[X1ANNEX XI

GENERAL RULES FOR ADAPTATION OF THE STANDARD TESTING REGIME SET OUT IN ANNEXES VII TO X

Editorial Information

X1 Substituted by Corrigendum 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 (Official Journal of the European Union L 396 of 30 December 2006).

Annexes VII to X set out the information requirements for all substances manufactured or imported in quantities of:

— one tonne or more in accordance with Article 12(1)(a),

— 10 tonnes or more in accordance with Article 12(1)(c),

— 100 tonnes or more in accordance with Article 12(1)(d), and

— 1 000 tonnes or more in accordance with Article 12(1)(e).

In addition to the specific rules set out in column 2 of Annexes VII to X, a registrant may adapt the standard testing regime in accordance with the general rules set out in Section 1 of this Annex. Under dossier evaluation the Agency may assess these adaptations to the standard testing regime.

[[F1]The requirements specific to nanoforms in this Annex are without prejudice to requirements applicable to other forms of a substance.**]**

Textual Amendments

F1 Inserted by Commission Regulation (EU) 2018/1881 of 3 December 2018 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards Annexes I, III,VI, VII, VIII, IX, X, XI, and XII to address nanoforms of substances (Text with EEA relevance).

1. TESTING DOES NOT APPEAR SCIENTIFICALLY NECESSARY

1.1. Use of existing data

1.1.1. Data on physical-chemical properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3)

Data shall be considered to be equivalent to data generated by the corresponding test methods referred to in Article 13(3) if the following conditions are met:

(1) adequacy for the purpose of classification and labelling and/or risk assessment;

(2) sufficient documentation is provided to assess the adequacy of the study; and

(3) the data are valid for the endpoint being investigated and the study is performed using an acceptable level of quality assurance.

1.1.2. Data on human health and environmental properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3)

Data shall be considered to be equivalent to data generated by the corresponding test methods referred to in Article 13(3) if the following conditions are met:

(1) adequacy for the purpose of classification and labelling and/or risk assessment;

(2) adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3);

(3) exposure duration comparable to or longer than the corresponding test methods referred to in Article 13(3) if exposure duration is a relevant parameter; and

(4) adequate and reliable documentation of the study is provided.

[[F2]1.1.3. Historical human data

Historical human data, such as epidemiological studies on exposed populations, accidental or occupational exposure data and clinical studies, shall be considered.

The strength of the data for a specific human health effect depends, among other things, on the type of analysis and on the parameters covered and on the magnitude and specificity of the response and consequently the predictability of the effect. Criteria for assessing the adequacy of the data include:

(1) the proper selection and characterisation of the exposed and control groups;

(2) adequate characterisation of exposure;

(3) sufficient length of follow-up for disease occurrence;

(4) valid method for observing an effect;

(5) proper consideration of bias and confounding factors; and

(6) a reasonable statistical reliability to justify the conclusion.

In all cases adequate and reliable documentation shall be provided.

When nanoforms are covered by the registration the above approach shall address the nanoforms separately.**]**

Textual Amendments

F2 Substituted by Commission Regulation (EU) 2018/1881 of 3 December 2018 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards Annexes I, III,VI, VII, VIII, IX, X, XI, and XII to address nanoforms of substances (Text with EEA relevance).

[[F2]1.2. Weight of evidence

There may be sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property, while the information from each single source alone is regarded insufficient to support this notion.

There may be sufficient weight of evidence from the use of newly developed test methods, not yet included in the test methods referred to in Article 13(3) or from an international test method recognised by [F3]... the Agency as being equivalent, leading to the conclusion that a substance has or has not a particular dangerous property.

Textual Amendments

F3 Words in Annex 11 point 1.2 omitted (31.12.2020) by virtue of The REACH etc. (Amendment etc.) (EU Exit) Regulations 2019 (S.I. 2019/758), reg. 1(1), **Sch. 3 para. 8(2)**; 2020 c. 1, Sch. 5 para. 1(1)

Where sufficient weight of evidence for the presence or absence of a particular dangerous property is available:

further testing on vertebrate animals for that property shall be omitted,

further testing not involving vertebrate animals may be omitted.

