ANNEX II

Procedure and criteria for the approval of active substances, safeners and synergists pursuant to Chapter II

1. Evaluation

1.1. During the process of evaluation and decision-making provided for in Articles 4 to 21, the **[**[F1]assessing competent authority**]** shall cooperate with applicants to resolve any questions on the dossier quickly or to identify at an early stage any further explanations or additional studies necessary for the evaluation of the dossier, including information to eliminate the need for a restriction of the approval, 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 satisfaction of the requirements of this Regulation.

Textual Amendments

F1 Words in Annex 2 point 1.1 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(a)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

1.2. The evaluation by the **[**[F2]assessing competent authority**]** must be based on scientific principles and be made with the benefit of expert advice.

Textual Amendments

F2 Words in Annex 2 point 1.2 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(b)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

[[F3]1.2A In this Annex, "the assessing competent authority" has the meaning given by Article 7(1C) or 15(1A) as the case may be.**]**

Textual Amendments

F3 Annex 2 point 1.2A inserted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(c)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

1.3. [F4] . . . . . .

Textual Amendments

F4 Annex 2 point 1.3 omitted (31.12.2020) by virtue of The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(d)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

2. General decision-making criteria

2.1. Article 4 shall only be considered as complied with, where, on the basis of the dossier submitted, authorisation **[**[F5]by at least one competent authority**]** is expected to be

possible for at least one plant protection product containing that active substance for at least one of the representative uses.

Textual Amendments

F5 Words in Annex 2 point 2.1 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(e)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

2.2. Submission of further information

In principle an active substance, safener or synergist shall only be approved where a complete dossier is submitted.

In exceptional cases an active substance, safener or synergist may be approved even though certain information is still to be submitted where:

(a) the data requirements have been amended or refined after the submission of the dossier; or

(b) the information is considered to be confirmatory in nature, as required to increase confidence in the decision.

2.3. Restrictions on approval

Where necessary, the approval may be subject to conditions and restrictions as referred to in **[**F6Article 6(1)**]**.

Where the **[**F7assessing competent authority**]** considers that the dossier provided lacks certain information, to the effect that the active substance could only be approved subject to restrictions, it shall contact the applicant at an early stage to obtain more information which may possibly enable these restrictions to be removed.

Textual Amendments

F6 Words in Annex 2 point 2.3 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(f)(i)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

F7 Words in Annex 2 point 2.3 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(f)(ii)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

3. Criteria for the approval of an active substance

3.1. Dossier

The dossiers submitted pursuant to **[**F8Article 7(1D)**]** shall contain the information needed to establish, where relevant, Acceptable Daily Intake (ADI), Acceptable Operator Exposure Level (AOEL) and Acute Reference Dose (ARfD).

In the case of an active substance, safener or synergist for which one or more representative uses includes use on feed or food crops or leads indirectly to residues in food or feed, the dossier submitted pursuant to **[**F8Article 7(1D)**]** shall contain the information necessary to carry out a risk assessment and for enforcement purposes.

The dossier shall in particular:

(a) permit any residue of concern to be defined;

(b) reliably predict the residues in food and feed, including succeeding crops;

(c) reliably predict, where relevant, the corresponding residue level reflecting the effects of processing and/or mixing;

(d) permit a maximum residue level to be defined and to be determined by appropriate methods in general use for the commodity and, where appropriate, for products of animal origin where the commodity or parts of it is fed to animals;

(e) permit, where relevant, concentration or dilution factors due to processing and/or mixing to be defined.

The dossier submitted pursuant to **[**[F8]Article 7(1D)**]** shall be sufficient to permit, where relevant, an estimate of the fate and distribution of the active substance in the environment, and its impact on non-target species.

Textual Amendments

F8 Words in Annex 2 point 3.1 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(g)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

3.2. Efficacy

An active substance alone or associated with a safener or synergist shall only be approved where it has been established for one or more representative uses that the plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use is sufficiently effective. This requirement shall be evaluated in accordance with the uniform principles for evaluation and authorisation of plant protection products referred to in **[**[F9]Article 29(6)(a) in relation to the relevant constituent territory**]**.

Textual Amendments

F9 Words in Annex 2 point 3.2 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(h)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

3.3. Relevance of metabolites

Where applicable the documentation submitted shall be sufficient to permit the establishment of the toxicological, ecotoxicological or environmental relevance of metabolites.

