conditions in the various areas for which an authorisation is granted. However, the application rates and the number of applications may not give rise to undesirable effects such as the development of resistance in the target organism.
- 3.4. Member States shall ensure that decisions taken to grant authorisations consider integrated pest management as set out in Directive 2009/128/EC. In particular, Member States shall ensure that a warning phrase is indicated on the label in case negative effects are expected on beneficial organisms that are deliberately released as part of integrated pest management strategies.
- 3.5. Since the evaluation is to be based on data concerning a limited number of representative non-target species, Member States shall ensure that use of plant protection products does not have any long-term repercussions for the abundance and diversity of non-target species.
- 3.6. Before issuing an authorisation, Member States shall ensure that the label of the plant protection product:
- (a) fulfils the requirements setting out in Regulation (EU) No 547/2011;
 - (b) also contains the information on protection of operators, workers, bystanders and residents required by EU legislation on worker protection;
 - (c) specifies in particular the conditions or restrictions under which the plant protection product may or may not be used as referred to in points 3.1 to 3.5 of this general introduction.

The authorisation shall mention the particulars indicated in Regulation (EC) No 1272/2008 of the European Parliament and of the Council (*).

- 3.7. Before issuing authorisations, Member States shall:
- (a) ensure that the proposed packaging is in accordance with the provisions of Regulation (EC) No 1272/2008;
 - (b) ensure that the following procedures are in accordance with the relevant regulatory provisions:
 - the procedures for destruction of the plant protection product,
 - the procedures for neutralisation of any adverse effects of the plant protection product if it is accidentally dispersed, and
 - the procedures for the decontamination and destruction of the packaging.
- 3.8. No authorisation shall be granted unless all the requirements referred to in Section 2 of Part A or Section 2 of Part B (as applicable) are satisfied. However:
- (a) when one or more of the specific decision-making requirements referred to in points 2.1, 2.2, 2.3 or 2.7 of Part A, or point 2.3 of Part B, respectively, are not satisfied, authorisations shall be granted only where the advantages of the use of the plant protection product under the proposed conditions of use outweigh the possible adverse effects of its use. Any restrictions on use of the plant protection product relating to non-compliance with some of the aforementioned requirements must be mentioned on the label, and non-compliance with the requirements referred to in point 2.7 of Part A (if Part A applies) shall not compromise proper use of the plant protection product. These advantages can be in terms of:
 - advantages for and compatibility with integrated control measures or organic farming,
 - facilitating strategies to minimise the risk of development of resistance,
 - the need for a greater diversity of types of active substances or biochemical modes of action, e.g. for use in strategies to avoid accelerated breakdown in the soil,
 - reduced risk for operators and consumers,
 - reduced contamination of the environment and reduced impact on non-target species.
 - (b) where the criteria referred to in point 2.6 of Part A or point 2.4 of Part B, respectively, are not fully satisfied because of limitations in current analytical science and technology, authorisation shall be granted for a limited period if the methods submitted prove adequate for the purposes intended. In this case, the applicant shall be required to develop and submit analytical methods that are in accordance with those criteria by a specific deadline. The authorisation shall be reviewed on expiry of that deadline;
 - (c) where the reproducibility of the submitted analytical methods referred to in point 2.6 of Part A or point 2.4 of Part B, respectively has only been verified in two laboratories, an authorisation shall be granted for 1 year to permit the applicant to demonstrate the reproducibility of those methods in accordance with agreed criteria in at least a third laboratory.
- 3.9. Where an authorisation has been granted in accordance with the requirements provided for in this Annex, Member States may, by virtue of Article 44 of Regulation (EC) No 1107/2009:
- (a) define, where possible, preferably in close cooperation with the applicant, measures to improve the efficacy of the plant protection product; and/or
 - (b) define, where possible, in close cooperation with the applicant, measures to reduce further the exposure that could occur during and after use of the plant protection product.

(*) Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (OJ L 353, 31.12.2008, p. 1).

Member States shall inform applicants of any measures identified under (a) or (b) and shall require applicants to provide any supplementary data and information necessary to demonstrate efficacy or acceptability of risks arising under the changed conditions.

- 3.10. Member States shall ensure, as far as it is practically possible, that for all active substances contained in plant protection products that are considered for an authorisation, the applicant has taken into account all available relevant knowledge and information in scientific literature at the time of submission of the dossier on the plant protection product.

PART A

Uniform principles for evaluation and authorisation of chemical plant protection products

1. EVALUATION

Member States shall, for the evaluation of the data and information submitted in support of applications, and without prejudice to the general principles of Section 2 of the general introduction, implement the following principles.

1.1. Efficacy

- 1.1.1. Where the proposed use concerns the control of or protection against an organism, Member States shall evaluate the possibility that this organism could be harmful under the agricultural, plant health and environmental (including climatic) conditions in the area of the proposed use.

- 1.1.2. Where the proposed use concerns an effect other than the control of or protection against an organism, Member States shall evaluate whether significant damage, loss or inconvenience could occur under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use if the plant protection product were not used.

- 1.1.3. Member States shall evaluate the efficacy data on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013 having regard to the degree of control or the extent of the effect desired and having regard to the relevant experimental conditions such as:

- the choice of the crop or cultivar,
- the agricultural and environmental (including climatic) conditions,
- the presence and density of the harmful organism,
- the development stage of crop and organism,
- the amount of the plant protection product used,
- if required on the label, the amount of adjuvant added,
- the frequency and timing of the applications,
- the type of application equipment.

- 1.1.4. Member States shall evaluate the performance of the plant protection product in a range of agricultural, plant health and environmental (including climatic) conditions likely to be encountered in practice in the area of proposed use and in particular:

- (i) the level, consistency and duration of the effect sought in relation to the dose in comparison with a suitable reference product or products and an untreated control;
- (ii) where relevant, effect on yield or reduction of loss in storage, in terms of quantity and/or quality, in comparison with a suitable reference product or products and an untreated control.

Where no suitable reference product exists, Member States shall evaluate the performance of the plant protection product to determine whether there is a consistent and defined benefit under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use.

- 1.1.5. Where the product label includes requirements for use of the plant protection product with other plant protection products and/or with adjuvants as a tank mix, Member States shall make the evaluations referred to in points 1.1.1 to 1.1.4 in relation to the information supplied for the tank mix.

Where the product label includes recommendations for use of the plant protection product with other plant protection products and/or with adjuvants as a tank mix, Member States shall evaluate the appropriateness of the mix and of its conditions of use.

1.2. **Absence of unacceptable effects on plants or plant products**

- 1.2.1. Member States shall evaluate the degree of adverse effects on the treated crop after use of the plant protection product in accordance with the proposed conditions of use in comparison, where relevant, with a suitable reference product or products, where they exist, and/or an untreated control.

(a) This evaluation shall take into consideration the following information:

- (i) the efficacy data provided for in the Annex to Regulation (EU) No 284/2013;
- (ii) other relevant information on the plant protection product such as nature of the preparation, dose, method of application, number and timing of applications;
- (iii) all relevant information on the active substance as provided for in of the Annex to Regulation (EU) No 283/2013, including mode of action, vapour pressure, volatility and water solubility.

(b) This evaluation shall include:

- (i) the nature, frequency, level and duration of observed phytotoxic effects and the agricultural, plant health and environmental (including climatic) conditions that affect them;
- (ii) the differences between main cultivars with regard to their sensitivity to phytotoxic effects;
- (iii) the part of the treated crop or plant products where phytotoxic effects are observed;
- (iv) the adverse impact on the yield of the treated crop or plant products in terms of quantity and/or quality;
- (v) the adverse impact on treated plants or plant products to be used for propagation, in terms of viability, germination, sprouting, rooting and establishment;
- (vi) where volatile products are concerned, the adverse impact on adjacent crops.

- 1.2.2. Where the available data indicate that the active substance or significant metabolites, degradation and reaction products persist in soils and/or in or on plant substances in significant quantities after use of the plant protection product in accordance with the proposed conditions of use, Member States shall evaluate the degree of adverse effects on subsequent crops. This evaluation shall be carried out as specified in point 1.2.1.

- 1.2.3. Where the product label includes requirements for use of the plant protection product with other plant protection products or with adjuvants as a tank mix, the evaluation as specified in point 1.1.1 shall be carried out in relation to the information supplied for the tank mix.

1.3. **Impact on vertebrates to be controlled**

Where the proposed use of the plant protection product aims to have an effect on vertebrates, Member States shall evaluate the mechanism by which this effect is obtained and the observed effects on the behaviour and health of the target animals; when the intended effect is to kill the target animal they shall evaluate the time necessary to obtain the death of the animal and the conditions under which death occurs.

This evaluation shall take into consideration the following information:

- (i) all relevant information as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof, including the toxicological and metabolism studies;

- (ii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013, including toxicological studies and efficacy data.

1.4. Impact on human or animal health

1.4.1. Impact on human or animal health arising from the plant protection product

1.4.1.1. Member States shall evaluate operator exposure to the active substance and/or to toxicologically relevant compounds in the plant protection product likely to occur under the proposed conditions of use (including in particular dose, application method and climatic conditions) using by preference realistic data on exposure and, if such data are not available, a suitable, validated calculation model.

(a) This evaluation shall take into consideration the following information:

- (i) the toxicological and metabolism studies as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof including the acceptable operator exposure level (AOEL). The acceptable operator exposure level is the maximum amount of active substance to which the operator may be exposed without any adverse health effects. The AOEL is expressed as milligrams of the chemical per kilogram body weight of the operator. The AOEL is based on the highest level at which no adverse effect is observed in tests in the most sensitive relevant animal species or, if appropriate data are available, in humans;
- (ii) other relevant information on the active substances such as physical and chemical properties;
- (iii) the toxicological studies provided for in the Annex to Regulation (EU) No 284/2013, including where appropriate dermal absorption studies;
- (iv) other relevant information as provided for in the Annex to Regulation (EU) No 284/2013 such as:
 - composition of the preparation,
 - nature of the preparation,
 - size, design and type of packaging,
 - field of use and nature of crop or target,
 - method of application including handling, loading and mixing of product,
 - exposure reduction measures recommended,
 - protective clothing recommendations,
 - maximum application rate,
 - minimum spray application volume stated on the label,
 - number and timing of applications.

(b) This evaluation shall be made for each type of application method and application equipment proposed for use of the plant protection product as well as for the different types and sizes of containers to be used, taking account of mixing, loading operations, application of the plant protection product and cleaning and routine maintenance of application equipment.

1.4.1.2. Member States shall examine information relating to the nature and characteristics of the packaging proposed with particular reference to the following aspects:

- the type of packaging,
- its dimensions and capacity,
- the size of the opening,
- the type of closure,
- its strength, leakproofness and resistance to normal transport and handling,
- its resistance to and compatibility with the contents.

1.4.1.3. Member States shall examine the nature and characteristics of the protective clothing and equipment proposed with particular reference to the following aspects:

- obtainability and suitability,
- ease of wearing taking into account physical stress and climatic conditions.

1.4.1.4. Member States shall evaluate the possibility of exposure of other humans (bystanders or workers exposed after the application of the plant protection product) or animals to the active substance and/or to other toxicologically relevant compounds in the plant protection product under the proposed conditions of use.

This evaluation shall take into consideration the following information:

- (i) the toxicological and metabolism studies on the active substance as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof, including the acceptable operator exposure level;
- (ii) the toxicological studies provided for in the Annex to Regulation (EU) No 284/2013, including where appropriate dermal absorption studies;
- (iii) other relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013 such as:
 - re-entry periods, necessary waiting periods or other precautions to protect humans and animals,
 - method of application, in particular spraying,
 - maximum application rate,
 - maximum spray application volume,
 - composition of the preparation,
 - excess remaining on plants and plant products after treatment,
 - further activities whereby workers are exposed.

1.4.2. Impact on human and animal health arising from residues

1.4.2.1. Member States shall evaluate the specific information on toxicology as provided for in the Annex to Regulation (EU) No 283/2013 and in particular:

- the determination of an acceptable daily intake (ADI),
- the identification of metabolites, degradation and reaction products in treated plants or plant products,
- behaviour of residues of the active substance and its metabolites from the time of application until harvest, or in the case of postharvest uses, until outloading of stored plant products.

1.4.2.2. Prior to evaluating the residue levels in the reported trials or in products of animal origin Member States shall examine the following information:

- data on the proposed good agricultural practice, including data on application as provided for in the Annex to Regulation (EU) No 284/2013 and proposed pre-harvest intervals for envisaged uses, or withholding periods or storage periods, in the case of post-harvest uses,
- nature of the preparation,
- analytical methods and the residue definition.

1.4.2.3. On the basis of suitable statistical models Member States shall evaluate the residue levels observed in the reported trials. This evaluation shall be made for each proposed use and shall take into consideration:

- (i) the proposed conditions of use of the plant protection product;
- (ii) the specific information on residues in or on treated plants, plant products, food and feed as provided for in the Annex to Regulation (EU) No 284/2013 and the distribution of residues between edible and non-edible parts;

- (iii) the specific information on residues in or on treated plants, plant products, food and feed as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;
- (iv) the realistic possibilities of extrapolating data from one crop to another.

1.4.2.4. Member States shall evaluate the residue levels observed in products of animal origin, taking into consideration the information provided for in Section 8 of Part A of the Annex to Regulation (EU) No 284/2013 and residues resulting from other uses.

1.4.2.5. Member States shall estimate the potential exposure of consumers through diet and, where relevant, other ways of exposure, using a suitable calculation model. This evaluation shall take account, where relevant, of other sources of information such as other authorised uses of plant protection products containing the same active substance or which give rise to the same residues.

1.4.2.6. Member States shall, where relevant, estimate the exposure of animals, taking into account the residue levels observed in treated plants or plant products intended to be fed to animals.

1.5. Influence on the environment

1.5.1. Fate and distribution in the environment

In the evaluation of the fate and distribution of the plant protection product in the environment, Member States shall have regard to all aspects of the environment, including biota, and in particular to the following:

1.5.1.1. Member States shall evaluate the possibility of the plant protection product reaching the soil under the proposed conditions of use; if this possibility exists they shall estimate the rate and the route of degradation in the soil, the mobility in the soil and the change in the total concentration (extractable and non-extractable ⁽³⁾) of the active substance and of relevant metabolites, degradation and reaction products that could be expected in the soil in the area of envisaged use after use of the plant protection product in accordance with the proposed conditions of use.

This evaluation shall take into consideration the following information:

- (i) the specific information on fate and behaviour in soil as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;
- (ii) other relevant information on the active substance such as:
 - molecular weight,
 - solubility in water,
 - octanol/water partition coefficient,
 - vapour pressure,
 - volatilisation rate,
 - dissociation constant,
 - photodegradation rate and identity of breakdown products,
 - hydrolysis rate in relation to pH and identity of breakdown products.
- (iii) all information on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013, including the information on distribution and dissipation in soil;
- (iv) where relevant, other authorised uses of plant protection products in the area of proposed use containing the same active substance or which give rise to the same residues.

⁽³⁾ Non-extractable residues (sometimes referred to as 'bound' or 'non-extracted' residues) in plants and soils are defined as chemical species originating from pesticides used in accordance with good agricultural practice that cannot be extracted by methods which do not significantly change the chemical nature of these residues. These non-extractable residues are not considered to include fragments through metabolic pathways leading to natural products.

- 1.5.1.2. Member States shall evaluate the possibility of the plant protection product reaching the groundwater under the proposed conditions of use; if this possibility exists, they shall estimate, using a suitable calculation model validated at EU level, the concentration of the active substance and of relevant metabolites, degradation and reaction products that could be expected in the groundwater in the area of envisaged use after use of the plant protection product in accordance with the proposed conditions of use.

As long as there is no validated EU calculation model, Member States shall base their evaluation especially on the results of mobility and persistence in soil studies as provided for in the Annex to Regulation (EU) No 283/2013 and to Regulation (EU) No 284/2013.

This evaluation shall also take into consideration the following information:

- (i) the specific information on fate and behaviour in soil and water as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;
- (ii) other relevant information on the active substance such as:
 - molecular weight,
 - solubility in water,
 - octanol/water partition coefficient,
 - vapour pressure,
 - volatilisation rate,
 - hydrolysis rate in relation to pH and identity of breakdown products,
 - dissociation constant;
- (iii) all information on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013, including the information on distribution and dissipation in soil and water;
- (iv) where relevant, other authorised uses of plant protection products in the area of envisaged use containing the same active substance or which give rise to the same residues;
- (v) where relevant, data on dissipation including transformation and sorption in the saturated zone;
- (vi) where relevant, data on the procedures for drinking water abstraction and treatment in the area of envisaged use;
- (vii) where relevant, monitoring data on the presence or absence of the active substance and relevant metabolites, degradation or reaction products in groundwater as a result of previous use of plant protection products containing the same active substance or which give rise to the same residues; such monitoring data shall be interpreted in a consistent scientific way.

- 1.5.1.3. Member States shall evaluate the possibility of the plant protection product reaching surface water under the proposed conditions of use; if this possibility exists they shall estimate, using a suitable calculation model validated at EU level, the short-term and long-term predicted concentration of the active substance and of metabolites, degradation and reaction products that could be expected in the surface water in the area of envisaged use after use of the plant protection product in accordance with the proposed conditions of use.

