COMMISSION REGULATION (EU) 2022/477

of 24 March 2022

amending Annexes VI to X to Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

(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 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 ([1]), and in particular Article 131 thereof,

Whereas:

(1) Regulation (EC) No 1907/2006 lays down specific registration duties and obligations on manufacturers, importers and downstream users to generate data on substances they manufacture, import or use, to assess the risks related to those substances and to develop and recommend appropriate risk management measures.

(2) Annex VI to Regulation (EC) No 1907/2006 sets out information requirements referred to in Article 10, point (a)(i) to (v) and (x), of that Regulation. Annexes VII to X to that Regulation set out standard information requirements for substances manufactured or imported in quantities of 1 tonne or more, 10 tonnes or more, 100 tonnes or more and 1 000 tonnes or more.

(3) In June 2019, the Commission and the European Chemicals Agency ('the Agency') concluded in the REACH Evaluation Joint Action Plan ([2]) that certain information requirements in the Annexes to Regulation (EC) No 1907/2006 should be amended to provide more clarity on the obligations of registrants regarding the submission of information.

(4) To increase clarity of the registrants' obligations, a number of information requirements in Annexes VII to X to Regulation (EC) No 1907/2006 and the general rules for adaptation of the standard testing regime in Annex XI to that Regulation have been amended by Commission Regulation (EU) 2021/979 ([3]) but in line with the objectives of the REACH Evaluation Joint Action Plan a number of information requirements remain to be clarified.

(5) Requirements concerning the general registrant information and substance identification information which a registrant is to submit for general registration purposes, laid down in Annex VI, sections 1 and 2, to Regulation (EC) No 1907/2006 should therefore be amended.

([1]) OJ L 396, 30.12.2006, p. 1.

([2]) European Commission and European Chemicals Agency REACH Evaluation Joint Action Plan of June 2019 (https://echa.europa.eu/documents/10162/21877836/final_echa_com_reach_evaluation_action_plan_en.pdf/0003c9fc-652e-5f0b-90f9-dff9d5371d17).

([3]) Commission Regulation (EU) 2021/979 of 17 June 2021 amending Annexes VII to XI to Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (OJ L 216, 18.6.2021, p. 121).

(6) Certain specific rules for adaptation from the standard information requirements set out in Annexes VII to X to Regulation (EC) No 1907/2006 should be amended to align the terminology of the classification of hazardous substances to that used in Annex I, parts 2 to 5, to Regulation (EC) No 1272/2008 of the European Parliament and the Council ([4]).

(7) Specific rules for adaptation from the standard information laid down in Annex VII to Regulation (EC) No 1907/2006 on mutagenicity and aquatic toxicity should be amended for reasons of clarity and to ensure that useful information is provided. In particular, subsection 8.4 should be amended to clarify the consequences of a positive result in the *in vitro* gene mutation study, as well as the situations when the study required under point 8.4.1 does not need to be conducted. In addition, parts not referring to standard information required should be removed from column 1 of point 9.1.1, while column 2 of that point should describe more accurately the situations where the study does not need to be conducted and where long-term aquatic toxicity testing is required. Point 9.1.2 should also be modified to clarify when the study does not need to be conducted.

(8) The information requirements on testing for mutagenicity and for reproductive toxicity, and on ecotoxicological information in Annex VIII to Regulation (EC) No 1907/2006 should be amended in order to clarify the obligations of registrants. In particular, the rules on testing for mutagenicity in subsection 8.4 should specify the situations that do not require testing referred to in that Annex and the situations that require further testing referred to in Annex IX. Furthermore, the nomenclature of the studies in point 8.4.2 should be aligned with that of the corresponding technical guidance documents of the Organisation for Economic Cooperation and Development (OECD) ([5]). In addition, to ensure that useful information on reproductive and developmental toxicity is generated, the preferred animal species and the preferred administration routes for testing should be added to point 8.7.1, while certain specific rules for adaptation from the standard information requirements should be clarified. Finally, a subsection heading 9.1 for aquatic toxicity that was missing should be added and the information requirement on short-term toxicity testing on fish in point 9.1.3 should be amended in order to remove the parts that do not list standard information from column 1 and to clarify the situations when the test is not required in column 2. Subsections 9.2 on degradation and 9.3 on fate and behaviour in the environment should also be modified in order to better describe the situations requiring further information on degradation and bioaccumulation as well as further degradation and bioaccumulation studies.