3.4. Composition of the active substance, safener or synergist

3.4.1. The specification shall define the minimum degree of purity, the identity and maximum content of impurities and, where relevant, of isomers/diastereo-isomers and additives, and the content of impurities of toxicological, ecotoxicological or environmental concern within acceptable limits.

3.4.2. 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.

3.5. Methods of analysis

3.5.1. The methods of analysis of the active substance, safener or synergist 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 the active substance 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 has been carried out in accordance with the uniform principles for evaluation and authorisation of plant protection products referred to in **[**F10Article 29(6) (a) in relation to the relevant constituent territory**]**.

Textual Amendments

F10 Words in Annex 2 point 3.5.3 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(h)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

3.6. Impact on human health

3.6.1. Where relevant, an ADI, AOEL and ARfD shall be established. When establishing such values an appropriate safety margin of at least 100 shall be ensured taking into account the type and severity of effects and the vulnerability of specific groups of the population. When the critical effect is judged of particular significance, such as developmental neurotoxic or immunotoxic effects, an increased margin of safety shall be considered, and applied if necessary.

3.6.2. An active substance, safener or synergist shall only be approved if, on the basis of assessment of higher tier genotoxicity testing carried out in accordance with the data requirements for the active substances, safeners or synergists and other available data and information, including a review of the scientific literature F11... , it is not or has not to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as mutagen category 1A or 1B.

Textual Amendments

F11 Words in Annex 2 point 3.6.2 omitted (31.12.2020) by virtue of The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(i)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

3.6.3. An active substance, safener or synergist shall only be approved, if, on the basis of assessment of carcinogenicity testing carried out in accordance with the data requirements for the active substances, safener or synergist **[**F12in relation to the relevant constituent territory**]** and other available data and information, including a review of the scientific literature F13... , it is not or has not to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as carcinogen category 1A or 1B, unless the exposure of humans to that active substance, safener or synergist in a

plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with **[**F14Article 18A of Regulation (EC) No 396/2005 in relation to the relevant constituent territory**]**.

Textual Amendments

F12 Words in Annex 2 point 3.6.3 inserted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(j)(i)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

F13 Words in Annex 2 point 3.6.3 omitted (31.12.2020) by virtue of The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(j)(ii)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

F14 Words in Annex 2 point 3.6.3 substituted (31.12.2020) by The Pesticides (Maximum Residue Levels) (Amendment etc.) (EU Exit) Regulations 2019 (S.I. 2019/557), regs. 1(1), **13(2)(a)**; 2020 c. 1, Sch. 5 para. 1(1)

3.6.4. An active substance, safener or synergist shall only be approved if, on the basis of assessment of reproductive toxicity testing carried out in accordance with the data requirements for the active substances, safeners or synergists **[**F15in relation to the relevant constituent territory**]** and other available data and information, including a review of the scientific literature F16... , it is not or has not to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 1A or 1B, unless the exposure of humans to that active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with **[**F17Article 18A of Regulation (EC) No 396/2005 in relation to the relevant constituent territory**]**.

Textual Amendments

F15 Words in Annex 2 point 3.6.4 inserted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(k)(i)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

F16 Words in Annex 2 point 3.6.4 omitted (31.12.2020) by virtue of The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(k)(ii)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

F17 Words in Annex 2 point 3.6.4 substituted (31.12.2020) by The Pesticides (Maximum Residue Levels) (Amendment etc.) (EU Exit) Regulations 2019 (S.I. 2019/557), regs. 1(1), **13(2)(b)**; 2020 c. 1, Sch. 5 para. 1(1)

3.6.5. An active substance, safener or synergist shall only be approved if, on the basis of the assessment of **[**F18nationally**]** or internationally agreed test guidelines or other available data and information, including a review of the scientific literature, reviewed by the **[**F19competent authority**]**, it is not considered to have endocrine disrupting properties that may cause adverse effect in humans, unless the exposure of humans to that active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other

conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with point (b) of Article 18(1) of Regulation (EC) No 396/2005.