If there is no validated EU calculation model, Member States shall base their evaluation especially on the results of mobility and persistence in soil studies and the information on run-off and drift as provided for in the Annex to Regulation (EU) No 283/2013 and to Regulation (EU) No 284/2013.

This evaluation shall also take into consideration the following information:

- (i) the specific information on fate and behaviour in soil and water as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;

- (ii) other relevant information on the active substance such as:
 - molecular weight,
 - solubility in water,
 - octanol/water partition coefficient,
 - vapour pressure,
 - volatilisation rate,
 - hydrolysis rate in relation to pH and identity of breakdown products,
 - dissociation constant;
- (iii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013, including the information on distribution and dissipation in soil and water;
- (iv) possible routes of exposure:
 - drift,
 - run-off,
 - overspray,
 - discharge via drains,
 - leaching,
 - deposit from the atmosphere;
- (v) where relevant, other authorised uses of plant protection products in the area of envisaged use containing the same active substance or which give rise to the same residues;
- (vi) where relevant, data on the procedures for drinking water abstraction and treatment in the area of envisaged use.

1.5.1.4. Member States shall evaluate the possibility of the plant protection product being dissipated in the air under the proposed conditions of use; if this possibility exists they shall make the best possible estimation, using where appropriate a suitable, validated calculation model, of the concentration of the active substance and of relevant metabolites, degradation and reaction products that could be expected in the air after use of the plant protection product in accordance with the proposed conditions of use.

This evaluation shall take into consideration the following information:

- (i) the specific information on fate and behaviour in soil, water and air as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;
- (ii) other relevant information on the active substance such as:
 - vapour pressure,
 - solubility in water,
 - hydrolysis rate in relation to pH and identity of breakdown products,
 - photochemical degradation in water and air and identity of breakdown products,
 - octanol/water partition coefficient;
- (iii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013, including the information on distribution and dissipation in air.

1.5.1.5. Member States shall evaluate the procedures for destruction or decontamination of the plant protection product and its packaging.

1.5.2. Impact on non-target species

When calculating toxicity/exposure ratios Member States shall take into consideration toxicity to the most sensitive relevant organism used in the tests.

1.5.2.1. Member States shall evaluate the possibility of exposure of birds and other terrestrial vertebrates to the plant protection product under the proposed conditions of use; if this possibility exists they shall evaluate the extent of the short-term and long-term risk to be expected for these organisms, including their reproduction, after use of the plant protection product in accordance with the proposed conditions of use.

(a) This evaluation shall take into consideration the following information:

- (i) the specific information relating to toxicological studies on mammals and to the effects on birds and other non-target terrestrial vertebrates, including effects on reproduction, and other relevant information concerning the active substance as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;
- (ii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013, including the information on effects on birds and other non-target terrestrial vertebrates;
- (iii) where relevant, other authorised uses of plant protection products in the area of envisaged use containing the same active substance or which give rise to the same residues.

(b) This evaluation shall include:

- (i) the fate and distribution, including persistence and bioconcentration, of the active substance and of relevant metabolites, breakdown and reaction products in the various parts of the environment after application of the plant protection product;
- (ii) the estimated exposure of the species likely to be exposed at the time of application or during the period that residues are present, taking into account all relevant routes of exposure such as ingestion of the formulated product or treated food, predation on invertebrates, feeding on vertebrate prey, contact by overspraying or with treated vegetation;
- (iii) a calculation of the acute, short-term and, where necessary, long-term toxicity/exposure ratio. The toxicity/exposure ratios are defined as respectively the quotient of LD_{50} , LC_{50} or non-observable effects of concentration (NOEC) expressed on an active substance basis and the estimated exposure expressed in mg/kg body weight.

1.5.2.2. Member States shall evaluate the possibility of exposure of aquatic organisms to the plant protection product under the proposed conditions of use; if this possibility exists they shall evaluate the degree of short-term and long-term risk to be expected for aquatic organisms after use of the plant protection product in accordance with the proposed conditions of use.

(a) This evaluation shall take into consideration the following information:

- (i) the specific information relating to the effects on aquatic organisms as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;
- (ii) other relevant information on the active substance such as:
 - solubility in water,
 - octanol/water partition coefficient,
 - vapour pressure,
 - volatilisation rate,
 - KOC,
 - biodegradation in aquatic systems and in particular the ready biodegradability,
 - photodegradation rate and identity of breakdown products,
 - hydrolysis rate in relation to pH and identity of breakdown products.
- (iii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013 and in particular the effects on aquatic organisms;

- (iv) where relevant, other authorised uses of plant protection products in the area of envisaged use, containing the same active substance or which give rise to the same residues.

(b) This evaluation shall include:

- (i) the fate and distribution of residues of the active substance and of relevant metabolites, breakdown and reaction products in water, sediment or fish;
- (ii) a calculation of the acute toxicity/exposure ratio for fish and Daphnia. This ratio is defined as the quotient of respectively acute LC₅₀ or EC₅₀ and the predicted short-term environmental concentration;
- (iii) a calculation of the algal growth inhibition/exposure ratio for algae. This ratio is defined as the quotient of the EC₅₀ and the predicted short-term environmental concentration;
- (iv) a calculation of the long-term toxicity/exposure ratio for fish and Daphnia. The long-term toxicity/exposure ratio is defined as the quotient of the NOEC and the predicted long-term environmental concentration;
- (v) where relevant, the bioconcentration in fish and possible exposure of predators of fish, including humans;
- (vi) if the plant protection product is to be applied directly to surface water, the effect on the change of surface water quality, such as pH or dissolved oxygen content.

1.5.2.3. Member States shall evaluate the possibility of exposure of honeybees to the plant protection product under the proposed conditions of use; if this possibility exists they shall evaluate the short-term and long-term risk to be expected for honeybees after use of the plant protection product in accordance with the proposed conditions of use.

(a) This evaluation shall take into consideration the following information:

- (i) the specific information on toxicity to honeybees as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;
- (ii) other relevant information on the active substance such as:
 - solubility in water,
 - octanol/water partition coefficient,
 - vapour pressure,
 - photodegradation rate and identity of breakdown products,
 - mode of action (e. g. insect growth regulating activity);
- (iii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013, including the toxicity to honeybees;
- (iv) where relevant, other authorised uses of plant protection products in the area of envisaged use, containing the same active substance or which give rise to the same residues.

(b) This evaluation shall include:

- (i) the ratio between the maximum application rate expressed in grams of active substance per hectare and the contact and oral LD₅₀ expressed in µg of active substance per bee (hazard quotients) and where necessary the persistence of residues on or, where relevant, in the treated plants;
- (ii) where relevant, the effects on honeybee larvae, honeybee behaviour, colony survival and development after use of the plant protection product in accordance with the proposed conditions of use.

1.5.2.4. Member States shall evaluate the possibility of exposure of beneficial arthropods other than honeybees to the plant protection product under the proposed conditions of use; if this possibility exists they shall assess the lethal and sublethal effects on these organisms to be expected and the reduction in their activity after use of the plant protection product in accordance with the proposed conditions of use.

This evaluation shall take into consideration the following information:

- (i) the specific information on toxicity to honeybees and other beneficial arthropods as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;
- (ii) other relevant information on the active substance such as:
 - solubility in water,
 - octanol/water partition coefficient,
 - vapour pressure,
 - photodegradation rate and identity of breakdown products,
 - mode of action (e. g. insect growth regulating activity);
- (iii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013 such as:
 - effects on beneficial arthropods other than bees,
 - toxicity to honeybees,
 - available data from biological primary screening,
 - maximum application rate,
 - maximum number and timetable of applications;
- (iv) where relevant, other authorised uses of plant protection products in the area of envisaged use, containing the same active substance or which give rise to the same residues.

1.5.2.5. Member States shall evaluate the possibility of exposure of earthworms and other non-target soil macro-organisms to the plant protection product under the proposed conditions of use; if this possibility exists they shall evaluate the degree of short-term and long-term risk to be expected to these organisms after use of the plant protection product in accordance with the proposed conditions of use.

(a) This evaluation shall take into consideration the following information:

- (i) the specific information relating to the toxicity of the active substance to earthworms and to other non-target soil macro-organisms as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;
- (ii) other relevant information on the active substance such as:
 - solubility in water,
 - octanol/water partition coefficient,
 - K_d for adsorption,
 - vapour pressure,
 - hydrolysis rate in relation to pH and identity of breakdown products,
 - photodegradation rate and identity of breakdown products,
 - DT_{50} and DT_{90} for degradation in the soil.
- (iii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013, including the effects on earthworms and other non-target soil macro-organisms;
- (iv) where relevant, other authorised uses of plant protection products in the area of envisaged use, containing the same active substance or which give rise to the same residues.

(b) This evaluation shall include:

- (i) the lethal and sublethal effects;
- (ii) the predicted initial and long-term environmental concentration;

(iii) a calculation of the acute toxicity/exposure ratio (defined as the quotient of LC_{50} and predicted initial environmental concentration) and of the long-term toxicity/exposure ratio (defined as the quotient of the NOEC and predicted long-term environmental concentration);

(iv) where relevant, the bioconcentration and persistence of residues in earthworms.

1.5.2.6. Member States shall, where the evaluation carried out under point 1.5.1.1 does not exclude the possibility of the plant protection product reaching the soil under the proposed conditions of use, evaluate the impact on microbial activity such as the impact on nitrogen and carbon mineralisation processes in the soil after use of the plant protection product in accordance with the proposed conditions of use.

This evaluation shall take into consideration the following information:

- (i) all relevant information on the active substance, including the specific information relating to the effects of non-target soil micro-organisms as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;
- (ii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013, including the effects on non-target soil micro-organisms;
- (iii) where relevant, other authorised uses of plant protection products in the area of proposed use, containing the same active substance or which give rise to the same residues;
- (iv) all available information from biological primary screening.

1.6. Analytical methods

Member States shall evaluate the analytical methods proposed for post-registration control and monitoring purposes, to determine:

1.6.1. for formulation analysis:

the nature and quantity of the active substance(s) in the plant protection product and, where appropriate, any toxicologically, ecotoxicologically or environmentally significant impurities and co-formulants.

This evaluation shall take into consideration the following information:

- (i) the data on analytical methods as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;
- (ii) the data on analytical methods as provided for in the Annex to Regulation (EU) No 284/2013 and in particular:
 - the specificity and linearity of the proposed methods,
 - the importance of interferences,
 - the precision of the proposed methods (intralaboratory repeatability and interlaboratory reproducibility);
- (iii) the limit of detection and determination of the proposed methods for impurities.

1.6.2. for residue analysis:

the residues of the active substance, metabolites, breakdown or reaction products resulting from authorised uses of the plant protection product and which are of toxicological, ecotoxicological or environmental significance.

This evaluation shall take into consideration the following information:

- (i) the data on analytical methods as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;

- (ii) the data on analytical methods as provided for in the Annex to Regulation (EU) No 284/2013 and in particular:
 - the specificity of the proposed methods,
 - the precision of the proposed methods (intralaboratory repeatability and interlaboratory reproducibility),
 - the recovery rate of the proposed methods at appropriate concentrations;
- (iii) the limit of detection of the proposed methods;
- (iv) the limit of determination of the proposed methods.

1.7. Physical and chemical properties

1.7.1. Member States shall evaluate the actual active substance content of the plant protection product and its stability during storage.

1.7.2. Member States shall evaluate the physical and chemical properties of the plant protection product and in particular:

- where a suitable FAO (Food and Agriculture Organisation of the United Nations) specification exists, the physical and chemical properties addressed in that specification,
- where no suitable FAO specification exists, all the relevant physical and chemical properties for the formulation as referred to in the 'Manual on development and use of FAO and WHO specifications for pesticides'.

This evaluation shall take into consideration the following information:

- (i) the data on the physical and chemical properties of the active substance as provided for in the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof;
- (ii) the data on the physical and chemical properties of the plant protection product as provided for in the Annex to Regulation (EU) No 284/2013.

1.7.3. Where proposed label claims include requirements or recommendations for use of the plant protection product with other plant protection products or adjuvants as a tank mix, the physical and chemical compatibility of the products in the mixture must be evaluated.

2. DECISION-MAKING

These principles shall apply without prejudice to the general principles referred to in Section 3 of the general introduction.

2.1. Efficacy

2.1.1. Where the proposed uses include recommendations for the control of or protection against organisms which are not considered to be harmful on the basis of experience acquired or scientific evidence under normal agricultural, plant health and environmental (including climatic) conditions in the areas of proposed use or where the other intended effects are not considered to be beneficial under those conditions, no authorisation shall be granted for those uses.

2.1.2. The level, consistency and duration of control or protection or other intended effects must be similar to those resulting from the use of suitable reference products. If no suitable reference product exists, the plant protection product must be shown to give a defined benefit in terms of the level, consistency and duration of control or protection or other intended effects under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use.

2.1.3. Where relevant, yield response when the product is used and reduction of loss in storage must be quantitatively and/or qualitatively similar to those resulting from the use of suitable reference products. If no suitable reference product exists, the plant protection product must be shown to give a consistent and defined quantitative and/or qualitative benefit in terms of yield response and reduction of loss in storage under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use.

2.1.4. Conclusions as to the performance of the preparation must be valid for all areas of the Member State in which it is to be authorised, and must hold for all conditions under which its use is proposed, except where the proposed label specifies that the preparation is intended for use in certain specified circumstances (e.g. light infestations, particular soil types or particular growing conditions).

2.1.5. Where proposed label claims include requirements for use of the preparation with other specified plant protection products or adjuvants as a tank mix, the mixture must achieve the desired effect and comply with the principles referred to in points 2.1.1 to 2.1.4.

Where proposed label claims include recommendations for use of the preparation with specified plant protection products or adjuvants as a tank mix, Member States shall not accept the recommendations unless they are justified.

2.2. **Absence of unacceptable effects on plants or plant products**

2.2.1. There must be no relevant phytotoxic effects on treated plants or plant products except where the proposed label indicates appropriate limitations of use.

2.2.2. There must be no reduction of yield at harvest due to phytotoxic effects below that which could be obtained without the use of the plant protection product, unless this reduction is compensated for by other advantages such as an enhancement of the quality of the treated plants or plant products.

2.2.3. There must be no unacceptable adverse effects on the quality of treated plants or plant products, except in the case of adverse effects on processing where proposed label claims specify that the preparation must not be applied to crops to be used for processing purposes.

2.2.4. There must be no unacceptable adverse effects on treated plants or plant products used for propagation or reproduction, such as effects on viability, germination, sprouting, rooting and establishment, except where proposed label claims specify that the preparation should not be applied to plants or plant products to be used for propagation or reproduction.

2.2.5. There must be no unacceptable impact on succeeding crops, except where proposed label claims specify that particular crops, which would be affected, must not be grown following the treated crop.

2.2.6. There must be no unacceptable impact on adjacent crops, except where proposed label claims specify that the preparation should not be applied when particular sensitive adjacent crops are present.

2.2.7. Where proposed label claims include requirements for use of the preparation with other plant protection products or adjuvants, as a tank mix, the mixture must comply with the principles referred to in points 2.2.1 to 2.2.6.

2.2.8. The proposed instructions for cleaning the application equipment must be both practical and effective so that they can be applied with ease to ensure the removal of residual traces of the plant protection product which could subsequently cause damage.

2.3. **Impact on vertebrates to be controlled**

An authorisation for a plant protection product intended to eliminate vertebrates shall be granted only when:

- death is synchronous with the extinction of consciousness, or
- death occurs immediately, or
- vital functions are reduced gradually without signs of obvious suffering.

For repellent products, the intended effect shall be obtained without unnecessary suffering and pain for the target animals.

2.4. Impact on human or animal health

2.4.1. Impact on human or animal health arising from the plant protection product

- 2.4.1.1. No authorisation shall be granted if the extent of operator exposure in handling and using the plant protection product under the proposed conditions of use, including dose and application method, exceeds the AOEL.

Moreover, the conditions of the authorisation shall be in compliance with the limit value established for the active substance and/or toxicologically relevant compound(s) of the product in accordance with Council Directive 98/24/EC ⁽⁶⁾ and in accordance with Directive 2004/37/EC of the European Parliament and of the Council ⁽⁷⁾.

- 2.4.1.2. Where the proposed conditions of use require use of items of protective clothing and equipment, no authorisation shall be granted unless those items are effective and in accordance with the relevant EU provisions and are readily obtainable by the user and unless it is feasible to use them under the circumstances of use of the plant protection product, taking into account climatic conditions in particular.

- 2.4.1.3. Plant protection products which because of particular properties or if mishandled or misused could lead to a high degree of risk must be subject to particular restrictions such as restrictions on the size of packaging, formulation type, distribution, use or manner of use.