In all cases adequate and reliable documentation shall be provided.

When nanoforms are covered by the registration the above approach shall address the nanoforms separately.**]**

[[F2]1.3. Qualitative or Quantitative structure-activity relationship ((Q)SAR)

Results obtained from valid qualitative or quantitative structure-activity relationship models ((Q)SARs) may indicate the presence or absence of a certain dangerous property. Results of (Q)SARs may be used instead of testing when the following conditions are met:

— results are derived from a (Q)SAR model whose scientific validity has been established,

— the substance falls within the applicability domain of the (Q)SAR model,

— results are adequate for the purpose of classification and labelling and/or risk assessment, and

— adequate and reliable documentation of the applied method is provided.

The Agency in collaboration with [F4]... interested parties shall develop and provide guidance in assessing which (Q)SARs will meet these conditions and provide examples.

Textual Amendments

F4 Words in Annex 11 point 1.3 omitted (31.12.2020) by virtue of The REACH etc. (Amendment etc.) (EU Exit) Regulations 2019 (S.I. 2019/758), reg. 1(1), **Sch. 3 para. 8(3)**; 2020 c. 1, Sch. 5 para. 1(1)

When nanoforms are covered by the registration the above approach shall address the nanoforms separately.**]**

1.4. *In vitro* methods

Results obtained from suitable *in vitro* methods may indicate the presence of a certain dangerous property or may be important in relation to a mechanistic understanding, which may be important for the assessment. In this context, ‘suitable’ means sufficiently well developed according to internationally agreed test development criteria [F5]... for the entry of a test into the prevalidation **[**[F6]process**]**. Depending on the potential risk, immediate confirmation requiring testing beyond the information foreseen in Annexes VII or VIII or proposed confirmation

requiring testing beyond the information foreseen in Annexes IX or X for the respective tonnage level may be necessary.

Textual Amendments

F5 Words in Annex 11 point 1.4 omitted (31.12.2020) by virtue of The REACH etc. (Amendment etc.) (EU Exit) Regulations 2019 (S.I. 2019/758), reg. 1(1), **Sch. 3 para. 8(4)(a)**; 2020 c. 1, Sch. 5 para. 1(1)

F6 Word in Annex 11 point 1.4 substituted (31.12.2020) by The REACH etc. (Amendment etc.) (EU Exit) Regulations 2019 (S.I. 2019/758), reg. 1(1), **Sch. 3 para. 8(4)(b)**; 2020 c. 1, Sch. 5 para. 1(1)

If the results obtained from the use of such *in vitro* methods do not indicate a certain dangerous property, the relevant test shall nevertheless be carried out at the appropriate tonnage level to confirm the negative result, unless testing is not required in accordance with Annexes VII to X or the other rules in this Annex.

[[F2]Such confirmation may be waived if the following conditions are met:

(1) results are derived from an *in vitro* method whose scientific validity has been established by a validation study, according to internationally agreed validation principles;

(2) results are adequate for the purpose of classification and labelling and/or risk assessment; and

(3) adequate and reliable documentation of the applied method is provided.

When nanoforms are covered by the registration the above approach in points (1) to (3) shall address the nanoforms separately.**]**

1.5. Grouping of substances and read-across approach

[[F2]Substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as a group, or ‘ category ’ of substances. Application of the group concept requires that physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach). This avoids the need to test every substance for every endpoint. The Agency, after consulting with relevant stakeholders and other interested parties, shall issue guidance on technically and scientifically justified methodology for the grouping of substances [F7]....

Textual Amendments

F7 Words in Annex 11 point 1.5 omitted (31.12.2020) by virtue of The REACH etc. (Amendment etc.) (EU Exit) Regulations 2019 (S.I. 2019/758), reg. 1(1), **Sch. 3 para. 8(5)**; 2020 c. 1, Sch. 5 para. 1(1)

When nanoforms are covered by the registration the above approach shall address the nanoforms separately. For grouping different nanoforms of the same substance the molecular structural similarities alone cannot serve as a justification.