Textual Amendments

F18 Word in Annex 2 point 3.6.5 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(l)(i)(aa)** (with Sch. 1) (as amended by S.I. 2019/1410, regs. 1(2), **6(4)(a)**); 2020 c. 1, **Sch. 5 para. 1(1)**

F19 Words in Annex 2 point 3.6.5 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(l)(i)(bb)** (with Sch. 1) (as amended by S.I. 2019/1410, regs. 1(2), **6(4)(a)**); 2020 c. 1, **Sch. 5 para. 1(1)**

By 14 December 2013, the Commission shall present to the Standing Committee on the Food Chain and Animal Health a draft of the measures concerning specific scientific criteria for the determination of endocrine disrupting properties to be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 79(4).

F20 . . . . . .

Textual Amendments

F20 Words in Annex 2 point 3.6.5 omitted (31.12.2020) by virtue of The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(l)(ia)** (with Sch. 1) (as amended by S.I. 2019/1410, regs. 1(2), **6(4)(a)**); 2020 c. 1, **Sch. 5 para. 1(1)**

F20 . . . . . .

[F21 From **[X1**10 November 2018**]**, an active substance, safener or synergist shall be considered as having endocrine disrupting properties that may cause adverse effect in humans if, based on points (1) to (4) of the sixth paragraph, it is a substance that meets all of the following criteria, unless there is evidence demonstrating that the adverse effects identified are not relevant to humans:

(1) it shows an adverse effect in an intact organism or its progeny, which is a change in the morphology, physiology, growth, development, reproduction or life span of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences;

(2) it has an endocrine mode of action, i.e. it alters the function(s) of the endocrine system;

(3) the adverse effect is a consequence of the endocrine mode of action.

Editorial Information

X1 Substituted by Corrigendum to Commission Regulation (EU) 2018/605 of 19 April 2018 amending Annex II to Regulation (EC) No 1107/2009 by setting out scientific criteria for the determination of endocrine disrupting properties (Official Journal of the European Union L 101 of 20 April 2018).

Textual Amendments

F21 Inserted by Commission Regulation (EU) 2018/605 of 19 April 2018 amending Annex II to Regulation (EC) No 1107/2009 by setting out scientific criteria for the determination of endocrine disrupting properties (Text with EEA relevance).

The identification of an active substance, safener or synergist as having endocrine disrupting properties that may cause adverse effect in humans in accordance with the fifth paragraph shall be based on all of the following points:

(1) all available relevant scientific data (in vivo studies or adequately validated alternative test systems predictive of adverse effects in humans or animals; as well as in vivo, in vitro, or, if applicable, in silico studies informing about endocrine modes of action):

(a) scientific data generated in accordance with internationally agreed study protocols, in particular those listed in **[**[F22]guidance issued**]** in accordance with this Regulation;

(b) other scientific data selected applying a systematic review methodology, in particular following guidance on literature data **[**[F23]issued**]**, in accordance with this Regulation;

(2) an assessment of the available relevant scientific data based on a weight of evidence approach in order to establish whether the criteria set out in the fifth paragraph are fulfilled; in applying the weight of evidence determination, the assessment of the scientific evidence shall, in particular, consider all of the following factors:

(a) both positive and negative results;

(b) the relevance of the study designs, for the assessment of adverse effects and of the endocrine mode of action;

(c) the quality and consistency of the data, considering the pattern and coherence of the results within and between studies of a similar design and across different species;

(d) the route of exposure, toxicokinetic and metabolism studies;

(e) the concept of the limit dose, and international guidelines on maximum recommended doses and for assessing confounding effects of excessive toxicity;

(3) using a weight of evidence approach, the link between the adverse effect(s) and the endocrine mode of action shall be established based on biological plausibility, which shall be determined in the light of current scientific knowledge and under consideration of internationally agreed guidelines;

(4) adverse effects that are non-specific secondary consequences of other toxic effects shall not be considered for the identification of the substance as endocrine disruptor.**]**

Textual Amendments

F22 Words in Annex 2 point 3.6.5 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(l)(ii)(aa)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

F23 Words in Annex 2 point 3.6.5 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(l)(ii)(bb)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

3.7. Fate and behaviour in the environment

3.7.1. An active substance, safener or synergist shall only be approved where it is not considered to be a persistent organic pollutant (POP).

A substance that fulfils all three of the criteria of the points below is a POP.

3.7.1.1. Persistence

An active substance, safener or synergist fulfils the persistence criterion where there is evidence that the time it takes for a degradation of 50 % (DT50) in water is greater than 2 months, or that its DT50 in soil is greater than 6 months, or that its DT50 in sediment is greater than 6 months.