(9) Information requirements on testing for mutagenicity in Annex IX to Regulation (EC) No 1907/2006 should be amended to specify in points 8.4.4 and 8.4.5 the studies to be conducted in mammalian somatic cells and, when relevant, in mammalian germ cells, as well as the cases where such studies need to be conducted. In addition, the information requirements in point 8.7.2 on testing for pre-natal developmental toxicity in a first and second species and in point 8.7.3 for Extended One-Generation Reproductive Toxicity studies should be clarified with regard to the preferred animal species and the preferred administration routes for testing, as well as with regard to the possible deviations from the general rules. Finally, as regards the section on ecotoxicological information, certain information requirements on long-term toxicity testing on fish should be removed due to animal welfare reasons. The subsection 9.2 on degradation should also be amended to align the wording of point 9.2.3 concerning identification of degradation products with that of the related provision in Annex XIII, and to reflect the amended requirement on further degradation testing accordingly. The subsection 9.4 on effects on terrestrial organisms should also be amended to clarify that a long-term toxicity study should be proposed by the registrant or may be required by the Agency for substances that have a high potential to adsorb to soil or that are very persistent.

(10) Annex X to Regulation (EC) No 1907/2006 should be amended to clarify certain information requirements on mutagenicity, developmental and reproductive toxicity and ecotoxicological information. In particular, the amendments should describe the situations meeting the requirement for a second *in-vivo* somatic cell study or a second *in-vivo* germ cell study and specify the need to conduct such studies in mammalian species. Those studies should be listed together with the mutagenicity concerns they are to address. In addition, the information requirements on pre-natal developmental toxicity and Extended One-Generation Reproductive Toxicity studies should be amended to clarify the need for a study in, and the choice of, a second species, as well as the preferred administration routes for testing and the deviations from the general rules. Furthermore, the reference to a specific requirement on biotic degradation in point 9.2.1 is no longer necessary and should therefore be deleted, while

([4]) 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).

([5]) OECD TG 473 and 487.

relevant specific rules for adaptation in subsection 9.2 should be amended accordingly. Finally, it should be clarified in subsection 9.4, as well as point 9.5.1 that in addition to degradation products, long-term toxicity testing of transformation products is required to investigate their effects on terrestrial and sediment organisms.

(11) Regulation (EC) No 1907/2006 should therefore be amended accordingly.

(12) The proposed amendments aim at providing clarifications of certain standard information requirements and specific rules for their adaptation, as well as at increasing the legal certainty of the evaluation practices already applied by the Agency. Nevertheless, it cannot be discarded that as a result of the amendments, certain registration dossiers will need to be updated. The application of this Regulation should therefore be deferred.

(13) The measures provided for in this Regulation are in accordance with the opinion of the Committee established under Article 133 of Regulation (EC) No 1907/2006,

HAS ADOPTED THIS REGULATION:

Article 1

Annexes VI to X to Regulation (EC) No 1907/2006 are 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*.

It shall apply from 14 October 2022.

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

Done at Brussels, 24 March 2022.

For the Commission
The President
Ursula VON DER LEYEN

ANNEX

Regulation (EC) No 1907/2006 is amended as follows:

(1) Annex VI is amended as follows:

(a) point 1.1.1 is replaced by the following:

'1.1.1. Name, address, telephone number and email address';

(b) the following point 1.1.4 is added:

'1.1.4. Where an only representative has been appointed in accordance with Article 8(1), the following information regarding the natural or legal person established outside the Union who appointed the only representative: name, address, telephone number, email address, contact person, location of the production site(s) or formulation site(s), as appropriate, company website, as appropriate and national company identification number(s), as appropriate.';

(c) subsection 1.2 is replaced by the following:

'1.2. Joint submission of data

Articles 11 and 19 provide for the possibility for the lead registrant to submit parts of the registration information on behalf of other member registrants.

When, in accordance with Article 11(1), the lead registrant submits information referred to in Article 10, point (a)(iv), (vi), (vii) and (ix), the lead registrant shall describe the composition(s), nanoform or set of similar nanoforms to which this information relates in accordance with points 2.3.1 to 2.3.4 and subsection 2.4 of this Annex. Each member registrant relying on information submitted by the lead registrant shall indicate which information thus submitted pertains to which composition, nanoform or set of similar nanoforms of the substance that the registrant identifies in accordance with Article 10, point (a)(ii), and Article 11(1).