Moreover, those plant protection products may not be authorised for use by non-professional users which are classified as:

- (i) acute toxicity category 1 and 2 for any route of uptake, provided the ATE (acute toxicity estimate) of the product does not exceed 25 mg/kg bw for the oral route of uptake or 0,25 mg/l/4h for the inhalation of dust, mist or fume;
 - (ii) STOT (single exposure), category 1 (oral), provided their classification is due to the presence of classified substances showing significant non-lethal toxic effects at guidance values below 25 mg/kg bw;
 - (iii) STOT (single exposure), category 1 (dermal), provided their classification is due to the presence of classified substances showing significant non-lethal toxic effects at guidance values below 50 mg/kg bw;
 - (iv) STOT (single exposure), category 1 (inhalation of gas/vapour), provided their classification is due to the presence of classified substances showing significant non-lethal toxic effects at guidance values below 0,5 mg/l/4h;
 - (v) STOT (single exposure), category 1 (inhalation of dust/mist/fume), provided their classification is due to the presence of classified substances showing significant non-lethal toxic effects at guidance values below 0,25 mg/l/4h.
- 2.4.1.4. Waiting and re-entry safety periods or other precautions must be such that the exposure of bystanders or workers exposed after the application of the plant protection product does not exceed the AOEL levels established for the active substance or toxicologically relevant compound(s) in the plant protection product nor any limit values established for those compounds in accordance with the EU provisions referred to in point 2.4.1.1.
- 2.4.1.5. Waiting and re-entry safety periods or other precautions must be established in such a way that no adverse impact on animals occurs.
- 2.4.1.6. Waiting and re-entry periods or other precautions to ensure that the AOEL levels and limit values are respected must be realistic; if necessary special precautionary measures must be prescribed.

⁽⁶⁾ Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC) (OJ L 131, 5.5.1998, p. 11).

⁽⁷⁾ Directive 2004/37/EC of the European Parliament and of the Council of 29 April 2004 on the protection of workers from the risks related to exposure to carcinogens or mutagens at work (Sixth individual Directive within the meaning of Article 16(1) of Council Directive 89/391/EEC) (OJ L 158, 30.4.2004, p. 50).

2.4.2. Impact on human or animal health arising from residues

- 2.4.2.1. Authorisations must ensure that residues occurring reflect the minimum quantities of the plant protection product necessary to achieve adequate control corresponding to good agricultural practice, applied in such a manner (including pre-harvest intervals or withholding periods or storage periods) that the residues at harvest, slaughter or after storage, as appropriate, are reduced to a minimum.
- 2.4.2.2. Where the new circumstances under which the plant protection product is to be used do not correspond to those under which a MRL (maximum residue limit) was established previously, Member States shall not grant an authorisation for the plant protection product unless the applicant can provide evidence that its recommended use shall not exceed the MRL established under Regulation (EC) No 396/2005 of the European Parliament and of the Council ⁽⁸⁾.
- 2.4.2.3. Where a MRL exists Member States shall not grant an authorisation for the plant protection product unless the applicant can provide evidence that its recommended use shall not exceed that MRL, or unless a new MRL has been established under Regulation (EC) No 396/2005.
- 2.4.2.4. In the cases referred to in points 2.4.2.2, each application for an authorisation must be accompanied by a risk assessment taking into account worst-case potential exposure of consumers in the Member State concerned on the basis of good agricultural practice.

Taking into account all registered uses, the proposed use shall not be authorised if the best possible estimate of dietary exposure exceeds the ADI.

- 2.4.2.5. Where the nature of residues is affected during processing, a separate risk assessment may need to be carried out under the conditions provided for in point 2.4.2.4.
- 2.4.2.6. Where the treated plants or plant products are intended to be fed to animals, residues occurring shall not have an adverse effect on animal health.

2.5. Influence on the environment

2.5.1. Fate and distribution in the environment

- 2.5.1.1. No authorisation shall be granted if the active substance and, where they are of significance from the toxicological, ecotoxicological or environmental point of view, metabolites and breakdown or reaction products, after use of the plant protection product under the proposed conditions of use:

- during tests in the field, persist in soil for more than 1 year (i.e. $DT_{90} > 1$ year and $DT_{50} > 3$ months), or
- during laboratory tests, form non-extractable residues in amounts exceeding 70 % of the initial dose after 100 days with a mineralisation rate of less than 5 % in 100 days,

unless it is scientifically demonstrated that under field conditions there is no accumulation in soil at such levels that unacceptable residues in succeeding crops occur and/or that unacceptable phytotoxic effects on succeeding crops occur and/or that there is an unacceptable impact on the environment, in accordance with the relevant requirements provided for in points 2.5.1.2, 2.5.1.3, 2.5.1.4 and 2.5.2.

- 2.5.1.2. No authorisation shall be granted if the concentration of the active substance or of relevant metabolites, degradation or reaction products in groundwater, may be expected to exceed, as a result of use of the plant protection product under the proposed conditions of use, the lower of the following limit values:

- (i) the maximum permissible concentration laid down by Council Directive 98/83/EC ⁽⁹⁾; or

⁽⁸⁾ Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC (OJ L 70, 16.3.2005, p. 1).

⁽⁹⁾ Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption (OJ L 330, 5.12.1998, p. 32).

- (ii) the maximum concentration laid down when approving the active substance in accordance with Regulation (EC) No 1107/2009, on the basis of appropriate data, in particular toxicological data, or, where that concentration has not been laid down, the concentration corresponding to one tenth of the ADI laid down when the active substance was approved in accordance with Regulation (EC) No 1107/2009,

unless it is scientifically demonstrated that under relevant field conditions the lower concentration is not exceeded.

2.5.1.3. No authorisation shall be granted if the concentration of the active substance or of relevant metabolites, breakdown or reaction products to be expected after use of the plant protection product under the proposed conditions of use in surface water:

- exceeds, where the surface water in or from the area of envisaged use is intended for the abstraction of drinking water, concentrations above which compliance with drinking water quality established in accordance with Directive 2000/60/EC of the European Parliament and of the Council ⁽¹⁰⁾ is compromised, or
- has an impact deemed unacceptable on non-target species, including animals, in accordance with the relevant requirements provided for in point 2.5.2.

The proposed instructions for use of the plant protection product, including procedures for cleaning application equipment, must be such that the likelihood of accidental contamination of surface water is reduced to a minimum.

2.5.1.4. No authorisation shall be granted if the airborne concentration of the active substance under the proposed conditions of use is such that either the AOEL or the limit values for operators, bystanders or workers as referred to in point 2.4.1 are exceeded.

2.5.2. Impact on non-target species

2.5.2.1. Where there is a possibility of birds and other non-target terrestrial vertebrates being exposed, no authorisation shall be granted if:

- the acute and short-term toxicity/exposure ratio for birds and other non-target terrestrial vertebrates is less than 10 on the basis of LD₅₀ or the long-term toxicity/exposure ratio is less than 5, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact occurs after use of the plant protection product in accordance with the proposed conditions of use,
- the bioconcentration factor (BCF, related to fat tissue) is greater than 1, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable effects occur — directly or indirectly — after use of the plant protection product in accordance with the proposed conditions of use.

2.5.2.2. Where there is a possibility of aquatic organisms being exposed, no authorisation shall be granted if:

- the toxicity/exposure ratio for fish and Daphnia is less than 100 for acute exposure and less than 10 for long-term exposure, or
- the algal growth inhibition/exposure ratio is less than 10, or
- the maximum bioconcentration factor (BCF) is greater than 1 000 for plant protection products containing active substances which are readily biodegradable or greater than 100 for those which are not readily biodegradable,

⁽¹⁰⁾ Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy (OJ L 327, 22.12.2000, p. 1).

unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact on the viability of exposed species (predators) occurs — directly or indirectly — after use of the plant protection product in accordance with the proposed conditions of use.

- 2.5.2.3. Where there is a possibility of honeybees being exposed, no authorisation shall be granted if the hazard quotients for oral or contact exposure of honeybees are greater than 50, unless it is clearly established through an appropriate risk assessment that under field conditions there are no unacceptable effects on honeybee larvae, honeybee behaviour, or colony survival and development after use of the plant protection product in accordance with the proposed conditions of use.
- 2.5.2.4. Where there is a possibility of beneficial arthropods other than honeybees being exposed, no authorisation shall be granted if more than 30 % of the test organisms are affected in lethal or sublethal laboratory tests conducted at the maximum proposed application rate, unless it is clearly established through an appropriate risk assessment that under field conditions there is no unacceptable impact on those organisms after use of the plant protection product in accordance with the proposed conditions of use. Any claims for selectivity and proposals for use in integrated pest management systems shall be substantiated by appropriate data.
- 2.5.2.5. Where there is a possibility of earthworms being exposed, no authorisation shall be granted if the acute toxicity/exposure ratio for earthworms is less than 10 or the long-term toxicity/exposure ratio is less than 5, unless it is clearly established through an appropriate risk assessment that under field conditions earthworm populations are not at risk after use of the plant protection product in accordance with the proposed conditions of use.
- 2.5.2.6. Where there is a possibility of non-target soil micro-organisms being exposed, no authorisation shall be granted if the nitrogen or carbon mineralisation processes in laboratory studies are affected by more than 25 % after 100 days, unless it is clearly established through an appropriate risk assessment that under field conditions there is no unacceptable impact on microbial activity after use of the plant protection product in accordance with the proposed conditions of use, taking account of the ability of micro-organisms to multiply.

2.6. Analytical methods

The methods proposed must reflect the state of the art. The following criteria must be met in order to permit validation of the analytical methods proposed for post-registration control and monitoring purposes:

2.6.1. for formulation analysis:

the method must be able to determine and to identify the active substance(s) and where appropriate any toxicologically, ecotoxicologically or environmentally significant impurities and co-formulants;

2.6.2. for residue analysis:

- (i) the method must be able to determine and confirm residues of toxicological, ecotoxicological or environmental significance;
- (ii) the mean recovery rates should be between 70 % and 110 % with a relative standard deviation of ≤ 20 %;
- (iii) the repeatability must be less than the following values for residues in foodstuffs:

Residue level mg/kg	Difference mg/kg	Difference in %
0,01	0,005	50
0,1	0,025	25
1	0,125	12,5
>1		12,5

Intermediate values shall be determined by interpolation from a log-log graph;

- (iv) the reproducibility must be less than the following values for residues in foodstuffs:

Residue level mg/kg	Difference mg/kg	Difference in %
0,01	0,01	100
0,1	0,05	50
1	0,25	25
>1		25

Intermediate values are determined by interpolation from a log-log graph;

- (v) in the case of residue analysis in treated plants, plant products, foodstuffs, feedingstuffs or products of animal origin, except where the MRL or the proposed MRL is at the limit of determination, the sensitivity of the methods proposed must satisfy the following criteria:

Limit of determination in relation to the proposed provisional or EU MRL:

MRL (mg/kg)	limit of determination (mg/kg)
> 0,5	0,1
0,5 – 0,05	0,1 – 0,02
< 0,05	MRL × 0,5

2.7. Physical and chemical properties

2.7.1 Where an appropriate FAO specification exists, that specification must be met.

2.7.2. Where no appropriate FAO specification exists, the physical and chemical properties of the product must meet the following requirements

- (a) Chemical properties:

Throughout the shelf-life period, the difference between the stated and the actual content of the active substance in the plant protection product must not exceed the following values:

Declared content in g/kg or g/l at 20 °C	Tolerance
up to 25	± 15 % homogeneous formulation
	± 25 % non-homogeneous formulation
more than 25 up to 100	± 10 %
more than 100 up to 250	± 6 %
more than 250 up to 500	± 5 %
more than 500	± 25 g/kg or ± 25 g/l

- (b) Physical properties:

The plant protection product must fulfil the physical criteria (including storage stability) specified for the relevant formulation type in the 'Manual on the development and use of FAO and WHO specifications for plant protection products'.

- 2.7.3. Where the proposed label claims include requirements or recommendations for use of the preparation with other plant protection products or adjuvants as a tank mix and/or where the proposed label includes indications on the compatibility of the preparation with other plant protection products as a tank mix, those products or adjuvants must be physically and chemically compatible in the tank mix.

PART B

UNIFORM PRINCIPLES FOR EVALUATION AND AUTHORISATION OF PLANT PROTECTION PRODUCTS CONTAINING AN ACTIVE SUBSTANCE THAT IS A MICRO-ORGANISM

Definitions

For the purposes of Part B, in addition to general introduction, the following definitions apply:

- (1) **‘strain’** means a genetic variant of an organism in its taxonomic level (species) that is made up of the descendants of a single isolation in pure culture from the original matrix (e.g. the environment) and usually is made up of a succession of cultures ultimately derived from an initial single colony;
- (2) **‘Microbial Pest Control Agent as manufactured’ (‘MPCA as manufactured’)** means the outcome of the manufacturing process of the micro-organism(s) intended to be used as active substance in plant protection products, consisting of the micro-organism(s) and any additives, metabolites (including metabolites of concern), chemical impurities (including relevant impurities), contaminating micro-organisms (including relevant contaminating micro-organisms) and the spent medium/rest fraction resulting from the manufacturing process or, in case of a continuous manufacturing processes where a strict separation between the manufacturing of the micro-organism(s) and the production process of the plant protection product is not possible, a non-isolated intermediate;
- (3) **‘relevant contaminating micro-organism’** means a pathogenic/infective micro-organism unintentionally present in the MPCA as manufactured;
- (4) **‘spent medium/rest fraction’** means the fraction of the MPCA as manufactured consisting of remaining or transformed starting materials, and excluding the micro-organism(s) that is the active substance, metabolites of concern, additives, relevant contaminating micro-organisms, and relevant impurities;
- (5) **‘starting material’** means substances used in the manufacturing process of the MPCA as manufactured as substrate and/or buffering agent;
- (6) **‘ecological niche’** means an ecological function and actual physical spaces occupied by a particular species within the community or ecosystem;
- (7) **‘host range’** means the range of different biological host-species that can be infected by a microbial species or strain;
- (8) **‘infectivity’** means the ability of a micro-organism to cause an infection;
- (9) **‘infection’** means the non-opportunistic introduction or entry of a micro-organism into a susceptible host, where the micro-organism is able to reproduce to form new infective units and persist in the host, whether or not it causes pathological effects or disease;
- (10) **‘pathogenicity’** means the non-opportunistic ability of a micro-organism to inflict injury and damage to the host upon infection;
- (11) **‘non-opportunistic’** means a condition under which a micro-organism exerts an infection or inflicts injury or damage when the host is not weakened by a predisposing factor (e.g. immune system impaired by an unrelated cause);
- (12) **‘opportunistic infection’** means an infection occurring in a host weakened by a predisposing factor (e.g. immune system impaired by an unrelated cause);
- (13) **‘virulence’** means the degree of pathogenicity that a pathogenic micro-organism is able to exert in the host;

- (14) **‘metabolite of concern’** means a metabolite produced by the micro-organism under assessment, with known toxicity or known relevant antimicrobial activity, which is present in the MPCA as manufactured at levels that may present a risk to human health, animal health or the environment, and/or for which it cannot be adequately justified that *in-situ* production of the metabolite is not relevant for the risk assessment;
- (15) **‘background level of a metabolite’** means a level of a metabolite that is likely to occur in relevant European environments (including also sources different than those of plant protection) and/or in food and feed (e.g. edible plant parts), when the micro-organisms are in conditions to grow, reproduce and to produce such metabolite in presence of a host or availability of carbon and nutrient sources, under consideration of high host densities and nutrients;
- (16) **‘in-situ production’** means the production of a metabolite by the micro-organism after application of the plant protection product containing that micro-organism;
- (17) **‘antibiosis’** means a relationship between two or more species in which one species is actively harmed (as by the production of toxins by the harming species);
- (18) **‘antimicrobial resistance’ (‘AMR’)** means the intrinsic or acquired ability of a micro-organism to multiply in the presence of an antimicrobial agent at concentrations which are relevant for therapeutic measures in human or veterinary medicine, making that substance therapeutically ineffective;
- (19) **‘antimicrobial agent’** means any antibacterial, antiviral, antifungal, anthelmintic or antiprotozoal agent that is a substance of natural, semi-synthetic, or synthetic origin that at *in vivo* concentrations kills or inhibits the growth of micro-organisms by interacting with a specific target;
- (20) **‘acquired antimicrobial resistance’** means a non-intrinsic and acquired novel resistance enabling a micro-organism to survive or multiply in the presence of an antimicrobial agent at concentrations higher than that which inhibits wild type strains of the same species;
- (21) **‘intrinsic antimicrobial resistance’** means all inherent properties of a microbial species that limit the action of antimicrobial agents thereby allowing it to survive and multiply in presence of the antimicrobial agents at concentrations that are relevant for their therapeutic uses. Inherent properties of micro-organisms are considered not transferable and can include structural characteristics such as lack of drug targets, the impermeability of cellular envelopes, activity of multidrug efflux pumps, or metabolic enzymes. An antimicrobial resistance gene is considered intrinsic if it is located on a chromosome in the absence of mobile genetic element and shared by the majority of wild type strains of the same species;
- (22) **‘relevant antimicrobial activity’** means the antimicrobial activity caused by relevant antimicrobial agents;
- (23) **‘relevant antimicrobial agents’** means all antimicrobial agents important for therapeutic use in humans or animals, as described in the latest available versions at the time of submission of the dossier:
- in a list adopted by means of Commission Regulation (EU) 2021/1760 ⁽¹⁾ in accordance with Article 37(5) of Regulation (EU) 2019/6 of the European Parliament and of the Council ⁽²⁾, or
 - by the World Health Organisation ⁽³⁾ in the lists of Critically Important Antimicrobials, Highly Important Antimicrobials and Important Antimicrobials for Human Medicine.

⁽¹⁾ Commission Delegated Regulation (EU) 2021/1760 of 26 May 2021 supplementing Regulation (EU) 2019/6 of the European Parliament and of the Council by establishing the criteria for the designation of antimicrobials to be reserved for the treatment of certain infections in humans (OJ L 353, 6.10.2021, p. 1).