3.7.1.2. Bioaccumulation

An active substance, safener or synergist fulfils the bioaccumulation criterion where there is:

— evidence that its bio-concentration factor or bioaccumulation factor in aquatic species is greater than 5 000 or, in the absence of such data, that the partition coefficient n-octanol/water (log Ko/w) is greater than 5, or

— evidence that the active substance, safener or synergist present other reasons for concern, such as high bioaccumulation in other non-target species, high toxicity or ecotoxicity.

3.7.1.3. Potential for long-range environmental transport:

An active substance, safener or synergist fulfils the potential for long-range environmental transport criterion where:

— measured levels of the active substance, safener or synergist in locations distant from the sources of its release are of potential concern,

— monitoring data show that long-range environmental transport of the active substance, safener or synergist, with the potential for transfer to a receiving environment, may have occurred via air, water or migratory species, or

— environmental fate properties and/or model results demonstrate that the active substance, safener or synergist has a potential for long-range environmental transport through air, water or migratory species, with the potential for transfer to a receiving environment in locations distant from the sources of its release. For an active substance safener or synergist that migrates significantly through the air, its DT50 in air is to be greater than 2 days.

3.7.2. An active substance, safener or synergist shall only be approved if it is not considered to be a persistent, bioaccumulative and toxic (PBT) substance.

A substance that fulfils all three of the criteria of the points below is a PBT substance.

3.7.2.1. Persistence

An active substance, safener or synergist fulfils the persistence criterion where:

— the half-life in marine water is higher than 60 days,

— the half-life in fresh or estuarine water is higher than 40 days,

— the half-life in marine sediment is higher than 180 days,

— the half-life in fresh or estuarine water sediment is higher than 120 days, or

— the half-life in soil is higher than 120 days.

Assessment of persistency in the environment shall be based on available half-life data collected under appropriate conditions, which shall be described by the applicant.

3.7.2.2. Bioaccumulation

An active substance, safener or synergist fulfils the bioaccumulation criterion where the bioconcentration factor is higher than 2 000.

Assessment of bioaccumulation shall be based on measured data on bioconcentration in aquatic species. Data from both freshwater and marine water species can be used.

3.7.2.3. Toxicity

An active substance, safener or synergist fulfils the toxicity criterion where:

— the long-term no-observed effect concentration for marine or freshwater organisms is less than 0,01 mg/l,

— the substance is classified as carcinogenic (category 1A or 1B), mutagenic (category 1A or 1B), or toxic for reproduction (category 1A, 1B or 2) pursuant to Regulation (EC) No 1272/2008, or

— there is other evidence of chronic toxicity, as identified by the classifications STOT RE 1 or STOT RE 2 pursuant to Regulation (EC) No 1272/2008.

3.7.3. An active substance, safener or synergist shall only be approved if it is not considered to be a very persistent and very bioaccumulative substance (vPvB).

A substance that fulfils both of the criteria of the points below is a vPvB substance.

3.7.3.1. Persistence

An active substance, safener or synergist fulfils the ‘very persistent’ criterion where:

— the half-life in marine, fresh- or estuarine water is higher than 60 days,

— the half-life in marine, fresh- or estuarine water sediment is higher than 180 days, or

— the half-life in soil is higher than 180 days.

3.7.3.2. Bioaccumulation

An active substance, safener or synergist fulfils the ‘very bioaccumulative’ criterion where the bioconcentration factor is greater than 5 000.

3.8. Ecotoxicology

3.8.1. An active substance, safener or synergist shall only be approved if the risk assessment demonstrates risks to be acceptable in accordance with the criteria laid down in the uniform principles for evaluation and authorisation of plant protection products referred to in **[**[F24]Article 29(6)(a) in relation to the relevant constituent territory**]** under realistic proposed conditions of use of a plant protection product containing the active substance, safener or synergist. The assessment must take into account the severity of effects, the uncertainty of the data, and the number of organism groups which the active substance, safener or synergist is expected to affect adversely by the intended use.

Textual Amendments

F24 Words in Annex 2 point 3.8.1 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(m)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

3.8.2. An active substance, safener or synergist shall only be approved if, on the basis of the assessment of **[**F25nationally**]** or internationally agreed test guidelines, it is not considered to have endocrine disrupting properties that may cause adverse effects on non-target organisms unless the exposure of non-target organisms to that active substance in a plant protection product under realistic proposed conditions of use is negligible.

