Council of the
European Union

Brussels, 10 February 2021
(OR. en)

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COVER NOTE

From:	Secretary-General of the European Commission, signed by Ms Martine DEPREZ, Director
date of receipt:	9 February 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 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)

Delegations will find attached document […](2021) XXX draft - D 070789/03 ANNEX.

Encl.: […](2021) XXX draft - D 070789/03 ANNEX

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ANNEX

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

(1) Annex VII is amended as follows:

(a) in the introductory part, the following paragraph is inserted after the sixth paragraph:

'Where a test method offers flexibility in the study design, for example in relation to the choice of dose levels, the chosen study design shall ensure that the data generated are adequate for hazard identification and risk assessment. To this end, testing shall be performed at appropriately high dose levels. If dose (concentration) selection is limited by the physicochemical properties or biological effects of the test substance, justification shall be provided.';

(b) in subsection 7.6, in column 1, the text is replaced by the following:

'7.6. Surface tension of an aqueous solution';	

(c) in subsection 7.7, in column 2, the following paragraph is added:

	'For metals and sparingly soluble metal compounds, information on transformation/ dissolution in aqueous media shall be provided.';

(d) in point 8.2.1, in column 2, the text is replaced by the following:

	'8.2.1. If results from a first in vitro study do not allow a conclusive decision on the classification of a substance or on the absence of eye irritation potential, (an)other in vitro study/studies for this endpoint shall be performed by the registrant or may be required by the Agency.'.

(2) Annex VIII is amended as follows:

(a) in the introductory part, the following paragraph is inserted after the fourth paragraph:

‘Where a test method offers flexibility in the study design, for example in relation to the choice of dose levels, the chosen study design shall ensure that the data generated are adequate for hazard identification and risk assessment. To this end, testing shall be performed at appropriately high dose levels. If dose (concentration) selection is limited by the physicochemical properties or biological effects of the test substance, justification shall be provided.’;

(b) in subsection 8.1, in column 2, the first paragraph is replaced by the following:

	‘8.1. An in vivo study for skin corrosion/irritation shall be conducted only if the in vitro study/studies under points 8.1.1 and/or 8.1.2 of Annex VII is(are) not applicable, or the results of this/these study/studies is/are not adequate for classification and risk assessment.’;

(c) in subsection 8.2, in column 2, the first paragraph is replaced by the following:

	‘8.2 An in vivo study for serious eye damage/ eye irritation shall be conducted only if the in vitro study/studies) under point 8.2.1 of Annex VII is/are not applicable, or the results of this/these study/studies) are not adequate for classification and risk assessment.’;

(d) in point 8.6.1, in column 2, in the first paragraph, the first indent is replaced by the following:

	‘- a reliable sub-chronic (90 days) or chronic toxicity study is available or proposed by the registrant, provided that an appropriate species, dosage, solvent and route of administration are used, or’;

(e) in point 8.6.1, in column 2, the fourth and fifth paragraphs are replaced by the following:

	‘For nanoforms without high dissolution rate in biological media, the study shall include toxicokinetic investigations on, among others, the recovery period and, where relevant, lung

	clearance. Toxicokinetic investigations do not need to be performed if equivalent toxicokinetic information on the nanoform is already available. The sub-chronic toxicity study (90 days) (Annex IX, point 8.6.2) shall be proposed by the registrant**,** or may be required by the Agency if: the frequency and duration of human exposure indicates that a longer term study is appropriate; and one of the following conditions is met: — other available data indicate that the substance may have a dangerous property that cannot be detected in a short-term toxicity study, or − appropriately designed toxicokinetic studies reveal accumulation of the substance or its metabolites in certain tissues or organs which would possibly remain undetected in a short-term toxicity study but which are liable to result in adverse effects after prolonged exposure.’;

(f) in point 9.3.1, in column 2, the following paragraph is inserted after the first paragraph:

		‘The study may not be waived on the basis of low octanol-water partition coefficient alone, unless the adsorptive properties of the substance are solely driven by lipophilicity. For instance, the study may not be waived on the basis of low octanol-water

		partition coefficient alone if the substance is surface active or ionisable at environmental pH (pH 4 – 9).’.

(3) Annex IX is amended as follows:

(a) in the introductory part, the following paragraph is inserted after the fifth paragraph:

‘Where a test method offers flexibility in the study design, for example in relation to the choice of dose levels, the chosen study design shall ensure that the data generated are adequate for hazard identification and risk assessment. To this end, testing shall be performed at appropriately high dose levels. If dose (concentration) selection is limited by the physicochemical properties or biological effects of the test substance, justification shall be provided.’;

(b) in subsection 7.16, in column 2, the following indent is added:

	‘- or based on the structure, the substance does not have any chemical group that can dissociate.’;

(c) in subsection 7.17, in column 2, the following text is added:

	‘For hydrocarbon substances the kinematic viscosity shall be determined at 40°C.’;

(d) point 8.6.1 is deleted;

(e) in point 8.6.2, in column 2, in the first paragraph, the introductory sentence and the first and second indents are replaced by the following:

	‘8.6.2. The sub-chronic toxicity study (90 days) does not need to be conducted if: — a reliable short-term toxicity study (28 days) is available showing severe toxicity effects meeting the criteria for classifying the substance as STOT RE (category 1 or 2), for which the observed NOAEL-28 days, with the application of an appropriate uncertainty factor, allows the extrapolation towards the NOAEL-90 days for the

	same route of exposure, or — a reliable chronic toxicity study is available or proposed by the registrant, provided that an appropriate species and route of administration are used, or’;

(f) in point 8.6.2, in column 2, the fourth paragraph is replaced by the following:

	‘For nanoforms without high dissolution rate in biological media, the study shall include toxicokinetic investigations on, among others, the recovery period and, where relevant, lung clearance. Toxicokinetic investigations do not need to be performed if equivalent toxicokinetic information on the nanoform is already available.’