When, in accordance with Article 11(3), a registrant submits information referred to in Article 10, point (a)(iv), (vi), (vii) or (ix), separately, this registrant shall describe the composition(s), nanoform or set of similar nanoforms of the substance to which this information relates in accordance with points 2.3.1 to 2.3.4 and subsection 2.4 of this Annex.';

(d) point 1.3.1 is replaced by the following:

'1.3.1. Name, address, telephone number and email address';

(e) subsection 2.1 is replaced by the following:

'2.1. Name and any other identifier of each substance';

(f) point 2.1.1 is replaced by the following:

'2.1.1. Name(s) in the IUPAC nomenclature. If unavailable, other international chemical name(s)';

(g) point 2.1.3 is replaced by the following:

'2.1.3. EC number, i.e. Einecs, Elincs or NLP number, or the number assigned by the Agency (if available and appropriate)';

(h) point 2.1.5 is replaced by the following:

'2.1.5. Other identity code, such as customs number (if available)';

(i) subsection 2.2 is replaced by the following:

'2.2. Information related to molecular and structural formula or crystal structure of each substance';

(j) point 2.2.1 is replaced by the following:

'2.2.1. Molecular formula and structural formula (including SMILES notation and other representation if available) and description of crystal structure(s)';

(k) points 2.3.1 to 2.3.7 are replaced by the following:

'2.3.1. Degree of purity (%), if applicable

2.3.2. Names of constituents and impurities

In the case of a substance of unknown or variable composition, complex reaction products or biological materials (UVCB):

— names of constituents present at a concentration of ≥ 10 %;

— names of known constituents present at a concentration of < 10 %;

— for constituents that cannot be identified individually, description of groups of constituents based on chemical nature;

— description of the origin or source and the manufacturing process

2.3.3. Typical concentration and concentration range (in percentage) of constituents, groups of constituents that cannot be identified individually and impurities as specified in point 2.3.2

2.3.4. Names and typical concentration and concentration range (in percentage) of additives

2.3.5. All necessary qualitative analytical data specific for the identification of the substance, such as ultra-violet, infra-red, nuclear magnetic resonance, mass spectrum or diffraction data

2.3.6. All necessary quantitative analytical data specific for the identification of the substance, such as chromatographic, titrimetric, elemental analysis or diffraction data

2.3.7. Description of the analytical methods or the appropriate bibliographical references that are necessary for the identification of the substance (including the identification and quantification of its constituents and, where appropriate, its impurities and additives). The description shall consist of the experimental protocols followed and the relevant interpretation of the results reported under points 2.3.1 to 2.3.6. This information shall be sufficient to allow the methods to be reproduced.';

(l) point 2.4.6 is replaced by the following:

'2.4.6. Description of the analytical methods or the appropriate bibliographical references for the information elements in this subsection (2.4). The description shall consist of the experimental protocols followed and the relevant interpretation of the results reported under points 2.4.2 to 2.4.5. This information shall be sufficient to allow the methods to be reproduced.';

(m) the following subsection 2.5 is added:

'2.5. Any other available information relevant for the identification of the substance';

(n) subsection 3.5 is replaced by the following:

'3.5. General description of the identified use(s)';

(2) Annex VII is amended as follows:

(a) in subsection 8.4, in column 2, the text is replaced by the following:

	'8.4. In case of a positive result in the *in vitro* gene mutation study in bacteria referred to in point 8.4.1 of this Annex, which gives rise to concern, the registrant shall perform an *in vitro* study referred to in Annex VIII, point 8.4.2. Based on the positive result of any of those *in vitro* genotoxicity studies, the registrant shall propose, or the Agency may require, an appropriate *in vivo* study referred to in Annex IX, point 8.4.4. The *in vivo* study shall address the chromosomal aberration concern or the gene mutation concern or both, as appropriate. The *in vitro* gene mutation study in bacteria does not need to be conducted if this test is not applicable for the substance. In this case, the registrant shall provide a justification and perform an *in vitro* study referred to in Annex VIII, point 8.4.3. In case of a positive result in that study the registrant shall perform an *in vitro* cytogenicity study referred to in Annex VIII, point 8.4.2. Based on the positive result in any of those *in vitro* genotoxicity studies, or in case one of the Annex VIII *in vitro* tests is not applicable for the substance, the