Textual Amendments

F25 Words in Annex 2 point 3.8.2 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(n)(i)** (with Sch. 1) (as amended by S.I. 2019/1410, regs. 1(2), **6(4)(b)**); 2020 c. 1, **Sch. 5 para. 1(1)**

[F21From **[**X1 10 November 2018**]**, an active substance, safener or synergist shall be considered as having endocrine disrupting properties that may cause adverse effects on non-target organisms if, based on points (1) to (4) of the third paragraph, it is a substance that meets all of the following criteria, unless there is evidence demonstrating that the adverse effects identified are not relevant at the (sub)population level for non-target organisms:

(1) it shows an adverse effect in non-target organisms, which is a change in the morphology, physiology, growth, development, reproduction or life span of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences;

(2) it has an endocrine mode of action, i.e. it alters the function(s) of the endocrine system;

(3) the adverse effect is a consequence of the endocrine mode of action.

The identification of an active substance, safener or synergist as having endocrine disrupting properties that may cause adverse effects on non-target organisms in accordance with the second paragraph shall be based on all of the following points:

(1) all available relevant scientific data (in vivo studies or adequately validated alternative test systems predictive of adverse effects in humans or animals; as well as in vivo, in vitro, or, if applicable, in silico studies informing about endocrine modes of action):

(a) scientific data generated in accordance with internationally agreed study protocols, in particular, those listed in **[**F26guidance issued**]** in accordance with this Regulation;

(b) other scientific data selected applying a systematic review methodology, in particular following guidance on literature data listed in **[**F27guidance issued**]** in accordance with this Regulation;

(2) an assessment of the available relevant scientific data based on a weight of evidence approach in order to establish whether the criteria set out in the second paragraph are fulfilled; in applying the weight of evidence determination, the assessment of the scientific evidence shall consider all of the following factors:

(a) both positive and negative results, discriminating between taxonomic groups (e.g. mammals, birds, fish, amphibians) where relevant;

(b) the relevance of the study design for the assessment of the adverse effects and its relevance at the (sub)population level, and for the assessment of the endocrine mode of action;

(c) the adverse effects on reproduction, growth/development, and other relevant adverse effects which are likely to impact on (sub)populations. Adequate, reliable and representative field or monitoring data and/or results from population models shall as well be considered where available;

(d) the quality and consistency of the data, considering the pattern and coherence of the results within and between studies of a similar design and across different taxonomic groups;

(e) the concept of the limit dose and international guidelines on maximum recommended doses and for assessing confounding effects of excessive toxicity;

(3) using a weight of evidence approach, the link between the adverse effect(s) and the endocrine mode of action shall be established based on biological plausibility, which shall be determined in the light of current scientific knowledge and under consideration of internationally agreed guidelines;

(4) Adverse effects that are non-specific secondary consequences of other toxic effects shall not be considered for the identification of the substance as endocrine disruptor with respect to non-target organisms.**]**

Textual Amendments

F26 Words in Annex 2 point 3.8.2 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(n)(ii)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

F27 Words in Annex 2 point 3.8.2 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(n)(ii)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

3.8.3. An active substance, safener or synergist shall be approved only if it is established following an appropriate risk assessment on the basis of **[**[F28]nationally**]** or internationally agreed test guidelines, that the use under the proposed conditions of use of plant protection products containing this active substance, safener or synergist:

— will result in a negligible exposure of honeybees, or

— has no unacceptable acute or chronic effects on colony survival and development, taking into account effects on honeybee larvae and honeybee behaviour.

Textual Amendments

F28 Word in Annex 2 point 3.8.3 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(o)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

3.9. Residue definition

An active substance, safener or synergist shall only be approved if, where relevant, a residue definition can be established for the purposes of risk assessment and for enforcement purposes.

3.10. Fate and behaviour concerning groundwater

An active substance shall only be approved where it has been established for one or more representative uses, that consequently after application of the plant protection product consistent with realistic conditions on use, the predicted concentration of the active substance or of metabolites, degradation or reaction products in groundwater complies with the respective criteria of the uniform principles for evaluation and authorisation of plant protection products referred to in **[**F29Article 29(6)(a) in relation to the relevant constituent territory**]**.