⁽²⁾ Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC (OJ L 4, 7. 1.2019, p.43).

⁽³⁾ <https://www.who.int/publications/i/item/9789241515528>.

1. EVALUATION

Member States shall consider during the evaluations that:

- micro-organisms are living organisms capable of replication that may be naturally present in high numbers in the environment, and the specific micro-organism under assessment may already be occurring in relevant European environments at a relevant taxonomic level,
- the biological properties and the mode of action of a micro-organism are the first and crucial step in the evaluation process, because they define which are the relevant aspects and elements on which the evaluation should focus, and also which aspects are not relevant for a robust informed decision making,
- extensive information on the micro-organism under assessment (at the relevant taxonomic level) may be available in the public domain (e.g. history of use, peer-reviewed scientific literature). Best use of this information shall be made. Where applicable, regulatory experimental studies may be needed to determine the specific properties of the micro-organism under evaluation.

Metabolism is inherent of all living organisms. If secondary metabolites that are known to be hazardous to humans or other non-target organisms have been identified during the assessment of the micro-organism, the evaluation of a plant protection product containing this micro-organism shall include an assessment of the risk due to exposures to such metabolites expected from the intended use.

Member States shall implement the following principles in the evaluation of the data and information submitted in support of applications, without prejudice to the general principles prescribed in Section 2 of the general introduction.

1.1. Identity and manufacturing information

An overall assessment is necessary for those data on the identity and manufacturing information required according to Section 1 of Part B of the Annex to Regulation (EU) No 283/2013 and Section 1 of Part B of the Annex to Regulation (EU) No 284/2013.

1.1.1. Identity of the micro-organism contained in the plant protection product

Member States shall verify the identity of the micro-organism that is the active substance based on information provided under point 1.3 of Part B of the Annex to Regulation (EU) No 283/2013.

Furthermore, Member States shall evaluate if the MPCA as manufactured used for manufacturing of the plant protection product complies with specification of the MPCA as manufactured characterised and quantified as required in point 1.4 of Part B of the Annex to Regulation (EU) No 283/2013 (e.g. in terms of content and identity of the micro-organism(s), metabolites of concern, additives, relevant contaminating micro-organisms, and relevant impurities).

1.1.2. Quality control of the production of the micro-organism contained in the plant protection product

Member States shall evaluate the quality assurance criteria proposed for the production of the active substance. Process control, good manufacturing practice, operational practices, process flows, cleaning practices, microbial monitoring and hygiene conditions shall be present and ensure stable quality of the MPCA as manufactured.

1.1.3. Identity of the plant protection product

Member States shall evaluate the detailed quantitative and qualitative information provided on the composition of the plant protection product as required in point 1.4 of Part B of the Annex to Regulation (EU) No 284/2013, e.g. micro-organism (active substance), metabolites of concern, relevant impurities, relevant contaminating micro-organisms, co-formulants, safeners and synergists.

1.1.4. Quality control of the plant protection product

Member States shall evaluate the quality assurance criteria proposed, in particular whether strict maintenance of environmental conditions and quality control analysis during the manufacturing process have been assured by the producer, in order to ensure compliance with the limits for relevant contaminating micro-organisms, relevant impurities and metabolites of concern.

1.2. **Biological, physical, chemical and technical properties**

Member States shall carry out an overall assessment of the information on biological, physical, chemical, and technical properties of the plant protection product provided under Section 2 of Part B of the Annex to Regulation (EU) No 283/2013 and Section 2 of Part B of the Annex to Regulation (EU) No 284/2013.

1.2.1. Biological properties of the micro-organism in the plant protection product

1.2.1.1. Member States shall evaluate information on the origin, occurrence and history of use of the micro-organism contained the plant protection product, giving particular relevance to both the location from which the strain was isolated, and the geographical distribution of the micro-organism at the relevant highest taxonomic level in relevant European environments.

1.2.1.2. Member States shall evaluate information on the ecology and the life cycle of the micro-organism, taking also into consideration the population densities of the micro-organism in relation to host densities as provided for in point 2.3 of Part B of the Annex to Regulation (EU) No 283/2013. In particular, for bacteriophages, the lysogenic and lytic properties of the virus shall be evaluated.

1.2.1.3. Member States shall evaluate information on the mode of action on the target organisms for the plant protection product to identify potential risks and function of the active substance that is a micro-organism according to the proposed conditions of use. In particular, Member States shall evaluate the role of possible infectivity, pathogenicity, toxicity and relevant antimicrobial activity in the mode of action against the target organism. If applicable, factors that enhance the pathogenicity/virulence of a micro-organism and environmental factors affecting a pathogenic mode of action shall be described.

Information on the mode of action can be a very valuable tool in identifying potential risks and purpose of the micro-organism in the plant protection product.

Aspects to be considered in the evaluation are, for instance:

- (a) invertebrate pathogenicity;
- (b) parasitisation;
- (c) competition for the ecological niche (e.g. nutrients, habitats);
- (d) endophytic growth;
- (e) interference with the virulence of a pathogenic target organism;
- (f) induction of plant defence;
- (g) antibiosis.

1.2.1.4. Member States shall evaluate data provided on the host range of the micro-organism, taking into account any available information on the relationship of the micro-organism to known pathogens to humans, animals, plants and other non-target species, at the most appropriate taxonomic level.

1.2.1.5. Member States shall evaluate information on growth requirements, by defining limiting factors e.g. UV light, humidity, pH, temperatures and other relevant agro-environmental conditions influencing the growth of the micro-organism.

1.2.1.6. Member States shall evaluate the genetic stability of a micro-organism that is a non-virulent variant of a plant pathogen virus, taking into consideration the likelihood of the micro-organisms to regain virulence, and the risk that could be caused by this occurrence.

- 1.2.1.7. In order to determine whether the micro-organism produces metabolites of concern, Member States shall take into account the information on production, toxicity and exposure concerning metabolites as provided for in points 2.8, 6.1, 6.2, 5.5, 7.2 and 8.8 of Part B of the Annex to Regulation (EU) No 283/2013.
- 1.2.1.8. For bacteria, Member States shall evaluate information on phenotypical resistance to relevant antimicrobial agents. Member States shall evaluate, taking into consideration that resistance genes in bacteria can be horizontally transmitted, and that this may potentially interfere with the effectiveness of relevant antimicrobial agents, information on the presence and transferability of genes coding for resistance to such antimicrobial agents.
- 1.2.2. Physical, chemical and technical properties of the plant protection product
- 1.2.2.1. Member States shall evaluate shelf-life and storage stability of the plant protection product, taking into account the packaging, optimal (recommended) storage temperature, and light conditions. Possible changes in composition due to growth or decline of the micro-organism or of relevant contaminating micro-organisms, or the production of metabolites of concern during storage, etc., shall be considered.
- 1.2.2.2. Member States shall evaluate the physical and chemical properties of the plant protection product and the retention of these characteristics after storage and take into consideration, unless a suitable FAO specification exists, all relevant physical and chemical properties of the plant protection product.
- 1.2.2.3. Where the proposed label includes requirements or recommendations for use of the plant protection product in combination with other plant protection products or adjuvants as a tank mix, Member states shall evaluate whether the plant protection product is physically and chemically compatible with those other plant protection products or adjuvants in the tank mix.
- 1.3. **Efficacy**
- Member States shall evaluate the efficacy of the plant protection product based on those data submitted in accordance with Section 6 of Part B of the Annex to Regulation (EU) No 284/2013.
- 1.3.1. Where the proposed use concerns the control of or protection against an organism, Member States shall evaluate if the target organism could be a danger to plant health under the agricultural and environmental (including climatic) conditions in the area of the proposed use.
- 1.3.2. Member States shall evaluate whether significant damage to plants or plant products or loss in yields could occur under the agricultural and environmental (including climatic) conditions in the area of proposed use, if the plant protection product was not used.
- 1.3.3. Member States shall evaluate the efficacy data provided for in Part B of the Annex to Regulation (EU) No 284/2013 for the plant protection product, having regard to the degree of control or the extent of the effect desired and to relevant experimental conditions such as:
- (a) the choice of the crop or cultivar;
 - (b) the agricultural and environmental (including climatic) conditions (if necessary for a specific use such data/information shall also be given for the time before and after application);
 - (c) the presence and density of the target organism;
 - (d) the development stage of crop and target organism;
 - (e) the application rate of the plant protection product;
 - (f) if required on the label, the application rate of adjuvant to be added;
 - (g) the frequency and timing of the applications;
 - (h) the type of application equipment to be used;
 - (i) the need for any special cleaning measures for the application equipment before and after use.

1.3.4. Member States shall evaluate the efficacy of the plant protection product under the range of agricultural, plant health and environmental (including climatic) conditions likely to be encountered in practice in the area of proposed use. The evaluation shall include the compatibility with integrated pest management. In particular, consideration shall be paid to:

- (a) the level, consistency and duration of the effect sought in relation to the proposed dose;
- (b) the comparison of the proposed dose with a suitable reference product or products, where they exist, and an untreated control;
- (c) where relevant, the effect on yield or reduction of loss in storage, in terms of quantity and/or quality, in comparison with a suitable reference product or products, where they exist, and an untreated control;
- (d) the risk of occurrence and development of resistance or cross-resistance in populations of target organism.

Where no suitable reference product exists, Member States shall evaluate the efficacy of the plant protection product to determine whether there is a consistent and defined benefit under the agricultural, plant health and environmental (including climatic) conditions likely to be encountered in practice in the area of proposed use.

1.3.5. Member States shall evaluate possible occurrence of adverse effects and their degree, on the treated crop after use of the plant protection product in accordance with the proposed conditions of use in comparison, where relevant, with a suitable reference product or products, where they exist, and/or an untreated control.

- (a) This evaluation shall take into consideration the following information:
 - (i) efficacy data;
 - (ii) other relevant information on the plant protection product such as nature of the plant protection product, dose, method of application, number and timing of applications, incompatibility with other crop treatments;
 - (iii) all relevant information on the micro-organism, including biological properties e.g. mode of action, survival, host range specificity.
- (b) This evaluation shall include:
 - (i) the nature, frequency, level and duration of observed phytotoxic/phytopathogenic effects and the agricultural, plant health and environmental (including climatic) conditions that affect them;
 - (ii) differences between main cultivars with regard to their sensitivity to phytotoxic/phytopathogenic effects;
 - (iii) the part of the treated crop or plant products where phytotoxic/phytopathogenic effects are observed;
 - (iv) adverse impact on the yield of the treated crop or plant products in terms of quantity and/or quality, and on transformation processes;
 - (v) adverse impact on treated plants or plant products to be used for propagation, in terms of viability, germination, sprouting, rooting and establishment;
 - (vi) where micro-organisms are disseminated, in particular for weed control, any adverse impact on adjacent crops.

1.3.6. Where the proposed label of the plant protection product includes recommendations or requirements for the use of the plant protection product with other plant protection products and/or adjuvants as a tank mix, Member States shall make the evaluations referred to in points 1.3.3 to 1.3.5 with regard to the information supplied for the tank mix, and shall evaluate the appropriateness of the mix and of its conditions of use.

1.3.7. Member States shall evaluate potential effects (e.g. antagonism, fungicidal effects) on the activity of the micro-organism after mixing or spraying in sequence (or employing other relevant types of applications) with other plant protection products in accordance with the instructions proposed by the applicant on the label.

- 1.3.8. Where the available data indicate that the micro-organism has adverse effects on plants, or that metabolites of concern that have adverse effects on plants can persist in soil, and/or persist in/on plants in significant quantities after use of the plant protection product in accordance with the proposed conditions of use, Member States shall evaluate the degree of adverse effects on succeeding crops, taking into consideration the relevant information provided for under point 6.6 of Part B of the Annex to Regulation (EU) No 284/2013.
- 1.3.9. Member States shall evaluate potential negative effects of the micro-organism on beneficial organisms, either deliberately released, or as part of other practices (e.g. conservation biological control), taking into consideration the relevant information provided for under point 6.7 of Part B of the Annex to Regulation (EU) No 284/2013.
- 1.3.10. Where the proposed use of a plant protection product is intended to have an effect on vertebrates, Member States shall evaluate the mechanism by which this effect is obtained and the observed effects on the behaviour and health of the target animals. When the intended effect is to kill the target animal they shall evaluate the time necessary to obtain the death of the animal and the conditions under which death occurs.

This evaluation shall take into consideration the following information:

- (a) all relevant information as provided for under Part B of the Annex to Regulation (EU) No 283/2013 and the results of the evaluation thereof, including the toxicological studies;
 - (b) all relevant information on the plant protection product as provided for under Part B of the Annex to Regulation (EU) No 284/2013, including toxicological studies and efficacy data.
- 1.3.11. If there is evidence of development of resistance of the target organism towards the plant protection product requiring a resistance management strategy, the Member State shall evaluate if the submitted resistance management strategy, required according to point 6.4 of Part B of the Annex to Regulation (EU) No 284/2013, addresses this adequately and sufficiently.

1.4. **Identification/detection and quantification methods**

Member States shall assess data on the identification/detection and quantification methods submitted in accordance with Section 4 of Part B of the Annex to Regulation (EU) No 283/2013 and Section 5 of Part B of the Annex to Regulation (EU) No 284/2013.

Member States shall evaluate the analytical methods proposed for control and monitoring purposes, of the micro-organism both in the plant protection product and, where relevant, in or on edible parts of treated crops. In addition, where relevant, the analytical methods relating to metabolites of concern and relevant impurities present in the plant protection product shall also be evaluated. Appropriate validation data shall be provided by the applicant as regards the pre-authorisation analytical methods and post-authorisation monitoring methods. Methods that are considered suitably validated for post-authorisation monitoring shall be clearly identified.

1.4.1. Analytical methods for the plant protection product

The evaluation concerning analytical methods for the plant protection product shall take into consideration the relevant information provided for under point 4.1 of Part B of the Annex to Regulation (EU) No 283/2013 and under point 5.1 of Part B of the Annex to Regulation (EU) No 284/2013.

1.4.1.1. Analytical methods for micro-organisms

Member States shall evaluate the methods proposed to identify and quantify the micro-organism, and especially methods that discriminate that micro-organism from closely related strains. These methods shall include the most appropriate molecular analytical and phenotypic methods, to allow unequivocal distinction between the micro-organism under assessment, and other strains belonging to the same species. Member States shall also evaluate the methods proposed to identify and quantify relevant contaminating micro-organisms.

1.4.1.2. Analytical methods for metabolites of concern, relevant impurities, additives, co-formulants, safeners and synergist

Where applicable, Member States shall evaluate the analytical methods proposed to identify and quantify metabolites of concern identified according to point 2.8 of Part B of the Annex to Regulation (EU) No 283/2013, relevant impurities, co-formulants, safeners and synergists.

1.4.2. Analytical methods for the determination of residues and density of the micro-organism

Member States shall take into consideration the relevant information provided for under point 4.2 of Part B of the Annex to Regulation (EU) No 283/2013 and under point 5.2 of Part B of the Annex to Regulation (EU) No 284/2013.

1.4.2.1. Density of the micro-organism

Member States shall evaluate the methods proposed to identify and quantify the density of the micro-organism, where relevant, on and/or in crops, in foodstuffs and feeding stuffs, in animal and human body tissues and fluids, in relevant environmental compartment.

1.4.2.2. Residues of metabolites of concern

Member States shall evaluate the analytical methods proposed to identify and quantify residues of metabolites of concern, where relevant, on and/or in crops, in foodstuffs and feeding stuffs, in animal and human body tissues and fluids, in relevant environmental compartment.

1.5. **Impact on human and animal health**

Member States shall evaluate data on human and animal (i.e. species normally fed and kept by humans or food-producing animals) health submitted in accordance with Sections 5 and 6 of Part B of the Annex to Regulation (EU) No 283/2013 and Sections 7 and 8 of Part B of the Annex to Regulation (EU) No 284/2013.

The most important aspects that shall be assessed are:

- infectivity and pathogenicity;
- toxicity of metabolites of concern, safeners, synergists, and relevant impurities;
- relevant antimicrobial activity of metabolites present in the plant protection product;
- susceptibility to relevant antimicrobial agents to ensure the availability of sufficient treatment options in case of an opportunistic infection.

These aspects comprise a complex set of interactions between micro-organisms and the hosts, and need to be assessed in an integrated way and applying a weight of evidence approach.

An assessment of infectivity and pathogenicity is always necessary.

1.5.1. Effects on human or animal health arising from the plant protection product

1.5.1.1. Availability of sufficient treatment options against the micro-organism contained in the plant protection product shall be evaluated.