	registrant shall propose, or the Agency may require, an appropriate *in vivo* study referred to in Annex IX, point 8.4.4. The *in vivo* study shall address the chromosomal aberration concern or the gene mutation concern or both, as appropriate. The *in vitro* gene mutation study in bacteria referred to in point 8.4.1 and follow-up testing do not need to be conducted in any of the following cases: — the substance is known to cause germ cell mutagenicity, meeting the criteria for classification in the hazard class germ cell mutagenicity category 1A or 1B, and appropriate risk management measures are implemented, — the substance is known to be a genotoxic carcinogen, meeting the criteria for classification both in the hazard class germ cell mutagenicity category 1A, 1B or 2 and in the hazard class carcinogenicity category 1A or 1B, and appropriate risk management measures are implemented.’;

(b) in point 8.4.1, in column 2, the text is replaced by the following:

	‘8.4.1. The *in vitro* gene mutation study in bacteria does not need to be conducted for nanoforms where it is not appropriate. In such case, an *in vitro* study referred to in Annex VIII, point 8.4.3, shall be provided.’;

(c) in point 9.1.1, in column 1, the second paragraph is deleted.

(d) in point 9.1.1, in column 2, the text is replaced by the following:

	‘9.1.1. The study does not need to be conducted in any of the following cases: — there are factors indicating that short-term aquatic toxicity is unlikely to occur, for instance if the substance is highly insoluble in water or the substance is unlikely to cross biological membranes, — a long-term aquatic toxicity study on invertebrates is available. For nanoforms, the study may not be waived on the basis of high insolubility in water alone. The registrant may propose long-term toxicity testing instead of short-term toxicity testing. Long-term toxicity testing on invertebrates (preferred species *Daphnia*), (Annex IX, point 9.1.5) shall be proposed by the registrant or may be required by the Agency when it is unlikely that short-term toxicity testing can provide a true measure of the intrinsic aquatic toxicity of the substance, for instance: — if the substance is poorly water soluble (solubility below 1 mg/L), or — for nanoforms with low dissolution rate in the relevant test media.’;

(e) in point 9.1.2, in column 2, the text is replaced by the following:

	'9.1.2. The study does not need to be conducted if there are factors indicating that aquatic toxicity is unlikely to occur for instance if the substance is highly insoluble in water or the substance is unlikely to cross biological membranes. For nanoforms, the study may not be waived on the basis of high insolubility in water alone.';

(3) Annex VIII is amended as follows:

(a) in subsection 8.4, in column 2, the following text is added:

	'8.4. The studies referred to in points 8.4.2 and 8.4.3 do not need to be conducted in any of the following cases: — adequate data from the corresponding *in vivo* study, (namely *in vivo* chromosomal aberration (or micronucleus) study regarding point 8.4.2 or *in vivo* mammalian gene mutation study regarding point 8.4.3), are available, — the substance is known to cause germ cell mutagenicity, meeting the criteria for classification as germ cell mutagen category 1A or 1B, and appropriate risk management measures are implemented, — the substance is known to be a genotoxic carcinogen, meeting the criteria for classification both in the hazard class germ cell mutagenicity category 1A, 1B or 2 and in the hazard class carcinogenicity category 1A or 1B, and appropriate risk management measures are implemented. In case of a positive result in any of the *in vitro* genotoxicity studies referred to in Annex VII or this Annex, which gives rise to concern, the registrant shall propose, or the Agency may require, an appropriate *in vivo* study referred to in Annex IX, point 8.4. The *in vivo* study shall address the chromosomal aberration concern or the gene mutation concern or both as appropriate. In case an *in vitro* mutagenicity study referred to in points 8.4.2 or 8.4.3 is not applicable for the substance, the registrant shall provide a justification and shall propose or the Agency may require an appropriate *in vivo* study referred to in Annex IX, point 8.4.4. The *in vivo* study shall address the chromosomal aberration concern or the gene mutation concern or both as appropriate.';

(b) in point 8.4.2, in column 1, the text is replaced by the following:

'8.4.2. *In vitro* mammalian chromosomal aberration study or *in vitro* mammalian micronucleus study';	

(c) in point 8.4.2, the text in column 2 is deleted;

(d) in point 8.4.3, the text in column 2 is deleted;