Textual Amendments

F29 Words in Annex 2 point 3.10 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(p)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

4. Candidate for substitution

An active substance shall be approved as a candidate for substitution pursuant to Article 24 where any of the following conditions are met:

— its ADI, ARfD or AOEL is significantly lower than those of the majority of the approved active substances within groups of substances/use categories,

— it meets two of the criteria to be considered as a PBT substance,

— there are reasons for concern linked to the nature of the critical effects (such as developmental neurotoxic or immunotoxic effects) which, in combination with the use/exposure patterns, amount to situations of use that could still cause concern, for example, high potential of risk to groundwater; even with very restrictive risk management measures (such as extensive personal protective equipment or very large buffer zones),

— it contains a significant proportion of non-active isomers,

— it is or is to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as carcinogen category 1A or 1B, if the substance has not been excluded in accordance with the criteria laid down in point 3.6.3,

— it is or is to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 1A or 1B if the substance has not been excluded in accordance with the criteria laid down in point 3.6.4,

— if, on the basis of the assessment of **[**F30nationally**]** or internationally agreed test guidelines or other available data and information F31... , it is considered to have endocrine disrupting properties that may cause adverse effects in humans if the substance has not been excluded in accordance with the criteria laid down in point 3.6.5.

Textual Amendments

F30 Word in Annex 2 point 4 substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(q)(i)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

F31 Words in Annex 2 point 4 omitted (31.12.2020) by virtue of The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(q)(ii)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

[F32 5. Low-risk active substances

5.1. Active substances other than micro-organisms

5.1.1. An active substance, other than a micro-organism, shall not be considered as being of low-risk where it corresponds to any of the following:

(a) it is or has to be classified in accordance with Regulation (EC) No 1272/2008 as any of the following:

— carcinogenic category 1A, 1B or 2,
— mutagenic category 1A, 1B or 2,
— toxic to reproduction category 1A, 1B or 2,
— skin sensitiser category 1,
— serious damage to eye category 1,
— respiratory sensitiser category 1,
— acute toxicity category 1, 2 or 3,
— specific Target Organ Toxicant, category 1 or 2,
— toxic to aquatic life of acute and chronic category 1 on the basis of appropriate standard tests,
— explosive,
— skin corrosive, category 1A, 1B or 1C;

(b) it has been identified as priority substance **[**F33 and is listed in Annex 10 to**]** Directive 2000/60/EC;

(c) it is deemed to be an endocrine disruptor;

(d) it has neurotoxic or immunotoxic effects.

Textual Amendments

F33 Words in Annex 2 point 5.1.1(b) substituted (31.12.2020) by The Plant Protection Products (Miscellaneous Amendments) (EU Exit) Regulations 2019 (S.I. 2019/556), regs. 1(1), **14(3)(r)** (with Sch. 1); 2020 c. 1, Sch. 5 para. 1(1)

5.1.2. An active substance, other than a micro-organism, shall not be considered as being of low-risk where it is persistent (half-life in soil is more than 60 days) or its bio-concentration factor is higher than 100.

However, a naturally occurring active substance which does not correspond to any of points (a) to (d) of point 5.1.1 may be considered as being of low-risk, even if it is persistent (half-life in soil is more than 60 days) or its bio-concentration factor is higher than 100.

5.1.3. An active substance, other than a micro-organism, emitted and used by plants, animals and other organisms for communication, shall be considered as being of low- risk where it does not correspond to any of points (a) to (d) of point 5.1.1.

5.2. Micro-organisms

5.2.1. An active substance which is a micro-organism may be considered as being of low-risk unless at strain level it has demonstrated multiple resistance to anti-microbials used in human or veterinary medicine.

5.2.2. Baculoviruses shall be considered as being of low-risk unless at strain level they have demonstrated adverse effects on non-target insects.**]**

Textual Amendments

F32 Substituted by Commission Regulation (EU) 2017/1432 of 7 August 2017 amending Regulation (EC) No 1107/2009 of the European Parliament and the Council concerning the placing of plant protection products on the market as regards the criteria for the approval of low-risk active substances (Text with EEA relevance).

Changes to legislation:
There are currently no known outstanding effects for the Regulation (EC) No 1107/2009 of the European Parliament and of the Council, ANNEX II.