1.5.1.2. Member States shall evaluate infectivity and pathogenicity of the micro-organism and toxicity of metabolites of concern and relevant impurities. This evaluation shall take into consideration the following information:

- (a) the available information on infectivity and pathogenicity (e.g. based on biological properties, peer-reviewed literature, animal studies performed by the applicant) as provided for in Part B of the Annex to Regulation (EU) No 283/2013. For micro-organisms, infectivity and pathogenicity tests on animals may not always be suitable for extrapolation to humans due to differences between humans and test animals (e.g. immune system, microbiome). Micro-organisms might have a narrow host range, hence it cannot always be assumed

that a micro-organism that does cause disease in the animals tested has the same result in humans, and vice-versa. Information available and provided by the applicant, as required in points 2.1, 2.3, 2.4, 2.6 and 5.1 of Part B of the Annex to Regulation (EU) No 283/2013, and/or retrieved from any other reliable sources (e.g. Qualified Presumption of Safety, peer-reviewed literature) may provide robust and reliable scientific indication on infectivity and pathogenicity of the micro-organism. Where an applicant provides a summary of information already available on infectivity and pathogenicity of the micro-organism, as described in point 5.2 of Part B of the Annex to Regulation (EU) No 283/2013, Member States shall assess such scientific evidence provided by the applicant using a weight of evidence approach, in order to evaluate whether the possible non-submission of certain studies required in points 5.3.1 and 5.4 of Part B of the Annex to Regulation (EU) No 283/2013 is justified. The evaluation shall take into consideration the following principles:

- to avoid unnecessary animal testing, in a first instance infectivity and pathogenicity shall be assessed on the basis of existing information as provided for under point 5.2 of Part B of the Annex to Regulation (EU) No 283/2013;
- infectivity and pathogenicity studies described in point 5.3.1 of Part B of the Annex to Regulation (EU) No 283/2013 may be necessary;
- further specific studies may be required, as indicated in point 5.4 of Part B of the Annex to Regulation (EU) No 283/2013. For instance, if there are indications of infectivity, or any adverse effects, further testing shall be conducted, taking into account the exposure scenario and an observation period suitable for the micro-organisms, to allow observing a clearance in the host. The choice of appropriate timing of the observational period may be based on available information such as biological properties of the micro-organism or other relevant available information.

The evaluation of available information and possible animal studies performed by the applicant, shall take into consideration the ability of the micro-organism to infect, persist or grow in the mammalian host, and its ability to cause effects or reactions in the host. Parameters that indicate the absence of ability to persist and multiply in the host, and the absence of ability to produce adverse effects in a host, include clearance from the body, if relevant. Replication temperatures may be different from mammalian body temperature, possibly indicating low likelihood of persistence and multiplication in the host. However, temperature adaptation may occur, and this parameter alone shall not be considered sufficient to conclude on persistence and multiplication of the micro-organism in the host. Evaluation based on relevant parameters of study results and available information shall lead to an assessment of the possible effects of occupational exposure.

- (b) the available information on toxicity (e.g. based on biological properties, peer-reviewed literature, animal studies performed by the applicant) as described in points 2.8 and 5.5 of Part B of the Annex to Regulation (EU) No 283/2013, and Section 7 of Part B of the Annex to Regulation (EU) No 284/2013. Information available on toxicity, such as from published literature, medical information, Integrated Approach to Testing and Assessment (IATA), results of CLP calculation rules in accordance with Regulation (EC) No 1272/2008, or bridging data from similar plant protection products, may provide robust and reliable scientific indication on the toxicity of relevant chemical substances contained in the plant protection product, and be used for classification and labelling. Where an applicant provides information available on human and animal toxicity of (chemical substances present in) the plant protection product (including *in vitro* and *ex vivo* data), Member States shall assess such scientific evidence provided by the applicant using a weight of evidence approach, in order to evaluate whether the possible non-submission of certain studies required in points 7.3.1 to 7.3.6 of Part B of the Annex to Regulation (EU) No 284/2013 is justified. The evaluation shall take into consideration the following principles:

- to avoid unnecessary animal testing, in a first instance toxicity shall be assessed on the basis of existing information as provided for in point 7.2 of Part B of the Annex to Regulation (EU) No 284/2013;
- toxicity studies may be necessary;
- further specific studies may be required taking into consideration the intended use, according to the provisions of points 2.8 and 5.5 of Part B of the Annex to Regulation (EU) No 283/2013, and of points 7.4 and 7.7 of Part B of the Annex to Regulation (EU) No 284/2013.

The evaluation of available information and possible animal studies performed by the applicant, shall take into consideration the ability of metabolites of concern, safeners, synergists, and relevant impurities to cause adverse effects on humans or animals. Evaluation based on relevant parameters of the tests shall lead to an assessment of the possible effects of non-dietary exposure, taking into account the intensity and duration of exposure under the proposed conditions of use.

(c) other relevant information provided for under Part B of the Annex to Regulation (EU) No 284/2013, such as:

- composition of the plant protection product,
- nature of the plant protection product,
- size, design and type of packaging.

1.5.1.3. Member States shall evaluate the effects to human and animal health related to non-dietary exposure of operators, workers, bystanders and residents to the micro-organism which is contained in the plant protection product, and the components which may be toxicologically relevant (e.g. metabolites of concern, relevant impurities), and which are likely to occur under the proposed conditions of use (including, in particular, dose, application method and climatic conditions). Realistic data on exposure levels to the plant protection product shall be used. If such data is not available, a suitable, and if possible validated, calculation model for plant protection products containing a micro-organism shall be employed. This evaluation shall take into consideration the following aspects:

(a) on the basis of the information referred to in point 1.5.1.2 the following overall end-points shall be established for single or repeated operator, worker, bystanders and residents exposure following the intended use, as regards:

- observed or expected infectivity and pathogenicity of the micro-organism(s) in the plant protection product,
- observed or expected adverse toxicological effects of the plant protection product due to metabolites of concern safeners, synergists, and/or relevant impurities.

(b) the evaluation of the exposure of the operator shall be made for each type of application method and application equipment proposed for the use of the plant protection product as well as for the different types and sizes of packaging containers to be used, taking into account mixing, loading operations, application of the plant protection product and cleaning and routine maintenance of application equipment. Where relevant, other authorised uses of the plant protection product in the area of envisaged use, concerning the same active substance or which give rise to the same residues, shall also be taken into account.

(c) the possibility of adverse effects in humans shall be assessed with regard to measured or estimated levels of human exposure as compared to the tested dose levels, as provided for under Section 7 of Part B of the Annex to Regulation (EU) No 284/2013. This risk assessment shall include consideration of e.g. mode of action, physical and chemical properties of the micro-organism and other components in the plant protection product, such as metabolites of concern, safeners, synergists and relevant impurities.

(d) other relevant information provided for under Part B of the Annex to Regulation (EU) No 284/2013, such as:

- field of use and nature of the crop or target,
- method of application including handling, mixing and loading of the plant protection product,
- exposure reduction measures recommended,
- protective clothing recommendations,
- maximum application rate,
- cleaning and routine maintenance of application equipment, , taking into account also seed treatment and good occupational practice,
- recommendation to be followed after application, such as re-entry period and working duration,

- minimum (spray) application volume stated on the label,
- number and timing of applications, including intervals between applications,
- re-entry periods, necessary waiting periods or other precautions to protect humans and animals,
- dried residues of the plant protection products on plants and plant products after treatment, taking into account the capacity of the micro-organism to grow *in situ*, and the influence of factors such as temperature, UV light, pH and the presence of certain substances,
- further information on exposure (e.g. operator/worker/bystander/resident exposure study, further activities whereby workers are exposed).

1.5.1.4. Member States shall evaluate information relating to the nature and characteristics of the packaging proposed, in particular the following aspects:

- (a) the type of packaging;
- (b) its dimensions and capacity;
- (c) the size of the opening;
- (d) the type of closure;
- (e) its strength, leak proofness and resistance to normal transport and handling;
- (f) its resistance to and compatibility with the contents.

1.5.1.5. Member States shall evaluate the nature and characteristics of the protective clothing and equipment proposed, in particular the following aspects:

- (a) obtainability and suitability;
- (b) effectiveness;
- (c) ease of wearing taking into account physical stress and climatic conditions;
- (d) resistance to and compatibility with the plant protection product.

1.5.1.6. Micro-organisms approved as active substances of plant protection product are not expected to be infective for humans. However, in order to ensure the availability of sufficient therapeutic measures in the event of opportunistic infections, Member States shall, where relevant based on biological properties of the micro-organism, evaluate the susceptibility of the micro-organism (except viruses) to antimicrobial agents.

1.5.2. Effects on human or animal health arising from residues of metabolites of concern

The evaluation of consumer exposure to residues of metabolites, for which a hazard to human and animal health was identified, is based either on the applicant's substantiated estimation or, in case where the substantiated estimation does not demonstrate an acceptable risk to consumers, on residue trials for metabolites of concern.

In cases provided for in point 6.1 of Part B of the Annex to Regulation (EU) No 283/2013, also information on viable micro-organisms may be required and assessed with the information on residues of metabolites of concern.

1.5.2.1. Member States shall evaluate the potential residue levels of metabolites of concern for which a hazard was identified to human or animal health in points 2.8 and 5.5 of Part B of Annex to Regulation (EU) No 283/2013. This evaluation shall be performed for each proposed use and shall take into account the following information:

- the intended use, including data on application and proposed pre-harvest intervals for envisaged uses or withholding periods or storage periods in the case of post-harvest uses;
- analytical methods as provided for under point 5.2 of Part B of the Annex to Regulation (EU) No 284/2013;

- the specific information on residues in/on treated plants, plant products, food and feed as provided for in Section 8 of Part B of the Annex to Regulation (EU) No 284/2013;
- realistic possibilities for extrapolating data from one crop to another.

Member States shall evaluate the potential exposure of consumers to metabolites of concern through diet using a suitable calculation model. This evaluation shall take into account, where relevant, other sources of the same metabolite of concern for which either maximum residue levels have been set in accordance with Regulation (EC) No 396/2005, or maximum tolerances have been set in accordance with Council Regulation (EEC) No 315/93 ⁽¹⁴⁾ on contaminants in food.

In cases where the estimation of residue levels does not demonstrate acceptable risk to consumers, Member States shall refine the evaluation, either based on data generated through residues trials, or on toxicity of metabolites of concern through determination of a toxicological endpoint, such as the acceptable daily intake (ADI), or, where appropriate, the Threshold of Toxicological Concern (TTC) value having regard to the specific information provided in accordance with point 6.2 of Part B of the Annex to Regulation (EU) No 283/2013.

- 1.5.2.2. Member States shall, where relevant, estimate the exposure of animals to residues of metabolites of concern, taking into account the residue levels estimated or measured in treated plants or plant products intended to be fed to animals.
- 1.5.2.3. Member States shall, where relevant, evaluate the residues of metabolites of concern estimated or measured in products of animal origin and their toxicity, taking into consideration the information provided for under points 2.8 and 5.5 and Section 6 of Part B of the Annex to Regulation (EU) No 283/2013.
- 1.5.2.4. Member States shall, where relevant, estimate the potential exposure of consumers to metabolites of concern through diet via the products of animal origin mentioned in point 1.5.2.3, using a suitable calculation model. This evaluation shall take account, where relevant, of other sources of the same metabolite of concern for which either maximum residue levels had been set in accordance with Regulation (EC) No 396/2005 (in case of authorised uses of the micro-organism producing it in biocidal or veterinary products), or maximum tolerances have been set in accordance with Regulation (EEC) No 315/93, where relevant.
- 1.5.2.5. Member States shall assess data on density of micro-organisms on edible parts of treated crops, if those are provided to support the estimation of residues of metabolites of concern produced *in-situ*. Data on density of micro-organisms on edible parts of treated crops is required only in few circumstances, as provided for in point 6.1 of Part B of Annex to Regulation (EU) No 283/2013, since micro-organisms which are infective or pathogenic to humans or other vertebrate animals will not be eligible for approval, and non-pathogenic micro-organisms are not expected to cause adverse effects to consumers, apart from possible production of metabolites of concern to be assessed in accordance with the points 1.5.2.1 to 1.5.2.4. Absence of viable micro-organisms on edible parts excludes the risk of *in-situ* production of metabolites of concern.

1.6. **Environmental occurrence of the micro-organism, including fate and behaviour of metabolites of concern**

Member States shall assess data on the environmental occurrence of the micro-organism, including fate and behaviour of metabolites of concern, submitted in accordance with Section 7 of Part B of the Annex to Regulation (EU) No 283/2013 and Section 9 of Part B of the Annex to Regulation (EU) No 284/2013.

The evaluation of the environmental occurrence of an active substance that is a micro-organism needs to take into account that micro-organisms may be already occurring in relevant European environments, have the ability to replicate and have the ability to become dormant allowing for the formation of seed banks of micro-organisms.

⁽¹⁴⁾ Council Regulation (EEC) No 315/93 of 8 February 1993 laying down Community procedures for contaminants in food (OJ L 37, 13.2.1993, p. 1).

The evaluation of the environmental exposure to the relevant components of the plant protection product, i.e. the micro-organism and metabolites of concern, shall be considered in order to conduct risk assessments as regards:

- non-target organisms (concerning the exposure to the micro-organism and to the metabolites of concern);
- humans via the environment (concerning the exposure to the metabolites of concern).

The evaluation of environmental exposure shall be based either on a substantiated estimation or, in case where this substantiated estimation does not demonstrate an acceptable risk, on experimental data. This experimental data may include measurements concerning the population dynamics of the micro-organism in specific environmental compartments upon use of the plant protection product, and the fate and behaviour of metabolites of concern.

1.6.1. Environmental occurrence of the micro-organism

Member States shall evaluate the possibility of exposure of soil and/or surface water to the micro-organism based on the intended use and the biological properties of the micro-organism. If the possibility of exposure cannot be excluded, Member States shall evaluate the estimated exposure of soil and/or surface water after the use of the plant protection product in accordance with the intended conditions of use.

For non-target organisms for which a hazard is identified, for instance based on the calculation of the predicted environmental density as provided for under point 7.1.1 of Part B of the Annex to Regulation (EU) No 283/2013, Member States shall evaluate the estimation of the exposure of the relevant non-target organisms to the micro-organism. This estimation shall be performed for each intended use and shall take into account the following information:

- the data on the proposed good agricultural practice, including data on application;
- nature of the plant protection product;
- analytical methods, as provided for under point 4.2 of Part B of the Annex to Regulation (EU) No 283/2013, and under point 5.2 of Part B of the Annex to Regulation (EU) No 284/2013;
- the specific information on occurrence of the micro-organism, e.g. possible increase of microbial density in the relevant environmental compartment compared to the occurrence at the relevant highest taxonomic level in European environments, as provided for under point 7.1 of Part B of the Annex to Regulation (EU) No 283/2013, and, where relevant, Section 9 of Part B of the Annex to Regulation (EU) No 284/2013;
- data extrapolated from one crop to another, if considered realistic by Member States;
- in addition, for micro-organisms not occurring in the relevant European environments at the relevant highest taxonomic level, and which are known to be pathogenic either for plants or for other organisms, the exposure of non-target organisms through colonised host organisms shall be evaluated taking into account also the information on the population density of the micro-organism in host organisms, and the exposure of non-target organisms to colonised host organisms.

1.6.2. Environmental fate and behaviour of the metabolites of concern

In case a hazard has been identified for humans and/or non-target organisms due to a metabolite of concern, as provided for under points 2.8, 5.5 and 8.8 of Part B of the Annex to Regulation (EU) No 283/2013, and Sections 7 and 10 of Part B of the Annex to Regulation (EU) No 284/2013, Member States shall estimate the concentrations in the relevant environmental compartments that lead to exposure of humans and non-target organisms for which the hazard has been identified. This estimation shall be performed for each intended use and shall take into account the following information:

- the data on the proposed good agricultural practice, including data on application;
- nature of the plant protection product;

- analytical methods, as provided for under point 4.2 of Part B of the Annex to Regulation (EU) No 283/2013, and under point 5.2 of Part B of the Annex to Regulation (EU) No 284/2013;
- the specific information on environmental fate and behaviour of the metabolite of concern present in the plant protection product, as provided for under point 7.2 of Part B of the Annex to Regulation (EU) No 283/2013, and, if relevant, Section 9 of Part B of the Annex to Regulation (EU) No 284/2013;
- if available and if submitted by the applicant to perform a qualitative exposure assessment as provided for under point 7.2.2 of Part B of the Annex to Regulation (EU) No 283/2013, on background level of the same metabolite of concern in the relevant environmental compartments;
- realistic possibilities of extrapolating data from one crop to another.

1.7. Effects on non-target organisms

Member States shall assess data on the risks to non-target organisms that the plant protection product may cause submitted in accordance with Section 8 Part B of the Annex to Regulation (EU) No 283/2013 and Section 10 Part B of the Annex to Regulation (EU) No 284/2013.

This assessment shall take into consideration the biology of the micro-organism, the exposure of non-target organisms under field condition according to the proposed conditions of use, and shall take into consideration possible increase of microbial density in the relevant environmental compartment compared to the occurrence of the micro-organism in European environments at the relevant highest taxonomic level.

To assess the possibility of exposure the following information shall be taken into consideration:

- (a) conditions of use;
- (b) information on fate and behaviour as provided in Section 9 of Part B of the Annex to Regulation (EU) No 284/2013.

Where an applicant does not perform certain studies required in Section 8 of Part B of the Annex to Regulation (EU) No 283/2013 and Section 10 of Part B of the Annex to Regulation (EU) No 284/2013, Member States shall assess if the scientific evidence provided by the applicant using a weight of evidence approach justifies the non-submission of these data.

1.7.1. Member States shall evaluate the risks to terrestrial vertebrates after the use of the plant protection product in accordance with the proposed conditions of use and taking into account the evaluation criteria provided for in point 1.6.

- (a) Member States shall evaluate the risks to terrestrial vertebrates due to the micro-organism and its potential to infect and multiply in the host, taking into account the following information on the micro-organism:
 - mode of action;
 - other biological properties;
 - studies on mammalian infectivity and pathogenicity;
 - studies on avian infectivity and pathogenicity;
 - other relevant information on terrestrial vertebrate infectivity and pathogenicity.
- (b) Member States shall evaluate the risk to terrestrial vertebrates due to toxic effects of the plant protection product in accordance with relevant provisions referred to in point 1.5.2.1 of Part A.