(g) in subsection 8.7, in column 2, the text is replaced by the following:

	‘8.7. The studies do not need to be conducted if: - 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 carcinogenicity (category 1A or 1B), and appropriate risk management measures are implemented, or - 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, or

	- the substance is of low toxicological activity (a comprehensive and informative dataset showing no toxicity in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure. If a substance is known to have an adverse effect on sexual function and 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, then no further testing for sexual function and fertility shall be necessary. If 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, then no further testing for developmental toxicity shall be necessary.'

(h) in point 9.3.2, in column 2, the following paragraph is inserted after the first paragraph:

	'The study may not be waived on the basis of low octanol-water partition coefficient alone, unless the potential for bioaccumulation of the substance is solely driven by lipophilicity. For instance, the study may not be waived on the basis of low octanol-water partition coefficient alone if the substance is surface active or ionisable at environmental pH (pH 4 – 9).';

(i) in point 9.3.3, in column 2, the following paragraph is inserted after the first paragraph:

	'The study may not be waived on the basis of low octanol-water partition coefficient alone, unless the adsorptive properties of the substance are solely driven by lipophilicity. For instance, the study may not be waived on the basis of low octanol-water partition coefficient alone if the substance is surface active or ionisable at environmental pH (pH 4 – 9).'

(4) Annex X is amended as follows:

(a) in the introductory part, the following paragraph is inserted after the fifth paragraph:

'Where a test method offers flexibility in the study design, for example in relation to the choice of dose levels, the chosen study design shall ensure that the data generated are adequate for hazard identification and risk assessment. To this end, testing shall be performed at appropriately high dose levels. If dose (concentration) selection is limited by the physicochemical properties or biological effects of the test substance, justification shall be provided.';

(b) in subsection 8.7, in column 2, the text is replaced by the following:

	'8.7. The studies do not need to be conducted if: - 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 carcinogenicity (category 1A or 1B), and appropriate risk management measures are implemented, or - 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, or - the substance is of low toxicological activity (a comprehensive and informative dataset showing no toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure. If a substance is known to have an adverse effect on sexual function and 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, then no further testing for sexual function and fertility shall be necessary. If 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, then no further testing for developmental toxicity shall be necessary.'.

(5) Annex XI is amended as follows:

(a) section 1 ("TESTING DOES NOT APPEAR SCIENTIFICALLY NECESSARY") is amended as follows:

(i) under the header of subsection 1.1. ("Use of existing data"), the following text is added:

'Any data generated as from 1 June 2008 shall not be considered as existing data and shall not be subject to the general rules for adaptation laid down in this point (1.1).';

(ii) the header of point 1.1.1. is replaced by the following:

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

(iii) in subsection 1.2. ("Weight of evidence"), the text is replaced by the following:

'There is sufficient weight of evidence when information from several independent sources together enable, through a reasoned justification, a conclusion on the information requirement, while the information from each single source alone is insufficient to fulfil the information requirement. The justification must have regard to the information that would otherwise be obtained from the study that shall normally be performed for this information requirement.

There may also 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), leading to a reasoned justification that they provide the information that would enable a conclusion on the information requirement.

Weight of evidence may lead to the conclusion that a substance has or has not a particular property.

If there is sufficient weight of evidence, the information requirement is fulfilled. Consequently, further testing on vertebrate animals shall be omitted and further testing not involving vertebrate animals may be omitted.

In all cases, the information provided shall be adequate for the purpose of classification, labelling and/or risk assessment, and adequate and reliable documentation shall be provided, including:

- robust study summaries of the studies used as sources of information;
- a justification explaining why the sources of information together provide a conclusion on the information requirement.

When nanoforms are covered by the registration, the above approach shall address the nanoforms separately.';

(iv) in subsection 1.5. ("Grouping of substances and read-across approach"), the text is replaced by the following:

'Substances whose physicochemical, toxicological and ecotoxicological 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.

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 may not 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 any of the following:

(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;

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

Structural similarity for UVCB substances shall be established on the basis of similarities in the structures of the constituents, together with the concentration of these constituents and variability in the concentration of these constituents. If it can be demonstrated that the identification of all individual constituents is not technically possible or impractical, the structural similarity may be demonstrated by other means, to enable a quantitative and qualitative comparison of the actual composition between substances.

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

In all cases, results shall fulfil all of the following conditions:

- 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 study that shall normally be performed for a particular information requirement,
- cover an exposure duration comparable to or longer than the corresponding study that shall normally be performed for a particular information requirement if exposure duration is a relevant parameter.

In all cases, adequate and reliable documentation of the applied method shall be provided. Such documentation shall include:

- a robust study summary for each source study used in the adaptation;
- an explanation why the properties of the registered substance may be predicted from other substances in the group;
- supporting information to scientifically justify such explanation for prediction of properties.';

(b) section 3 ("SUBSTANCE-TAILORED EXPOSURE-DRIVEN TESTING") is amended as follows:

(i) subsection 3.1. is replaced by the following:

'3.1. Testing in accordance with Section 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. Testing in accordance with Section 8.6.1. of Annex VIII may be omitted only for registrants producing less than 100 tonnes per year per manufacturer or importer, based on the exposure scenario(s) developed in the Chemical Safety Report.'

(ii) point 3.2(a)(ii) is replaced by the following:

'(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. For this purpose and without prejudice to column 2 of Sections 8.6 and 8.7 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, and a DNEL derived from a screening test for reproductive/developmental toxicity shall not be considered appropriate to omit a prenatal developmental toxicity study or an extended one-generation reproductive toxicity study.'.