(e) in point 8.6.1, in column 2, the introductory wording of the sixth paragraph is replaced by the following:

	'Further studies shall be proposed by the registrant or may be required by the Agency in case of:';

(f) point 8.7.1 is replaced by the following:

'8.7.1. Screening for reproductive/developmental toxicity (OECD TG 421 or TG 422); the preferred species is the rat. The route of administration shall be oral if the substance is a solid or liquid, and inhalation if the substance is a gas; deviations may be made if scientifically justified, for example through evidence of equivalent or higher systemic exposure via another relevant route of human exposure or route-specific toxicity.	8.7.1. This study does not need to be conducted in any of the following cases: — the substance is known to be a genotoxic carcinogen, meeting the criteria for classification both in the hazard class germ cell mutagenicity category 1A, 1B or 2 and in the hazard class carcinogenicity category 1A or 1B, and appropriate risk management measures are implemented, — the substance is known to be a germ cell mutagen, meeting the criteria for classification in the hazard class germ cell mutagenicity category 1A or 1B and appropriate risk management measures are implemented, — relevant human exposure can be excluded in accordance with Annex XI, Section 3, — a pre-natal developmental toxicity study (OECD TG 414) referred to in Annex IX, point 8.7.2 or an Extended One-Generation Reproductive Toxicity Study (OECD TG 443) referred to in Annex IX, point 8.7.3 is available or proposed by the registrant; or a Two-Generation Reproductive Toxicity Study (OECD TG 416) is available, — a substance is known to have an adverse effect on sexual function or fertility, meeting the criteria for classification in the hazard class reproductive toxicity category 1A or 1B: May damage fertility (H360F), and the available data are adequate to support a robust risk assessment, — a substance is known to cause developmental toxicity, meeting the criteria for classification in the hazard class reproductive toxicity category 1A or 1B: May damage the unborn child (H360D), and the available data are adequate to support a robust risk assessment. In case of serious concerns about potential adverse effects on sexual function, fertility or development, the registrant shall propose, or the Agency may require either an Extended One-Generation Reproductive Toxicity Study (OECD TG 443), referred to in Annex IX, point 8.7.3, or a pre-natal developmental toxicity study (OECD TG 414), referred to in Annex IX, point 8.7.2, instead of the screening study (OECD TG 421 or 422) to address those concerns. Those serious concerns include among others: — adverse effects related to sexual function, fertility or development based on available information, not meeting the criteria for classification as reproductive toxicity category 1A or 1B, — possible developmental or reproductive toxicity of the substance predicted from information on structurally related substances, (Q)SAR estimates or *in vitro* methods.';

(g) in point 8.8.1, in column 2, the first paragraph is replaced by the following:

	'For nanoforms without high dissolution rate in biological media a toxicokinetics study shall be proposed by the registrant or may be required by the Agency in case such an assessment cannot be performed on the basis of relevant available information, including from the study conducted in accordance with 8.6.1';

(h) the following subsection 9.1 is inserted:

'9.1. Aquatic toxicity	9.1. Long-term aquatic toxicity testing referred to in Annex IX, subsection 9.1, in addition to short-term toxicity testing shall be proposed by the registrant or may be required by the Agency if the chemical safety assessment performed in accordance with Annex I indicates that it is needed to further investigate the effects on aquatic organisms, for example when further information is needed for the refinement of the PNEC or if additional toxicity information as set out in Annex XIII, point 3.2.3, would be necessary to assess PBT or vPvB properties of the substance. The choice of the appropriate test(s) shall be made on the basis of the results of the chemical safety assessment.';

(i) point 9.1.3 is replaced by the following:

'9.1.3. Short-term toxicity testing on fish	9.1.3. The study does not need to be conducted in any of the following cases: — there are factors indicating that short-term aquatic toxicity is unlikely to occur, for instance if the substance is highly insoluble in water or the substance is unlikely to cross biological membranes, — a long-term aquatic toxicity study on fish is available. For nanoforms, the study may not be waived on the basis of high insolubility in water alone. The registrant may propose long-term toxicity testing instead of short-term toxicity testing. Long-term toxicity testing on fish referred to in Annex IX, point 9.1.6, shall be proposed by the registrant or may be required by the Agency when it is unlikely that short-term toxicity testing can provide a true measure of the intrinsic aquatic toxicity of the substance, for instance: — if the substance is poorly water soluble (below 1 mg/L), or — for nanoforms with low dissolution rate in the relevant test media.';