1.7.2. Member States shall evaluate the risks to aquatic organisms after the use of the plant protection product in accordance with the proposed conditions of use and taking into account the evaluation criteria provided for in point 1.6.

- (a) Member States shall evaluate the risks to aquatic organisms due to the micro-organism and its potential to infect and multiply the host, taking into account the following information on the micro-organism:
 - its mode of action;

- other biological properties;
 - studies on infectivity and pathogenicity to aquatic organisms and/or other existing relevant information.
- (b) Member States shall evaluate the risk to aquatic organisms due to toxic effects of the plant protection product in accordance with relevant provisions referred to in point 1.5.2.2 of Part A.
- 1.7.3. Member States shall evaluate the risks to bees after the use of the plant protection product in accordance with the proposed conditions of use and taking into account the evaluation criteria provided for in point 1.6.
- (a) Member States shall evaluate the risks to bees due to the micro-organism and its potential to infect and multiply the host, taking into account the following information on the micro-organism:
- its mode of action;
 - other biological properties;
 - studies on infectivity and pathogenicity to bees and/or other existing relevant information.
- (b) Member States shall evaluate the risk to bees due to toxic effects of the plant protection product, in accordance with relevant provisions referred to in point 1.5.2.3 of Part A.
- 1.7.4. Member States shall evaluate the risks to non-target arthropods other than bees after the use of the plant protection product in accordance with the proposed conditions of use and taking into account the evaluation criteria provided for in point 1.6. Member States shall pay particular attention to the risks to beneficial organisms deliberately released for biocontrol purposes.
- (a) Member States shall evaluate the risks to arthropods other than bees due to the micro-organism and its potential to infect and multiply the host, taking into account the following information on the micro-organism:
- its mode of action;
 - other biological properties;
 - studies on infectivity and pathogenicity to honeybees and other arthropods and/or other existing relevant information.
- (b) Member States shall evaluate the risk to arthropods other than bees due to toxic effects of the plant protection product in accordance with relevant provisions referred to in point 1.5.2.4 of Part A.
- 1.7.5. Member States shall evaluate the risks to non-target meso- and macro-organisms in soil after the use of the plant protection product in accordance with the proposed conditions of use and taking into account the evaluation criteria provided for in point 1.6.
- (a) Member States shall evaluate the risks to meso- and macroorganisms in soil due to the micro-organism and its potential to infect and multiply the host, taking into account the following information on the micro-organism:
- its mode of action;
 - other biological properties;
 - studies on infectivity and pathogenicity to meso- and macro-organisms and/or other existing relevant information.
- (b) Member States shall evaluate the risk to meso- and macro-organisms in soil due to toxic effects of the plant protection product in accordance with relevant provisions referred to in point 1.5.2.5 of part A.

1.7.6. Member States shall evaluate the risks to non-target terrestrial plants after the use of the plant protection product in accordance with the proposed conditions of use and taking into account the evaluation criteria provided for in point 1.6.

(a) Member States shall evaluate the risks to terrestrial plants due to the micro-organism and its potential to infect and multiply the host, taking into account the following information on the micro-organism:

- its mode of action;
- other biological properties;
- studies on infectivity and pathogenicity to terrestrial plants;
- relatedness to known plant-pathogens.

(b) Member States shall evaluate the risk to terrestrial plants due to toxic effects of the plant protection product.

1.8. **Conclusions and proposals**

Member States shall draw conclusions on the need for further information and/or testing and the need for measures to limit the risks arising. Member States shall justify proposals for the classification and labelling of plant protection products.

2. **DECISION-MAKING**

The following principles shall apply without prejudice to the general principles referred to in Section 3 of the general introduction.

2.1. **Identity**

2.1.1. For each authorisation granted the Member States shall ensure that the active substance concerned has been approved in accordance with Regulation (EC) No 1107/2009.

2.1.2. For each authorisation granted the Member States shall set the specification as regards the composition of the plant protection product. The minimum and maximum content of the micro-organism that is the active substance contained in the plant protection product shall be defined. The content of metabolites of concern, relevant impurities, co-formulants, safeners and synergists in the plant protection product, and relevant contaminating micro-organisms derived from the production process shall to the extent possible be defined. Member States shall verify, based on the information provided in the dossier, that quality assurance on the manufacturing process allows levels of metabolites of concern, relevant impurities, and relevant contaminating micro-organisms to be controlled to an acceptable level.

2.1.3. No authorisation shall be granted unless the manufacturing processes of the MPCA as manufactured and the plant protection product ensure that the production of MPCA as manufactured and plant protection product is of consistent quality, as set out in the specification set out in point 2.1.2.

2.1.4. In accordance with Article 48 of Regulation (EC) No 1107/2009 and Directive 2001/18/EC of the European Parliament and of the Council ⁽¹⁵⁾, where the micro-organism has been genetically modified no authorisation shall be granted unless:

- the evaluation conducted in accordance with Directive 2001/18/EC as well as the relevant decision taken by the Member States has been provided by the applicant in the dossier, and
- an authorisation is granted in accordance with Part C of Directive 2001/18/EC under which that organism can be released into the environment, or placed on the market in a plant protection product.

2.1.5. Member States shall ensure that adequate quality control measures are applied to ensure the identity of the micro-organism and of the other components of the plant protection product.

⁽¹⁵⁾ Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC (OJ L 106, 17.4.2001, p. 1).

2.2. **Biological and technical properties**

- 2.2.1. No authorisation shall be granted for a plant protection product containing a micro-organism, if the micro-organism that is the active substance is a non-virulent variant of a plant pathogen virus, and the likelihood of regaining virulence and causing adverse effects in target and non-target plants through mutation, after application under the proposed conditions of use (including possible risk mitigation measures), is not negligible.

2.3. **Efficacy and absence of unacceptable effects on plants and plant products**

2.3.1. Efficacy

- 2.3.1.1. No authorisation shall be granted where, on the basis of experience acquired or scientific evidence under normal agricultural, plant health and environmental (including climatic) conditions, the proposed uses include:

- recommendations for the control of or protection against target organisms, or any other effects, which are not considered to cause adverse effects on crops, plants, or plant products; or,
- effects which are not considered to be beneficial under those conditions.

- 2.3.1.2. No authorisation shall be granted when the proposed minimum dose, or a range of minimum doses, necessary to achieve sufficient efficacy against a target pest or any other relevant benefit across the proposed use, i.e. the minimum effective dose, is not justified based on available information or efficacy trials.

- 2.3.1.3. The level, consistency and duration of control or protection or other intended effects shall be at least higher than those observed in the untreated control, and if possible similar to a suitable reference product. Where relevant, yield response when the plant protection product is used, or reduction of loss in storage, shall be quantitatively and/or qualitatively at least higher than those observed for the untreated control, and if possible similar to a suitable reference product. The plant protection product shall be shown to give a defined benefit under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use.

- 2.3.1.4. Conclusions as to the efficacy of the plant protection product shall be valid for all areas and conditions in which it is to be authorised.

- 2.3.1.5. Where the proposed label includes recommendations or requirements for use of the plant protection product with other specified plant protection products and/or adjuvants in a tank mix, spray sequences, or employing other relevant types of applications, or any other recommendations (e.g. weather conditions, soil conditions, irrigation application), Member States shall not accept the recommendations or requirements unless they are justified, if applicable, by supporting information and comply with the principles referred to in points 2.3.1.1 to 2.3.1.4.

- 2.3.1.6. Where negative interactions are expected between the plant protection product containing the micro-organism(s) and other plant protection products, which the label requires to use in tank mix, spray sequences, or employing other relevant types of applications, or other common practices (e.g. conservation biological control), affecting the efficacy of one or the others, Member States shall set appropriate conditions in the authorisation of the plant protection product containing the micro-organism(s), and they shall ensure that a warning labelling phrase is indicating such negative interaction.

2.3.2. Absence of unacceptable effects on plants and plant products

- 2.3.2.1. There shall be no relevant phytotoxic or pathogenic effects on treated plants or plant products, except where the proposed label indicates appropriate limitations of use.

- 2.3.2.2. There shall be no reduction of yield at harvest below that which could be obtained without the use of the plant protection product, unless this reduction is compensated for by other advantages beside the plant protection action, such as an enhancement of the quality of the treated plants or plant products.

- 2.3.2.3. There shall be no unacceptable adverse effects on the quality of treated plants or plant products, except in the case of adverse effects on food and feed transformation processes (e.g. wine making, brewing, bread making, or silage productions as feed) where proposed label specifies that the plant protection product shall not be applied to crops to be used in transformation processes.
- 2.3.2.4. There shall be no unacceptable adverse effects on treated plants or plant products used for propagation or reproduction, such as effects on viability, germination, sprouting, rooting and establishment, except where proposed label specifies that the plant protection product shall not be applied to plants or plant products to be used for propagation or reproduction.
- 2.3.2.5. There shall be no unacceptable impact on succeeding crops, except where proposed label specifies that particular crops, which would be affected, shall not be grown following the treated crop.
- 2.3.2.6. There shall be no unacceptable impact on adjacent crops, except where proposed label specifies that the plant protection product should not be applied when particular sensitive adjacent crops are present.
- 2.3.2.7. Where the proposed label of the plant protection product includes recommendations or requirements for the use with other plant protection products and/or adjuvants as a tank mix, the same criteria referred to in points 2.3.2.1 to 2.3.2.6 apply in relation to the information supplied for the tank mix.
- 2.3.2.8. The proposed instructions for cleaning the application equipment shall be both practical and effective so that they can be applied with ease so as to ensure the removal of residual traces of the plant protection product which could subsequently cause damage.

2.4 Identification/detection and quantification methods

The methods proposed shall reflect the most appropriate techniques. The following conditions shall be met in order to permit validation of the pre-authorisation analytical methods and, where relevant, the analytical methods proposed for post-authorisation control and monitoring purposes.

- 2.4.1. No authorisation shall be granted unless there is an adequate method of sufficient quality to identify and quantify the micro-organism in appropriate microbial unit, and any other components of the plant protection product, such as metabolites of concern, relevant impurities and co-formulants, which are relevant for human and animal health and/or the environment. For a plant protection product containing more than one micro-organism as active substance, the recommended methods should be capable of identifying and determining the content of each micro-organism independently of the others.
- 2.4.2. No authorisation shall be granted unless there is an adequate method for control and monitoring to identify and quantify residues of metabolites of concern for which MRL have been set. These methods shall involve the use of commonly available reagents and equipment. Methods shall be available for analysis of:
- (a) plants, plant products, foodstuffs of plant and animal origin and feeding stuffs if relevant residues occur. Residues are considered relevant if a MRL or a waiting or re-entry safety period or other such precaution is required;
 - (b) soil, water, air and/or body fluids and tissues, in those compartments where toxicologically, ecotoxicologically or environmentally relevant residues occur.

2.5 Impact on human and animal health

2.5.1 Effects on human and animal health arising from the plant protection product

When making a decision on the authorisation of the plant protection product containing (a) micro-organism(s), Member States shall consider possible effects on all human populations, namely professional users, non-professional users and humans exposed directly or indirectly through the diet or the environment, and on animals.

- 2.5.1.1. No authorisation shall be granted if it is concluded that the micro-organism is infective or causes unacceptable adverse health effects in humans or animals under the recommended conditions of use, including in a realistic worst case exposure scenario.
- 2.5.1.2. No authorisation shall be granted if, where relevant based on biological properties of the micro-organism, there are no sufficient treatment options which are effective against the micro-organism.
- 2.5.1.3. No authorisation shall be granted if the plant protection product has unacceptable toxic effects on humans or animals under the proposed conditions of use, including in a realistic worst-case exposure scenario.
- 2.5.1.4. All micro-organisms shall be regarded as potential sensitisers until a test method is validated and unless it is established by means of relevant information that there is no risk of sensitisation. Authorisations granted shall therefore specify, as a non-specific risk mitigation measure, that personal protective equipment (e.g. masks) shall be worn, taking into account the conditions of use, and that the exposure via inhalation to the plant protection product containing a micro-organism shall be minimised. In addition, the proposed conditions of use may require that specific risk mitigation measures are applied as envisaged by Article 6 of Regulation (EC) No 1107/2009.

Where the proposed conditions of use require personal protective equipment, no authorisation shall be granted unless those are:

- effective and in accordance with Regulation (EU) 2016/425 of the European Parliament and of the Council ⁽¹⁶⁾,
 - readily obtainable by the user,
 - feasibly usable under the claimed conditions of use of the plant protection product, taking into account climatic conditions in particular.
- 2.5.1.5. Plant protection products which, because of particular properties, or which, if mishandled or misused, could lead to unacceptable risk, shall be subject to particular restrictions such as restrictions on the size of packaging, preparation type, distribution, use or manner of use. In addition, plant protection products, which are classified as very toxic, shall not be authorised for use by non-professional users.
- 2.5.1.6. Waiting and re-entry safety periods or other precautions shall be established in such a way that no infection of or other adverse effects on bystanders, workers, or residents or animals exposed after application of the plant protection product are expected.
- 2.5.1.7. Waiting and re-entry periods or other precautions to ensure that no infection or adverse effects are expected shall be realistic; if necessary, special precautionary measures shall be prescribed.
- 2.5.1.8. The conditions of authorisation shall be in compliance with Council Directives 98/24/EC ⁽¹⁷⁾ and 89/656/EEC ⁽¹⁸⁾, and Directives 2000/54/EC ⁽¹⁹⁾ and 2004/37/EC of the European Parliament and of the Council. The experimental data and information relevant to the recognition of the symptoms of infection and on the effectiveness of first aid and therapeutic measures provided shall be considered.

⁽¹⁶⁾ Regulation (EU) 2016/425 of the European Parliament and of the Council of 9 March 2016 on personal protective equipment and repealing Council Directive 89/686/EEC (OJ L 81, 31.3.2016, p. 51).

⁽¹⁷⁾ Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC) (OJ L 131, 5.5.1998, p. 11).

⁽¹⁸⁾ Council Directive 89/656/EEC of 30 November 1989 on the minimum health and safety requirements for the use by workers of personal protective equipment at the workplace (third individual directive within the meaning of Article 16 (1) of Directive 89/391/EEC) (OJ L 393, 30.12.1989, p. 18).

⁽¹⁹⁾ Directive 2000/54/EC of the European Parliament and of the Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work (seventh individual directive within the meaning of Article 16(1) of Directive 89/391/EEC) (OJ L 262, 17.10.2000, p. 21).

2.5.2. Effects on human and animal health arising from residues

2.5.2.1. No authorisation shall be granted unless there is sufficient information for plant protection products containing an active substance that is a micro-organism, to decide that there is no harmful effect on human or animal health arising from exposure to the micro-organism and metabolites of concern remaining in or on plants or plant products.

2.5.2.2. No authorisation shall be granted where the treated plants or plant products are intended to be fed to animals and residues occurring have adverse effect on animal health.

2.6. Fate and behaviour in the environment

2.6.1. No authorisation shall be granted if, as a result of the use of the plant protection product under the proposed conditions, a contamination of surface water is expected by metabolites of concern, and:

- the surface water in or from the area of envisaged use is intended for the abstraction of drinking water; and
- this contamination exceeds the parameters or values established in accordance with Directive 2000/60/EC.

2.6.2. No authorisation shall be granted unless the proposed instruction for use of the plant protection product, including procedures for cleaning application equipment, are clearly described, and reduce to the minimum the likelihood of accidental contamination of surface water.

2.6.3. No authorisation shall be granted if, as a result of the use of the plant protection product under the proposed conditions, contamination of groundwater is expected by metabolites of concern, and this contamination exceeds the lower of the following limit values:

- (i) the maximum permissible concentration laid down by Council Directive 98/83/EC ⁽²⁰⁾; or
- (ii) the maximum concentration laid down when approving the active substance in accordance with Regulation (EC) No 1107/2009, based on appropriate data, in particular toxicological data, or, where that concentration has not been laid down, the concentration corresponding to one tenth of the ADI laid down when the active substance was approved ⁽²¹⁾ in accordance with Regulation (EC) No 1107/2009,

unless a consumer risk assessment demonstrates no unacceptable risk or it is scientifically demonstrated that under relevant field conditions the parameters or maximum concentrations is not contravened or exceeded.

2.7. Effects on non-target organisms

Member States shall ensure that the available information is sufficient to permit a decision to be taken as to whether there may be unacceptable effects on non-target organism groups indicated in Section 10 of Part B to the Annex of Regulation (EU) No 284/2013, due to exposure to the plant protection product containing a micro-organism following its intended use.

2.7.1. Where there is a possibility of terrestrial vertebrates being exposed according to the consideration done under point 1.6, no authorisation shall be granted:

- (a) if the micro-organism is pathogenic to terrestrial vertebrates,
- (b) in case of toxic effects of the plant protection product, if the acute and short-term toxicity/exposure ratio for terrestrial vertebrates is less than 10 on the basis of LD₅₀ (acute dietary risk assessment) or the long-term toxicity/exposure ratio is less than 5, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact occurs, directly or indirectly, after use of the plant protection product in accordance with the proposed conditions of use.