If nanoforms covered by a registration are grouped or placed in a ‘ category ’ with other forms, including other nanoforms, of the substance in the same registration the obligations above shall apply in the same manner.**]**

The similarities may be based on:

(1) a common functional group;

(2) the common precursors and/or the likelihood of common breakdown products via physical and biological processes, which result in structurally similar chemicals; or

(3) a constant pattern in the changing of the potency of the properties across the category.

If the group concept is applied, substances shall be classified and labelled on this basis.

In all cases results should:

— be adequate for the purpose of classification and labelling and/or risk assessment,

— have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3),

— cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter, and

— adequate and reliable documentation of the applied method shall be provided.

2. TESTING IS TECHNICALLY NOT POSSIBLE

Testing for a specific endpoint may be omitted, if it is technically not possible to conduct the study as a consequence of the properties of the substance: e.g. very volatile, highly reactive or unstable substances cannot be used, mixing of the substance with water may cause danger of fire or explosion or the radio-labelling of the substance required in certain studies may not be possible. The guidance given in the test methods referred to in Article 13(3), more specifically on the technical limitations of a specific method, shall always be respected.

[F8 3. SUBSTANCE-TAILORED EXPOSURE-DRIVEN TESTING

3.1. Testing in accordance with Sections 8.6 and 8.7 of Annex VIII and in accordance with Annex IX and Annex X may be omitted, based on the exposure scenario(s) developed in the Chemical Safety Report.

3.2. In all cases, adequate justification and documentation shall be provided. The justification shall be based on a thorough and rigorous exposure assessment in accordance with section 5 of Annex I and shall meet any one of the following criteria:

(a) the manufacturer or importer demonstrates and documents that all of the following conditions are fulfilled:

(i) the results of the exposure assessment covering all relevant exposures throughout the life cycle of the substance demonstrate the absence of or no significant exposure in all scenarios of the manufacture and all identified uses as referred to in Annex VI section 3.5;

(ii) a DNEL or a PNEC can be derived from results of available test data for the substance concerned taking full account of the increased uncertainty resulting from the omission of the information requirement, and that DNEL or PNEC is relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes [1] ;

(iii) the comparison of the derived DNEL or PNEC with the results of the exposure assessment shows that exposures are always well below the derived DNEL or PNEC;

(b) where the substance is not incorporated in an article the manufacturer or importer demonstrates and documents for all relevant scenarios that throughout the life cycle strictly controlled conditions as set out in Article 18(4)(a) to (f) apply;

(c) where the substance is incorporated in an article in which it is permanently embedded in a matrix or otherwise rigorously contained by technical means, it is demonstrated and documented that all of the following conditions are fulfilled:

(i) the substance is not released during its life cycle;

(ii) the likelihood that workers or the general public or the environment are exposed to the substance under normal or reasonably foreseeable conditions of use is negligible; and

(iii) the substance is handled according to the conditions set out in Article 18(4)(a) to (f) during all manufacturing and production stages including the waste management of the substance during these stages.

3.3. The specific conditions of use must be communicated through the supply chain in accordance with Article 31 or 32, as the case may be.**]]**

Textual Amendments

F8 Inserted by Commission Regulation (EU) No 143/2011 of 17 February 2011 amending Annex XIV to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals ('REACH') (Text with EEA relevance).

(1) **[**[X1]**[**[F8]For the purpose of subparagraph 3.2(a)(ii), without prejudice to column 2 of Section 8.7 of Annexes IX and X, a DNEL derived from a screening test for reproductive/developmental toxicity shall not be considered appropriate to omit a prenatal developmental toxicity study or a two-generation reproductive toxicity study. For the purpose of subparagraph 3.2(a)(ii), without prejudice to column 2 of section 8.6 of Annexes IX and X, a DNEL derived from a 28-day repeated dose toxicity study shall not be considered appropriate to omit a 90-day repeated dose toxicity study.**]]**

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Textual Amendments

F8 Inserted by Commission Regulation (EU) No 143/2011 of 17 February 2011 amending Annex XIV to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals ('REACH') (Text with EEA relevance).

Changes to legislation:
There are currently no known outstanding effects for the Regulation (EC) No 1907/2006 of the European Parliament and of the Council, ANNEX XI .