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COVER NOTE

From: Secretary-General of the European Commission, signed by Ms Martine DEPREZ, Director

date of receipt: 19 November 2021

To: Mr Jeppe TRANHOLM-MIKKELSEN, Secretary-General of the Council of the European Union

Subject: ANNEX to Commission Regulation (EU) .../...of XXX 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)

Delegations will find attached document D (2021) 76145/01 ANNEX.

Encl.: D (2021) 76145/01 ANNEX

EN
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 e-mail 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, e-mail 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 e-mail 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. Einescs, 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:

	<p>‘8.4. In case of a positive result in the <i>in vitro</i> 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 <i>in vitro</i> study referred to in Annex VIII, point 8.4.2. Based on the positive result of any of those <i>in vitro</i> genotoxicity studies, the registrant shall propose, or the Agency may require, an appropriate <i>in vivo</i> study referred to in Annex IX, point 8.4.4. The <i>in vivo</i> study shall address the chromosomal aberration concern or the gene</p>
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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.’;
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(b) in point 8.4.1, in column 2, the text is replaced by the following:

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

	<p>‘9.1.1. The study does not need to be conducted in any of the following cases:</p> <ul style="list-style-type: none"> — 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. <p>For nanoforms, the study may not be waived on the basis of high insolubility in water alone.</p> <p>The registrant may propose long-term toxicity testing instead of short-term toxicity testing.</p> <p>Long-term toxicity testing on invertebrates (preferred species <i>Daphnia</i>), (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:</p>
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	<ul style="list-style-type: none"> - if the substance is poorly water soluble (solubility below 1 mg/L), or - for nanoforms with low dissolution rate in the relevant test media.’;
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(e) in point 9.1.2, in column 2, the text is replaced by the following:

	<p>‘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.</p> <p>For nanoforms, the study may not be waived on the basis of high insolubility in water alone.’;</p>
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(3) Annex VIII is amended as follows:

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

	<p>‘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:</p> <ul style="list-style-type: none"> - adequate data from the corresponding <i>in vivo</i> study, (namely <i>in vivo</i> chromosomal aberration (or micronucleus) study regarding point 8.4.2 or <i>in vivo</i> 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,
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	<p>- 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.</p> <p>In case of a positive result in any of the <i>in vitro</i> 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 <i>in vivo</i> study referred to in Annex IX, point 8.4. The <i>in vivo</i> study shall address the chromosomal aberration concern or the gene mutation concern or both as appropriate.</p> <p>In case an <i>in vitro</i> 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 <i>in vivo</i> study referred to in Annex IX, point 8.4.4. The <i>in vivo</i> study shall address the chromosomal aberration concern or the gene mutation concern or both as appropriate.’;</p>
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- (b) in point 8.4.2, in column 1, the text is replaced by the following:

<p>‘ 8.4.2. <i>In vitro</i> mammalian chromosomal aberration study or <i>in vitro</i> mammalian micronucleus study’;</p>	
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- (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: ‘;
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- (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.	<p>8.7.1 This study does not need to be conducted in any of the following cases:</p> <ul style="list-style-type: none"> - 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
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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

	<p>information, not meeting the criteria for classification as reproductive toxicity category 1A or 1B,</p> <p>- possible developmental or reproductive toxicity of the substance predicted from information on structurally related substances, (Q)SAR estimates or <i>in vitro</i> methods.’;</p>
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(g) in point 8.8.1, in column 2, the first paragraph is replaced by the following:

	<p>‘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. ‘;</p>
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(h) the following subsection 9.1 is inserted:

‘ 9.1. Aquatic toxicity’	<p>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.</p> <p>The choice of the appropriate test(s) shall be made on the basis of the results of the</p>
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	chemical safety assessment.’;
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(i) point 9.1.3 is replaced by the following:

‘9.1.3. Short-term toxicity testing on fish	<p>9.1.3. The study does not need to be conducted in any of the following cases:</p> <ul style="list-style-type: none"> - 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. <p>For nanoforms, the study may not be waived on the basis of high insolubility in water alone.</p> <p>The registrant may propose long-term toxicity testing instead of short-term toxicity testing.</p> <p>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:</p> <ul style="list-style-type: none"> - if the substance is poorly water soluble (below 1 mg/L), or - for nanoforms with low dissolution rate in the relevant test media.’;
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(j) in subsection 9.2, in column 2, the text is replaced by the following:

	<p>‘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</p>
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	<p>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.</p> <p>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).</p> <p>The choice of the appropriate test(s) shall be made on the basis of the results of the chemical safety assessment.</p> <p>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. ’;</p>
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(k) in subpoint 9.2.2.1, in column 2, the text is replaced by the following:

	<p>‘9.2.2.1. The study does not need to be conducted in any of the following cases:</p> <ul style="list-style-type: none"> — 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. <p>For nanoforms, the study may not be waived on the basis of high insolubility in water alone.’;</p>
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(l) in subsection 9.3, in column 2, the following text is added:

	<p>‘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</p>
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	<p>of the substance in accordance with subsection 2.1. of that Annex.</p> <p>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.’;</p>
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(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:

<p>‘8.4. Mutagenicity’</p>	<p>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:</p> <ul style="list-style-type: none"> - 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.’;
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(c) the following points 8.4.4 and 8.4.5 are added:

<p>‘8.4.4. An appropriate <i>in vivo</i> mammalian somatic cell genotoxicity study, if there is a positive result in any of the <i>in vitro</i> genotoxicity studies referred to in Annex VII or Annex VIII, which gives rise to concern. The <i>in vivo</i> mammalian somatic cell genotoxicity study shall address the chromosomal aberration concern or the gene mutation concern or both, as appropriate.</p> <p>8.4.5. An appropriate <i>in vivo</i> mammalian germ cell genotoxicity study, if there is a positive result in an available <i>in vivo</i> mammalian somatic cell genotoxicity study, which gives rise to concern. The <i>in vivo</i> mammalian germ cell genotoxicity study shall address the chromosomal aberration concern or the gene mutation concern or both, as appropriate.</p>	<p>8.4.4. The <i>in vivo</i> mammalian somatic cell genotoxicity study does not need to be conducted if there are adequate results available from an appropriate <i>in vivo</i> mammalian somatic cell genotoxicity study.</p> <p>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.’;</p>
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(d) point 8.7.2 is replaced by the following:

<p>‘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</p>	<p>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</p>
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<p>higher systemic exposure via another relevant route of human exposure or route-specific toxicity.</p>	<p>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.’;</p>
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(e) in point 8.7.3, in column 1, the text is replaced by the following:

<p>‘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.’;</p>	
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(f) in point 8.7.3, in column 2, the introductory wording of the first paragraph is replaced by the following:

	<p>‘8.7.3. An Extended One-Generation Reproductive Toxicity Study with the extension of cohort 1B to include the F2</p>
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	generation shall be proposed by the registrant or may be required by the Agency if:’;
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(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:’;
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(h) in subsection 9.1, in column 2, the text is replaced by the following:

	<p>‘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.</p> <p>The choice of the test(s) shall be made on the basis of the results of the chemical safety assessment.’;</p>
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(i) point 9.1.6 is replaced by the following:

<p>‘9.1.6. Long-term toxicity testing on fish, (unless already provided as part of Annex VIII requirements).</p> <p>The information shall be provided for subpoint 9.1.6.1 or subpoint</p>	<p>9.1.6. Fish short-term toxicity tests on embryo and sac-fry stages (OECD TG 212) that were initiated before ...[<i>OP, please insert the date of entry into force of this amending Regulation</i>] shall be considered appropriate to address this standard information 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</p>
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9.1.6.3.	mode of action.'
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(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)';	
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(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)';	
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(m) in subsection 9.2, in column 2, the text is replaced by the following:

	<p>'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.</p> <p>The choice of the appropriate test(s) and test media shall be made on the basis of the results of the chemical safety assessment.';</p>
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(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';	
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(o) in subsection 9.4, in column 2, the text is replaced by the following:

	<p>‘9.4. These studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely.</p> <p>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.</p> <p>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.’;</p>
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(5) Annex X is amended as follows:

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

<p>‘8.4. Mutagenicity</p>	<p>‘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:</p> <ul style="list-style-type: none"> - 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
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	management measures are implemented.’;
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(b) the following points 8.4.6 and 8.4.7 are added:

‘8.4.6. A second <i>in vivo</i> mammalian somatic cell genotoxicity study, if there is a positive result in any of the <i>in vitro</i> 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 <i>in vivo</i> mammalian somatic cell genotoxicity study.	
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8.4.7. A second <i>in vivo</i> mammalian germ cell genotoxicity study, if there is a positive result in <i>in vivo</i> 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 <i>in vivo</i> 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.’;
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(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	Deviations from the default route of administration and deviations in the choice of
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<p>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.</p>	<p>species shall be scientifically justified.’;</p>
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(d) in point 8.7.3, in column 1, the text is replaced by the following:

<p>‘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.’;</p>	
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(e) in point 8.7.3, in column 2, the introductory wording of the first paragraph is replaced by the following:

	<p>‘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: ’;</p>
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(f) in point 8.7.3, in column 2, the introductory wording of the second paragraph is replaced by the following:

	<p>‘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:’;</p>
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(g) in subsection 9.2, in column 2, the text is replaced by the following:

	<p>‘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. ’;</p>
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(h) point 9.2.1 is deleted;

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

	<p>‘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.</p>
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	These studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely.’;
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(j) in point 9.5.1, in column 2, the text is replaced by the following:

	<p>‘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.</p> <p>The choice of the appropriate test(s) shall be made on the basis of the results of the chemical safety assessment.’</p>
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