⁽²⁰⁾ Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption (OJ L 330, 5.12.1998, p. 32).

⁽²¹⁾ Where the ADI is not available for a metabolite of concern, the default value of 0.1 µg/l applies.

- 2.7.2. Where there is a possibility of aquatic organisms being exposed according to the consideration done under point 1.6, no authorisation shall be granted:
- (a) if the micro-organism is pathogenic to aquatic organisms, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact on aquatic organism populations would occur after use of the plant protection product in accordance with the proposed conditions of use; or
 - (b) in case of toxic effects of the plant protection product if the:
 - toxicity/exposure ratio for fish and *Daphnia* is less than 100 for acute exposure and less than 10 for long-term exposure, or
 - algal growth inhibition/exposure ratio is less than 10,unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact on exposed species occurs, directly or indirectly, after use of the plant protection product in accordance with the proposed conditions of use.
- 2.7.3. Where the possibility of bees to be exposed cannot be excluded according to the consideration done under point 1.6, no authorisation shall be granted:
- (a) if the micro-organism is pathogenic to bees under the proposed conditions of use, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact is expected to occur to the populations of bees after use of the plant protection product in accordance with the proposed conditions of use; or
 - (b) in case of toxic effects of the plant protection product, as defined in the decision-making principles of point 2.5.2.3 of Part A.
- 2.7.4. Where there is a possibility of arthropods other than bees being exposed according to the consideration done under point 1.6, no authorisation shall be granted:
- (a) if the micro-organism is pathogenic to arthropods other than bees, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact is expected to occur to the populations of arthropods other than bees after use of the plant protection product in accordance with the proposed conditions of use; or
 - (b) in case of toxic effects of the plant protection product, as defined in the decision-making principles of point 2.5.2.4 of Part A, unless it is clearly established through an appropriate risk assessment that under field conditions there is no unacceptable impact on arthropods other than bees after use of the plant protection product in accordance with the proposed conditions of use. Any claims for selectivity and proposals for use in integrated pest management systems shall be substantiated by appropriate data.
- 2.7.5. Where the micro-organism was not isolated from the soil and there is a possibility of meso- and macro-organisms in soil being exposed according to the consideration done under point 1.6, no authorisation shall be granted:
- (a) if the micro-organism is pathogenic to meso- and macro-organisms in soil, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact on soil meso- and macro-organism populations occurs after use of the plant protection product in accordance with the proposed conditions of use; or
 - (b) in the case of toxic effects of the plant protection product, if the acute toxicity/exposure ratio for meso- and macro-organisms in soil is less than 10 or the long-term toxicity/exposure ratio is less than 5, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact on soil meso- and macro-organism populations occur after use of the plant protection product in accordance with the proposed conditions of use.

- 2.7.6. If the micro-organism has an herbicidal mode of action or it is closely related to a known plant pathogen, and there is a possibility of terrestrial plants being exposed to the micro-organism according to the consideration done under point 1.6, no authorisation shall be granted if the micro-organism is pathogenic to, or the plant protection product has toxic effects on, terrestrial plants. This criterion applies unless it is clearly established through an appropriate risk assessment that, under field conditions, no unacceptable impact on non-target terrestrial plant populations occurs after use of the plant protection product in accordance with the proposed conditions of use.'
-

COMMISSION IMPLEMENTING REGULATION (EU) 2022/1442**of 31 August 2022****amending Implementing Regulation (EU) 2017/1490 as regards the terms of authorisation of manganese chelate of amino acids hydrate as a feed additive for all animal species****(Text with EEA relevance)**

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition ⁽¹⁾, and in particular Article 13(3) thereof,

Whereas:

- (1) Regulation (EC) No 1831/2003 provides for the authorisation of additives for use in animal nutrition and for the grounds and procedures for granting such an authorisation.
- (2) The use of manganese chelate of amino acids hydrate as a feed additive was authorised for all animal species by Commission Implementing Regulation (EU) 2017/1490 ⁽²⁾.
- (3) In accordance with Article 13(1) of Regulation (EC) No 1831/2003, the Commission requested the European Food Safety Authority ('the Authority') to issue an opinion on whether the authorisation of manganese chelate of amino acids hydrate as a feed additive would still meet the conditions laid down in Article 5 of Regulation (EC) No 1831/2003, if modified as proposed by the applicant. That modification consists in the extension of the protein sources for the amino acids and in the introduction of a minimum specification for free amino acids and of a tighter specification of the manganese content. The request was accompanied by the relevant supporting data.
- (4) The Authority concluded in its opinion of 29 September 2021 ⁽³⁾ that the modifications of the terms of authorisation applied for do not modify the conclusions reached in the previous assessments on the safety for the target species, consumers, environment and efficacy of the feed additive. The Authority concluded that the additive should be considered a skin and eye irritant and a skin sensitiser and stated a potential risk due to exposure by inhalation. Therefore, the Commission considers that appropriate protective measures should be taken to prevent adverse effects on human health, in particular as regards the users of the additive. The Authority does not consider that there is a need for specific requirements of post-market monitoring. It also verified the report on the method of analysis of the feed additive in feed submitted by the Reference Laboratory set up by Regulation (EC) No 1831/2003.
- (5) The assessment of the proposed modifications to the authorisation shows that the conditions for authorisation as provided for in Article 5 of Regulation (EC) No 1831/2003, are satisfied.
- (6) For reasons of clarity, the composition of the additive should be modified to include the indication that the additive consists of a preparation.
- (7) Implementing Regulation (EU) 2017/1490 should therefore be amended accordingly.
- (8) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

⁽¹⁾ OJ L 268, 18.10.2003, p. 29.

⁽²⁾ Commission Implementing Regulation (EU) 2017/1490 of 21 August 2017 concerning the authorisation of manganous chloride tetrahydrate, manganese (II) oxide, manganous sulphate monohydrate, manganese chelate of amino acids hydrate, manganese chelate of protein hydrolysates, manganese chelate of glycine hydrate and dimanganese chloride trihydroxide as feed additives for all animal species (OJ L 216, 22.8.2017, p. 1).

⁽³⁾ EFSA Journal 2021;19(10):6895

HAS ADOPTED THIS REGULATION:

Article 1

In the Annex to Implementing Regulation (EU) 2017/1490, the entry for manganese chelate of amino acids hydrate is amended in accordance with the Annex to this Regulation.

Article 2

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 31 August 2022.

For the Commission
The President
Ursula VON DER LEYEN

ANNEX

Identification number of the additive	Name of the holder of authorisation	Additive	Composition, chemical formula, description, analytical method	Species or category of animal	Maximum age	Minimum content	Maximum content	Other provisions	End of period of authorisation
						Content of element (Mn) mg/kg of complete feed with a moisture content of 12 %			

Category of nutritional additives. Functional group: compound of trace elements

'3b504	-	Manganese chelate of amino acids hydrate	<i>Additive composition</i> Preparation of manganese amino acid complex where the manganese and the amino acids derived from soya protein are chelated via coordinate covalent bonds, as a powder with a minimum content of 8 % manganese.	All animal species	-	-	Fish: 100 (total (?)) Other species: 150 (total (?))	1. The additive shall be incorporated into feed in the form of a premixture. 2. For users of the additive and premixtures, feed business operators shall establish operational procedures and appropriate organisational measures to address the potential risks by inhalation, dermal contact or eyes contact, in particular due to the content of heavy metals, including nickel. Where risks cannot be reduced to an acceptable level by these procedures and measures, the additive and premixtures shall be used with appropriate personal protective equipment, including skin, eye and breathing protection.	11 September 2027
			<i>Characterisation of the active substance</i> Chemical formula: $Mn(x)_{1-3} nH_2O$, x = anion of any amino acid derived from acid hydrolysed soya protein; Maximum 10 % of molecules exceeding 1 500 Da.						

			<i>Analytical method (1)</i> For the quantification of amino acid content in the feed additive: — ion exchange chromatography with post-column derivatisation and optical detection (IEC-VIS/FLD) For the quantification of total manganese in the feed additive: — inductively coupled plasma-atomic emission spectrometry, ICP-AES (EN 15510 or EN 15621) or — atomic absorption spectrometry, AAS (ISO 6869) For the quantification of total manganese in premixtures: — inductively coupled plasma-atomic emission spectrometry, ICP-AES (EN 15510 or EN 15621) or — atomic absorption spectrometry, AAS (ISO 6869) or — inductively coupled plasma-mass spectrometry, ICP-MS (EN 17053) For the quantification of total manganese in feed materials and compound feed: — inductively coupled plasma-atomic emission spectrometry, ICP-AES (EN 15510 or EN 15621) or — atomic absorption spectrometry, AAS (Commission Regulation (EC) No 152/2009 (Annex IV-C) or ISO 6869) or — inductively coupled plasma-mass spectrometry, ICP-MS (EN 17053)						
--	--	--	---	--	--	--	--	--	--

3b504i	-	Manganese chelate of amino acids hydrate	<i>Additive composition</i> Preparation of manganese amino acid complex, where the manganese and the amino acids are chelated via coordinate covalent bonds, as a powder with a content of 8 – 9 % manganese and a minimum of 17 % free amino acids. <i>Characterisation of the active substance:</i> Chemical formula: $Mn(x)_{1-3} \cdot nH_2O$, where x is equal to any amino acid coming from hydrolysed protein sources from feathers or plants; Maximum 10 % of molecules exceeding 1 500 Da. <i>Analytical method ⁽¹⁾</i> For the quantification of amino acid content in the feed additive: — ion exchange chromatography with post-column derivatisation and optical detection (IEC-VIS/FLD), Commission Regulation 152/2009 (Annex III,F) and EN ISO 17180 For the quantification of total manganese in the feed additive: — inductively coupled plasma-atomic emission spectrometry, ICP-AES (EN 15510 or EN 15621) or — atomic absorption spectrometry, AAS (ISO 6869)	All animal species	-	-	Fish: 100 (total ⁽²⁾) Other species: 150 (total ⁽²⁾)	1. The additive shall be incorporated into feed in the form of a premixture. 2. For users of the additive and premixtures, feed business operators shall establish operational procedures and appropriate organisational measures to address the potential risks by inhalation, dermal contact or eyes contact, in particular due to the content of heavy metals, including nickel. Where risks cannot be reduced to an acceptable level by these procedures and measures, the additive and premixtures shall be used with appropriate personal protective equipment, including skin, eye and breathing protection. 3. For additives produced from hydrolysis of animal protein, the animal origin (<i>avian species</i>) shall be indicated on the label of the additive and premixtures	11 September 2027
--------	---	--	--	--------------------	---	---	--	---	-------------------

			For the quantification of total manganese in premixtures: — inductively coupled plasma-atomic emission spectrometry, ICP-AES (EN 15510 or EN 15621) or — atomic absorption spectrometry, AAS (ISO 6869) or — inductively coupled plasma-mass spectrometry, ICP-MS (EN 17053) For the quantification of total manganese in feed materials and compound feed: — inductively coupled plasma-atomic emission spectrometry, ICP-AES (EN 15510 or EN 15621) or — atomic absorption spectrometry, AAS (Commission Regulation (EC) No 152/2009 (Annex IV-C) or ISO 6869) or — inductively coupled plasma-mass spectrometry, ICP-MS (EN 17053)						
--	--	--	---	--	--	--	--	--	--

⁽¹⁾ Details of the analytical methods are available at the following address of the Reference Laboratory: <https://ec.europa.eu/jrc/en/eurl/feed-additives/evaluation-reports>.

⁽²⁾ The amount of inert manganese is not to be taken into consideration for the calculation of the total manganese content of the feed (manganese/kg complete feed).

COMMISSION IMPLEMENTING REGULATION (EU) 2022/1443**of 31 August 2022****concerning the non-approval of calcium propionate as a basic substance 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****(Text with EEA relevance)**

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard 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 and repealing Council Directives 79/117/EEC and 91/414/EEC ⁽¹⁾, and in particular Article 13(2) in conjunction with Article 23(5) thereof,

Whereas:

- (1) On 7 April 2020, the Commission received an application from Niacet B.V. ('the applicant') for the approval of calcium propionate as a basic substance to be used in plant protection as a fungicide in amenity grassland and on flower bulb and flower tuber crops. On 17 September 2021, the Commission received a revised application, which was accompanied by the information required under Article 23(3), second subparagraph, of Regulation (EC) No 1107/2009.
- (2) One relevant evaluation of calcium propionate, carried out in accordance with other Union legislation as referred to in Article 23(2) of Regulation (EC) No 1107/2009 was available, namely, an evaluation from the ANS Panel of the European Food Safety Authority ('the Authority') ⁽²⁾. The outcome of this evaluation has been taken into account by the Authority as well as by the Commission.
- (3) The Commission asked the Authority for scientific assistance. The Authority provided the Commission with a technical report on calcium propionate on 24 August 2021 ⁽³⁾. The Authority concluded that, even though no Union harmonised classification is available in the classification & labelling inventory ⁽⁴⁾ on the European Chemicals Agency (ECHA) website, the published information indicates that calcium propionate has eye-damaging effects. In addition, the Authority considers that further toxicological assessment of the toxicity of calcium propionate by inhalation is necessary if, as foreseen in the application, the substance is intended to be used in a spray application after dilution with water.
- (4) Additionally, the assessment of dermal toxicity, endocrine disrupting properties and immunotoxicity has not been provided.] by the applicant. No robust and exhaustive justifications were mentioned in the application.
- (5) The Authority also noted that an assessment of operator, worker, bystander and resident exposure is needed for each of the uses included in the application, but this was not provided, nor was a risk assessment of the impurities present in the basic substance.
- (6) Moreover, the Authority indicated that the potential for a build-up of the impurities lead, mercury and arsenic in the environment remains an open issue for the proposed use pattern, which requires a high application frequency.

⁽¹⁾ OJ L 309, 24.11.2009, p. 1.

⁽²⁾ EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources Added to Food), 2014. Scientific Opinion on the re-evaluation of propionic acid (E 280), sodium propionate (E 281), calcium propionate (E 282) and potassium propionate (E 283) as food additives. EFSA Journal 2014; 12(7):3779, 45 pp. doi:10.2903/j.efsa.2014.3779.

⁽³⁾ EFSA (European Food Safety Authority), 2021. Technical report on the outcome of the consultation with Member States and EFSA on the basic substance application for approval of calcium propionate to be used in plant protection as a fungicide in amenity grassland and on flower bulb and flower tuber crops. EFSA supporting publication 2021:EN-6834. 87pp. doi:10.2903/sp.efsa.2021.EN-6834.

⁽⁴⁾ C&L Inventory (europa.eu).

- (7) Finally, the Authority concluded that the intended uses and doses raise a concern regarding possible adverse effects of calcium propionate on non-target organisms, including bees and non-target arthropods, earthworms and other soil macro-organisms, soil micro-organisms, and organisms involved in biological methods of sewage treatment.
- (8) The Commission presented the review report, concluding that the approval criteria for basic substances are not fulfilled in the case of calcium propionate and that it is therefore appropriate not to approve it as a basic substance, as well as a draft of this Implementing Regulation to the Standing Committee on Plants, Animals, Food and Feed on 27 January 2022 and 18 May 2022, respectively.
- (9) The Commission invited the applicant to submit its comments on the technical report of the Authority and on the draft review report of the Commission. The applicant submitted its comments, which have been carefully examined.
- (10) However, despite the arguments put forward by the applicant, the concerns related to the substance could not be eliminated.
- (11) Consequently, it has not been established that the conditions laid down in Article 23 of Regulation (EC) No 1107/2009 are satisfied. It is therefore appropriate not to approve calcium propionate as a basic substance.
- (12) This Regulation does not prevent the submission of a further application for the approval of calcium propionate as a basic substance in accordance with Article 23(3) of Regulation (EC) No 1107/2009.
- (13) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

HAS ADOPTED THIS REGULATION:

Article 1

The substance calcium propionate is not approved as a basic substance.

Article 2

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 31 August 2022.

For the Commission
The President
Ursula VON DER LEYEN

COMMISSION IMPLEMENTING REGULATION (EU) 2022/1444**of 31 August 2022****concerning the non-approval of black soap E470a as a basic substance 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****(Text with EEA relevance)**

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard 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 and repealing Council Directives 79/117/EEC and 91/414/EEC ⁽¹⁾, and in particular Article 13(2) in conjunction with Article 23(5) thereof,

Whereas:

- (1) On 7 February 2020, the Commission received an application from the Institut Technique de l'Agriculture Biologique ('the applicant') for the approval of black soap E470a as a basic substance to be used in plant protection as an insecticide on arable crops, ornamental flower beds, house plants, plant trees, ornamental woody plants, ornamental crops, vegetables crops, berry fruit crops, pome fruit crops, stone fruit and olive tree crops; and as a fungicide on vegetables and ornamental plant crops. In September 2020 and February 2021, the Commission received revised applications, which were accompanied by the information required under Article 23(3), second subparagraph, of Regulation (EC) No 1107/2009.
- (2) Two relevant evaluations, carried out in accordance with other Union legislation as referred to in Article 23(2) of Regulation (EC) No 1107/2009, were available, namely, an evaluation from the ANS Panel of the European Food Safety Authority ('the Authority') ⁽²⁾ and a conclusion on the peer review from the Authority ⁽³⁾. The outcome of these evaluations have been taken into account by the Authority as well as by the Commission.
- (3) The Commission asked the Authority for scientific assistance. The Authority provided the Commission with a technical report on black soap E470a on 12 August 2021 ⁽⁴⁾. The Authority concluded that, even though no Union harmonised classification is available in the classification & labelling inventory ⁽⁵⁾ on the European Chemicals Agency (ECHA) website, the main hazard associated with black soap E470a is its irritation/corrosive properties.
- (4) The Authority also noted that the applicant had provided no evidence that the substance for which the approval is sought, is placed on the market in products that fulfil the food additive E470a specifications.