(j) in subsection 9.2, in column 2, the text is replaced by the following:

	‘9.2. Further information on degradation shall be generated or further degradation testing as described in Annex IX shall be proposed if the chemical safety assessment performed in accordance with Annex I indicates that it is needed to further investigate the degradation of the substance. That could for example be the case if additional information on degradation as set out in Annex XIII, point 3.2.1, is required to assess PBT or vPvB properties of the substance in accordance with subsection 2.1 of that Annex. For nanoforms that are not soluble, nor have high dissolution rate, such test(s) shall consider morphological transformation (e.g. irreversible changes in particle size, shape and surface properties, loss of coating), chemical transformation (e.g. oxidation, reduction) and other abiotic degradation (e.g. photolysis). The choice of the appropriate test(s) shall be made on the basis of the results of the chemical safety assessment. In case the generation of additional information requires further testing in accordance with Annex IX, the registrant shall propose or the Agency may require such testing.’;

(k) in subpoint 9.2.2.1, in column 2, the text is replaced by the following:

	‘9.2.2.1. The study does not need to be conducted in any of the following cases: — the substance is readily biodegradable, — the substance is highly insoluble in water, — based on the structure, the substance does not have chemical groups that can hydrolyse. For nanoforms, the study may not be waived on the basis of high insolubility in water alone.’;

(l) in subsection 9.3, in column 2, the following text is added:

	‘9.3. Further information on bioaccumulation shall be generated if additional information on bioaccumulation as set out in Annex XIII, point 3.2.2, is required to assess PBT or vPvB properties of the substance in accordance with subsection 2.1 of that Annex. In case the generation of additional information requires further testing in accordance with Annex IX or Annex X, the registrant shall propose or the Agency may require such testing.’;

(4) Annex IX is amended as follows:

(a) in point 7.16, the second bullet point in column 2 is deleted;

(b) subsection 8.4 is replaced by the following:

'8.4. Mutagenicity	8.4. The studies referred to in points 8.4.4 and 8.4.5 do not need to be conducted in any of the following cases: — the substance is known to cause germ cell mutagenicity, meeting the criteria for classification in the hazard class germ cell mutagenicity category 1A or 1B, and appropriate risk management measures are implemented, — the substance is known to be a genotoxic carcinogen, meeting the criteria for classification both in the hazard class germ cell mutagenicity category 1A, 1B or 2 and in the hazard class carcinogenicity category 1A or 1B, and appropriate risk management measures are implemented.';

(c) the following points 8.4.4 and 8.4.5 are added:

'8.4.4. An appropriate *in vivo* mammalian somatic cell genotoxicity study, if there is a positive result in any of the *in vitro* genotoxicity studies referred to in Annex VII or Annex VIII, which gives rise to concern. The *in vivo* mammalian somatic cell genotoxicity study shall address the chromosomal aberration concern or the gene mutation concern or both, as appropriate.	8.4.4. The *in vivo* mammalian somatic cell genotoxicity study does not need to be conducted if there are adequate results available from an appropriate *in vivo* mammalian somatic cell genotoxicity study.
8.4.5. An appropriate *in vivo* mammalian germ cell genotoxicity study, if there is a positive result in an available *in vivo* mammalian somatic cell genotoxicity study, which gives rise to concern. The *in vivo* mammalian germ cell genotoxicity study shall address the chromosomal aberration concern or the gene mutation concern or both, as appropriate.	8.4.5. The study does not need to be conducted if there is clear evidence that neither the substance nor its metabolites reach the germ cells.';

(d) point 8.7.2 is replaced by the following:

'8.7.2. Pre-natal developmental toxicity study (OECD TG 414) on one species; the preferred species is the rat or the rabbit. The route of administration shall be oral if the substance is a solid or liquid, and inhalation if the substance is a gas; deviations may be made if scientifically justified, for example through evidence of equivalent or higher systemic exposure via another relevant route of human exposure or route-specific toxicity.	8.7.2. An additional pre-natal developmental toxicity study in a second species, that is the other preferred species to the one used in the first study, shall be proposed by the registrant or may be required by the Agency if there is a concern for developmental toxicity based on the outcome of the first study and all other relevant data. That could be the case for example if the study on the first species shows developmental toxicity not meeting the criteria for classification in the hazard class reproductive toxicity category 1A or 1B; May damage the unborn child (H360D). Deviations from the default route of administration and deviations in the choice of species shall be scientifically justified.';