⁽¹⁾ OJ L 309, 24.11.2009, p. 1.

⁽²⁾ EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food), Younes M, Aggett P, Aguilar F, Crebelli R, Dusemund B, Filipic M, Frutos MJ, Galtier P, Gott D, Gundert-Remy U, Kuhnle GG, Leblanc J-C, Lillegaard IT, Moldeus P, Mortensen A, Oskarsson A, Stankovic I, Waalkens-Berendsen I, Woutersen RA, Wright M, Boon P, Chrysafidis D, Gürtler R, Mosesso P, Parent-Massin D, Tobback P, Cascio C, Rincon AM and Lambré C, 2018. Scientific Opinion on the re-evaluation of sodium, potassium and calcium salts of fatty acids (E 470a) and magnesium salts of fatty acids (E 470b) as food additives. EFSA Journal 2018;16(3):5180, 34 pp. DOI: <https://doi.org/10.2903/j.efsa.2018.5180>.

⁽³⁾ EFSA (European Food Safety Authority), 2013. Conclusion on the peer review of the pesticide risk assessment of the active substance Fatty acids C7 to C18 (approved under Regulation (EC) No 1107/2009 as Fatty acids C7 to C20). EFSA Journal 2013;11(1):3023. [62 pp.] doi:10.2903/j.efsa.2013.3023.

⁽⁴⁾ EFSA (European Food Safety Authority), 2021. Technical report on the outcome of the consultation with Member States and EFSA on the basic substance application for approval of black soap E470a to be used in plant protection as an insecticide on arable crops, ornamental flower beds, house plants, plant trees, ornamental woody plants, ornamental crops, vegetables crops, berry fruit crops, pome fruit crops, stone fruit and olive tree crops; and as a fungicide on vegetables and ornamental plant crops. EFSA supporting publication 2021:EN-6834. 87pp. doi:10.2903/sp.efsa.2021.EN-6834.

⁽⁵⁾ C&L Inventory (europa.eu).

- (5) Additionally, due to the absence of data, the Authority could not conclude its assessment of non-dietary risks for operators, workers, bystanders and residents. Moreover, a quantitative consumer risk assessment through dietary intake and drinking water could not be finalised.
- (6) The Commission presented the review report, concluding that the approval criteria for basic substances are not fulfilled in the case of black soap E470a and that it is therefore appropriate not to approve it as a basic substance, as well as a draft of this Implementing Regulation to the Standing Committee on Plants, Animals, Food and Feed on 30 March 2022 and 18 May 2022, respectively.
- (7) The Commission invited the applicant to submit its comments on the technical report of the Authority and on the Commission's draft review report. The applicant submitted its comments, which have been carefully examined.
- (8) However, despite the arguments put forward by the applicant, the concerns related to the safety of using this substance with regard to the protection of human health could not be eliminated.
- (9) Consequently, it has not been established that the conditions laid down in Article 23 of Regulation (EC) No 1107/2009 are satisfied. It is therefore appropriate not to approve black soap E470a as a basic substance.
- (10) This Regulation does not prevent the submission of a further application for the approval of black soap E470a as a basic substance in accordance with Article 23(3) of Regulation (EC) No 1107/2009.
- (11) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

HAS ADOPTED THIS REGULATION:

Article 1

The substance black soap E470a is not approved as a basic substance.

Article 2

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 31 August 2022.

For the Commission
The President
Ursula VON DER LEYEN

COMMISSION IMPLEMENTING REGULATION (EU) 2022/1445**of 31 August 2022****amending Implementing Regulation (EU) 2018/1039 as regards the terms of authorisation of copper (II) chelate of amino acids hydrate as a feed additive for all animal species****(Text with EEA relevance)**

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition ⁽¹⁾, and in particular Article 13(3) thereof,

Whereas:

- (1) Regulation (EC) No 1831/2003 provides for the authorisation of additives for use in animal nutrition and for the grounds and procedures for granting such an authorisation.
- (2) The use of copper (II) chelate of amino acids hydrate as a feed additive was authorised for all animal species by Commission Implementing Regulation (EU) 2018/1039 ⁽²⁾.
- (3) In accordance with Article 13(1) of Regulation (EC) No 1831/2003, the Commission requested the European Food Safety Authority ('the Authority') to issue an opinion on whether the authorisation of copper (II) chelate of amino acids hydrate as a feed additive would still meet the conditions laid down in Article 5 of Regulation (EC) No 1831/2003, if modified as proposed by the applicant. That modification consists in the extension of the protein sources for the amino acids and in the introduction of a minimum specification for free amino acids and of a tighter specification of the copper content. The request was accompanied by the relevant supporting data.
- (4) The Authority concluded in its opinion of 29 September 2021 ⁽³⁾ that the modifications of the terms of authorisation applied for do not modify the conclusions reached in the previous assessments on the safety for the target species, consumers, environment and efficacy of the additive above. The Authority concluded that the additive should be considered a skin and eye irritant and a skin sensitiser and stated a potential risk due to exposure by inhalation. Therefore, the Commission considers that appropriate protective measures should be taken to prevent adverse effects on human health, in particular as regards the users of the additive. The Authority does not consider that there is a need for specific requirements of post-market monitoring. It also verified the report on the method of analysis of the feed additive in feed submitted by the Reference Laboratory set up by Regulation (EC) No 1831/2003.
- (5) The assessment of the proposed modifications to the authorisation shows that the conditions for authorisation as provided for in Article 5 of Regulation (EC) No 1831/2003 are satisfied.
- (6) For reasons of clarity, the composition of the additive should be modified to include the indication that the additive consists of a preparation.
- (7) Implementing Regulation (EU) 2018/1039 should therefore be amended accordingly.

⁽¹⁾ OJ L 268, 18.10.2003, p. 29.

⁽²⁾ Commission Implementing Regulation (EU) 2018/1039 of 23 July 2018 concerning the authorisation of Copper(II) diacetate monohydrate, Copper(II) carbonate dihydroxy monohydrate, Copper(II) chloride dihydrate, Copper(II) oxide, Copper(II) sulphate pentahydrate, Copper(II) chelate of amino acids hydrate, Copper(II) chelate of protein hydrolysates, Copper(II) chelate of glycine hydrate (solid) and Copper(II) chelate of glycine hydrate (liquid) as feed additives for all animal species and amending Regulations (EC) No 1334/2003, (EC) No 479/2006 and (EU) No 349/2010 and Implementing Regulations (EU) No 269/2012, (EU) No 1230/2014 and (EU) 2016/2261 (OJ L 186, 24.7.2018, p. 3).

⁽³⁾ EFSA Journal 2021;19(10):6896.

- (8) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

HAS ADOPTED THIS REGULATION:

Article 1

In the Annex to Implementing Regulation (EU) 2018/1039, the entry of copper (II) chelate of amino acids hydrate is amended in accordance with the Annex to this Regulation.

Article 2

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 31 August 2022.

For the Commission
The President
Ursula VON DER LEYEN

ANNEX

Identification number of the additive	Name of the holder of authorisation	Additive	Composition, chemical formula, description, analytical method	Species or category of animal	Maximum age	Minimum content	Maximum content	Other provisions	End of period of authorisation
						Content of element (Cu) in mg/kg of complete feed with a moisture content of 12 %			
Category of nutritional additives. Functional group: compounds of trace elements									
‘3b406	-	Copper (II) chelate of amino acids hydrate	Additive composition Preparation of copper(II) amino acid complex where the copper and the amino acids derived from soya protein are chelated via coordinate covalent bonds, as a powder with a minimum content of 10 % copper	All animal species	-	-	Bovines before the start of rumination: 15 (total); Other bovines: 30 (total). Ovines: 15 (total). Caprines: 35 (total) Piglets: — suckling and weaned up to 4 weeks after weaning: 150 (total). — from 5 th week after weaning up to 8 weeks after weaning: 100 (total). Crustaceans: 50 (total). Other animals: 25 (total).	1. The additive shall be incorporated into feed in the form of a premixture. 2. The following words shall be included in the labelling: — For feed for ovines, if the level of copper in the feed exceeds 10 mg/kg: ‘The level of copper in this feed may cause poisoning in certain breeds of sheep.’ — For feed for bovines after the start of rumination, if the level of copper in the feed is less than 20 mg/kg: ‘The level of copper in this feed may cause copper deficiencies in cattle grazing pastures with high contents of molybdenum or sulphur.’ 3. For users of the additive and premixtures, feed business operators shall establish operational procedures and appropriate organisational measures to address the potential risks by inhalation, dermal contact or eyes contact, in particular due to the content of heavy metals. Where	13 August 2028
			Characterisation of the active substance Chemical formula: Cu(x) ₁₋₃ · nH ₂ O, x = anion of any amino acid from soya protein hydrolysate. Maximum 10 % of molecules exceeding 1 500 Da.						
			Analytical methods ⁽¹⁾ For the quantification of amino acid content in the feed additive: — ion exchange chromatography with post-column derivatisation and optical detection (IEC-VIS/FLD)						

			For the quantification of total copper in the feed additive: — inductively coupled plasma-atomic emission spectrometry, ICP-AES (EN 15510 or EN 15621) or — atomic absorption spectrometry, AAS (ISO 6869) For the quantification of total copper in premixtures: — inductively coupled plasma-atomic emission spectrometry, ICP-AES (EN 15510 or EN 15621) or — atomic absorption spectrometry, AAS (ISO 6869) or — inductively coupled plasma-mass spectrometry, ICP-MS (EN 17053) For the quantification of total copper in feed materials and compound feed: — inductively coupled plasma-atomic emission spectrometry, ICP-AES (EN 15510 or EN 15621) or — atomic absorption spectrometry, AAS (Commission Regulation (EC) No 152/2009 (Annex IV-C) or ISO 6869) or — inductively coupled plasma-mass spectrometry, ICP-MS (EN 17053)					risks cannot be reduced to an acceptable level by these procedures and measures, the additive and premixtures shall be used with appropriate personal protective equipment.	
--	--	--	--	--	--	--	--	--	--

3b406i	-	Copper (II) chelate of amino acids hydrate	<i>Additive composition</i> Preparation of copper (II) amino acid complex, where the copper and the amino acids are chelated via coordinate covalent bonds, as a powder with a content of 10-11 % copper and a minimum of 18 % free amino acids. <i>Characterisation of the active substance</i> Chemical formula: $\text{Cu}(\text{x})_{1-3} \cdot \text{nH}_2\text{O}$, where x is equal to any amino acid coming from hydrolysed protein sources from feathers or plants; Maximum 10 % of molecules exceeding 1 500 Da. <i>Analytical methods</i> ⁽¹⁾ For the quantification of amino acid content in the feed additive: — ion exchange chromatography with post-column derivatisation and optical detection (IEC-VIS/FLD), Commission Regulation 152/2009 (Annex III,F) and EN ISO 17180 For the quantification of total copper in the feed additive: — inductively coupled plasma-atomic emission spectrometry, ICP-AES (EN 15510 or EN 15621) or — atomic absorption spectrometry, AAS (ISO 6869)	All animal species	-	-	Bovines before the start of rumination: 15 (total); Other bovines: 30 (total). Ovines: 15 (total). Caprines: 35 (total) Piglets: suckling and weaned up to 4 weeks after weaning: 150 (total). from 5th week after weaning up to 8 weeks after weaning: 100 (total). Crustaceans: 50 (total). Other animals: 25 (total).	- The additive shall be incorporated into feed in the form of a premixture. - The following words shall be included in the labelling: - For feed for ovines, if the level of copper in the feed exceeds 10 mg/kg: 'The level of copper in this feed may cause poisoning in certain breeds of sheep.' - For feed for bovines after the start of rumination, if the level of copper in the feed is less than 20 mg/kg: 'The level of copper in this feed may cause copper deficiencies in cattle grazing pastures with high contents of molybdenum or sulphur.' - For users of the additive and premixtures, feed business operators shall establish operational procedures and appropriate organisational measures to address the potential risks by inhalation, dermal contact or eyes contact, in particular due to the content of heavy metals. Where risks cannot be reduced to an acceptable level by these procedures and measures, the additive and premixtures shall be used with appropriate personal protective equipment including skin, eye and breathing protection.	13 August 2028'
--------	---	--	--	--------------------	---	---	---	--	-----------------

			For the quantification of total copper in premixtures: — inductively coupled plasma-atomic emission spectrometry, ICP-AES (EN 15510 or EN 15621) or — atomic absorption spectrometry, AAS (ISO 6869) or — inductively coupled plasma-mass spectrometry, ICP-MS (EN 17053) For the quantification of total copper in feed materials and compound feed: — inductively coupled plasma-atomic emission spectrometry, ICP-AES (EN 15510 or EN 15621) or — atomic absorption spectrometry, AAS (Commission Regulation (EC) No 152/2009 (Annex IV-C) or ISO 6869) or — inductively coupled plasma-mass spectrometry, ICP-MS (EN 17053)				4. For additives produced from hydrolysis of animal protein, the animal origin (<i>avian species</i>) shall be indicated on the label of the additive and premixtures.'	
--	--	--	---	--	--	--	--	--

(¹) Details of the analytical methods are available at the following address of the Reference Laboratory: <https://ec.europa.eu/jrc/en/eurl/feed-additives/evaluation-reports>

CORRIGENDA

Corrigendum to Directive (EU) 2022/362 of the European Parliament and of the Council of 24 February 2022 amending Directives 1999/62/EC, 1999/37/EC and (EU) 2019/520, as regards the charging of vehicles for the use of certain infrastructures

(Official Journal of the European Union L 69 of 4 March 2022)

On page 15, Article 1, point 3, amending Article 7a(3), fourth subparagraph, second sentence, of Directive 1999/62/EC:

for: 'However, they shall comply with the limits set out in the first subparagraph as well as with the second subparagraph as soon as substantially amended charging arrangements enter into force and, at the latest, by 25 March 2030.'

read: 'However, they shall comply with the limits set out in the first subparagraph as well as with the third subparagraph as soon as substantially amended charging arrangements enter into force and, at the latest, by 25 March 2030.'

Corrigendum to Council Regulation (EU) 2022/515 of 31 March 2022 amending Regulation (EU) 2022/109 fixing for 2022 the fishing opportunities for certain fish stocks and groups of fish stocks applicable in Union waters and for Union fishing vessels in certain non-Union waters

(Official Journal of the European Union L 104 of 1 April 2022)

On page 32, Annex I, point (2), stock SRX/89-C., tables in note (2)

for:	‘Species: Undulate ray Raja undulata		Zone: Union waters of 8 (RJU/8-C.)
	Belgium	0	Precautionary TAC
	France	13	
	Portugal	10	
	Spain	10	
	Union	33	
	United Kingdom	0	
	TAC	66	
	Species: Undulate ray Raja undulata		Zone: Union waters of 9 (RJU/9-C.)
	Belgium	0	Precautionary TAC'
read:	France	20	
	Portugal	15	
	Spain	15	
	Union	50	
	United Kingdom	0	
	TAC	100	
	‘Species: Undulate ray Raja undulata		Zone: Union waters of 8 (RJU/8-C.)
	Belgium	0	Precautionary TAC
	France	13	
	Portugal	10	
	Spain	10	
	Union	33	
	United Kingdom	0	
	TAC	33	

Species:	Undulate ray <i>Raja undulata</i>	Zone:	Union waters of 9 (RJU/9-C.)
Belgium	0	Precautionary TAC'	
France	20		
Portugal	15		
Spain	15		
Union	50		
United Kingdom	0		
TAC	50		

Corrigendum to Regulation (EU) 2021/2115 of the European Parliament and of the Council of 2 December 2021 establishing rules on support for strategic plans to be drawn up by Member States under the common agricultural policy (CAP Strategic Plans) and financed by the European Agricultural Guarantee Fund (EAGF) and by the European Agricultural Fund for Rural Development (EAFRD) and repealing Regulations (EU) No 1305/2013 and (EU) No 1307/2013

(Official Journal of the European Union L 435 of 6 December 2021)

On page 153, footnote 1, third indent:

- for:* ‘— Regulation (EC) No 853/2004: Article 3(1), Annex III Section IX Chapter 1 (I-1 b, c, d, e; I-2 a (i, ii, iii), b (i, ii), c; I-3; I-4; I-5; II-A 1, 2, 3, 4; II-B 1(a, d), 2, 4 (a, b)), Annex III Section X Chapter 1(1),’
- read:* ‘— Regulation (EC) No 853/2004: Article 3(1), Annex III Section IX Chapter I (I-1 b, c, d, e; I-2 a (i, ii, iii), b (i, ii), c; I-3; I-4; I-5; II-A 1, 2, 3, 4; II-B 1(a, d), 2, 4 (a, b)), Annex III Section X Chapter I(1),’.
-

ISSN 1977-0677 (electronic edition)
ISSN 1725-2555 (paper edition)



Publications Office
of the European Union
L-2985 Luxembourg
LUXEMBOURG

EN