(e) in point 8.7.3, in column 1, the text is replaced by the following:

'8.7.3. Extended One-Generation Reproductive Toxicity Study (OECD TG 443), basic test design (cohorts 1A and 1B without extension to include an F2 generation), one species, if the available repeated dose toxicity studies (e.g. 28-day or 90-day studies, or OECD TG 421 or 422 screening studies) indicate adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity. The route of administration shall be oral if the substance is a solid or liquid, and inhalation if the substance is a gas; deviations may be made if scientifically justified, for example through evidence of equivalent or higher systemic exposure via another relevant route of human exposure or route-specific toxicity.';	

(f) in point 8.7.3, in column 2, the introductory wording of the first paragraph is replaced by the following:

	'8.7.3. An Extended One-Generation Reproductive Toxicity Study with the extension of cohort 1B to include the F2 generation shall be proposed by the registrant or may be required by the Agency if:';

(g) in point 8.7.3, in column 2, the introductory wording of the second paragraph is replaced by the following:

	'An Extended One-Generation Reproductive Toxicity Study including cohorts 2A/2B (developmental neurotoxicity) and/or cohort 3 (developmental immunotoxicity) shall be proposed by the registrant or may be required by the Agency in case of particular concerns on (developmental) neurotoxicity or (developmental) immunotoxicity justified by any of the following:';

(h) in subsection 9.1, in column 2, the text is replaced by the following:

	'9.1. Long-term toxicity testing other than the tests referred to in points 9.1.5 and 9.1.6 shall be proposed by the registrant or may be required by the Agency if the chemical safety assessment performed in accordance with Annex I indicates that it is needed to further investigate the effects of the substance on aquatic organisms. The choice of the test(s) shall be made on the basis of the results of the chemical safety assessment.';

(i) point 9.1.6 is replaced by the following:

'9.1.6. Long-term toxicity testing on fish, (unless already provided as part of Annex VIII requirements).	9.1.6. Fish short-term toxicity tests on embryo and sac-fry stages (OECD TG 212) that were initiated before 14 April 2022 shall be considered appropriate to address this standard in-

The information shall be provided for subpoint 9.1.6.1 or subpoint 9.1.6.3.	formation requirement provided that the substance is not highly lipophilic (log Kow > 4) or there is no indication of endocrine disrupting properties or any other specific mode of action.';

(j) subpoint 9.1.6.1 is replaced by the following:

'9.1.6.1. Fish early-life stage (FELS) toxicity test (OECD TG 210)';	

(k) subpoint 9.1.6.2 is deleted.

(l) subpoint 9.1.6.3 is replaced by the following:

'9.1.6.3. Fish juvenile growth test (OECD TG 215)';	

(m) in subsection 9.2, in column 2, the text is replaced by the following:

	'9.2. Further degradation testing shall be proposed by the registrant or may be required by the Agency if the chemical safety assessment performed in accordance with Annex I indicates that it is needed to further investigate the degradation of the substance and its transformation or degradation products. The choice of the appropriate test(s) and test media shall be made on the basis of the results of the chemical safety assessment.';

(n) in point 9.2.3, in column 1, the text is replaced by the following:

'9.2.3. Identification of transformation and abiotic and biotic degradation products';	

(o) in subsection 9.4, in column 2, the text is replaced by the following:

	'9.4. These studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely. In the absence of toxicity data for soil organisms, the equilibrium partitioning method may be applied to assess the hazard to soil organisms. Where the equilibrium partitioning method is applied to nanoforms, this shall be scientifically justified. The choice of the appropriate test(s) shall be made on the basis of the results of the chemical safety assessment. In particular for substances that have a high potential to adsorb to soil or that are very persistent, the registrant shall propose or the Agency may require long-term toxicity testing as referred to in Annex X instead of short-term toxicity testing.';

(5) Annex X is amended as follows:

(a) subsection 8.4. is replaced by the following:

'8.4. Mutagenicity	8.4. The studies referred to in points 8.4.6 and 8.4.7 do not need to be conducted in any of the following cases: — the substance is known to cause germ cell mutagenicity, meeting the criteria for classification in the hazard class germ cell mutagenicity category 1A or 1B, and appropriate risk management measures are implemented, — the substance is known to be a genotoxic carcinogen, meeting the criteria for classification both in the hazard class germ cell mutagenicity category 1A or 1B or 2 and in the hazard class carcinogenicity category 1A or 1B, and appropriate risk management measures are implemented.';

(b) the following points 8.4.6 and 8.4.7 are added:

'8.4.6. A second *in vivo* mammalian somatic cell genotoxicity study, if there is a positive result in any of the *in vitro* genotoxicity studies referred to in Annex VII or Annex VIII, which gives rise to both chromosomal aberration concern and gene mutation concern. The second study shall address chromosomal aberration or gene mutation, as appropriate, which has not been addressed by the first *in vivo* mammalian somatic cell genotoxicity study.	
8.4.7. A second *in vivo mammalian* germ cell genotoxicity study, if there is a positive result in *in vivo* mammalian somatic cell genotoxicity studies, which gives rise to both chromosomal aberration concern and gene mutation concern. The second study shall address the chromosomal aberration or gene mutation, as appropriate, which has not been addressed by the first *in vivo* mammalian germ cell genotoxicity study.	8.4.7. The study does not need to be conducted if there is clear evidence that neither the substance nor its metabolites reach the germ cells.';

(c) point 8.7.2 is replaced by the following:

'8.7.2. Pre-natal developmental toxicity study (OECD TG 414) in a second species, the preferred species is the rat or the rabbit, whichever was not used in the first study under Annex IX. The route of administration shall be oral if the substance is a solid or liquid, and inhalation if the substance is a gas; deviations may be made if scientifically justified, for example through evidence of equivalent or higher systemic exposure via another relevant route of human exposure or route-specific toxicity.	Deviations from the default route of administration and deviations in the choice of species shall be scientifically justified.';

(d) in point 8.7.3, in column 1, the text is replaced by the following:

'8.7.3. Extended One-Generation Reproductive Toxicity Study (OECD TG 443), basic test design (cohorts 1A and 1B without extension to include an F2 generation), one species, unless already provided as part of Annex IX requirements. The route of administration shall be oral if the substance is a solid or liquid, and inhalation if the substance is a gas; deviations may be made if scientifically justified, for example through evidence of equivalent or higher systemic exposure via another relevant route of human exposure or route-specific toxicity.';	

(e) in point 8.7.3, in column 2, the introductory wording of the first paragraph is replaced by the following:

	'An Extended One-Generation Reproductive Toxicity Study with the extension of cohort 1B to include the F2 generation shall be proposed by the registrant or may be required by the Agency if:';

(f) in point 8.7.3, in column 2, the introductory wording of the second paragraph is replaced by the following:

	'An Extended One-Generation Reproductive Toxicity Study including cohorts 2A/2B (developmental neurotoxicity) and/or cohort 3 (developmental immunotoxicity) shall be proposed by the registrant or may be required by the Agency in case of particular concerns on (developmental) neurotoxicity or (developmental) immunotoxicity justified by any of the following:';

(g) in subsection 9.2, in column 2, the text is replaced by the following:

	'9.2. Further degradation testing shall be proposed by the registrant or may be required by the Agency, if the chemical safety assessment performed in accordance with Annex I indicates that it is needed to further investigate the degradation of the substance and its transformation and degradation products. The choice of the appropriate test(s) and test media shall be made on the basis of the results of the chemical safety assessment.';

(h) point 9.2.1 is deleted;

(i) in subsection 9.4, in column 2, the text is replaced by the following:

	'9.4. Long-term toxicity testing shall be proposed by the registrant or may be required by the Agency if the results of the chemical safety assessment performed in accordance with Annex I indicates that it is needed to further investigate the effects of the substance or of transformation and degradation products on terrestrial organisms. The choice of the appropriate test(s) shall be made on the basis of the outcome of the chemical safety assessment.

	These studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely.’;

(j) in point 9.5.1, in column 2, the text is replaced by the following:

	‘9.5.1. Long-term toxicity testing shall be proposed by the registrant or may be required by the Agency if the results of the chemical safety assessment performed in accordance with Annex I indicates that it is needed to further investigate the effects of the substance or of relevant transformation and degradation products on sediment organisms. The choice of the appropriate test(s) shall be made on the basis of the results of the chemical safety assessment.’.