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From:	European Commission
date of receipt:	1 October 2014
To:	General Secretariat of the Council
Subject:	ANNEX to COMMISSION REGULATION (EU) No …/.. of XXX amending Annexes VIII, IX and X to 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 the Extended one-generation reproductive toxicity study

Delegations will find attached document D034185/03 Annex 1.

Encl.: D034185/03 Annex 1

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Annex

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

(1) In Annex VIII , in the table setting out the toxicological information, in column 2 (Specific Rules for Adaptation from Column 1), point 8.7.1. is replaced by the following:

	"8.7.1. This study does not need to be conducted if: — the substance is known to be a genotoxic carcinogen and appropriate risk management measures are implemented, or — the substance is known to be a germ cell mutagen and appropriate risk management measures are implemented, or — relevant human exposure can be excluded in accordance with Annex XI section 3, or — a pre-natal developmental toxicity study (Annex IX, 8.7.2) or, either an Extended One-Generation Reproductive Toxicity Study (B.56, OECD TG 443) (Annex IX, Section 8.7.3) or a two-generation study (B.35, OECD TG 416), is available. If a substance is known to have an adverse effect on fertility, meeting the criteria for classification as toxic for reproduction 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 fertility will be necessary. However, testing for developmental toxicity must be considered. If a substance is known to cause developmental toxicity, meeting the criteria for classification as toxic for reproduction 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 will be necessary. However, testing for effects on fertility must be considered. In cases where there are serious concerns about the potential for adverse effects on fertility or development, either an Extended One-Generation Reproductive Toxicity Study (Annex IX, Section 8.7.3) or a pre- natal developmental toxicity study (Annex IX, Section 8.7.2) may, as appropriate, be proposed by the registrant instead of the screening study."

(2) In Annex IX, in the table setting out the toxicological information, in column 1 (Standard Information Requirement) and column 2 (Specific Rules for Adaptation from Column 1) point 8.7.3. is replaced by the following:

"COLUMN 1 STANDARD INFORMATION REQUIRED	COLUMN 2 SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1
8.7.3. Extended One-Generation Reproductive Toxicity Study (B.56 of the Commission Regulation on test methods as specified in Article 13(3) or OECD 443), basic test design (cohorts 1A and 1B without extension to include a F2 generation), one species, most appropriate route of administration, having regard to the likely route of human exposure, if the available repeated dose toxicity studies (e.g. 28-day or 90-day studies, OECD 421 or 422 screening studies) indicate adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity.	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 in accordance with Articles 40 or 41, if: (a) the substance has uses leading to significant exposure of consumers or professionals, taking into account, *inter alia*, consumer exposure from articles, and (b) any of the following conditions are met: - the substance displays genotoxic effects in somatic cell mutagenicity tests *in vivo* which could lead to classifying it as Mutagen Category 2, or - there are indications that the internal dose for the substance and/or any of its metabolites will reach a steady state in the test animals only after an extended exposure, or - there are indications of one or more relevant modes of action related to endocrine disruption from available in vivo studies or non-animal approaches. 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 accordance with Articles 40 or 41, in case of particular concerns on (developmental) neurotoxicity or (developmental) immunotoxicity justified by any of the following: - existing information on the substance itself derived from relevant available in vivo or non-animal approaches (e.g. abnormalities of the CNS, evidence of adverse effects on the nervous or immune system in studies on adult animals or animals exposed prenatally), or - specific mechanisms/modes of action of the substance with an association to (developmental) neurotoxicity and/or (developmental) immunotoxicity (e.g. cholinesterase inhibition or relevant changes in thyroidal hormone levels

	associated to adverse effects), or - existing information on effects caused by substances structurally analogous to the substance being studied, suggesting such effects or mechanisms/modes of action. Other studies on developmental neurotoxicity and/or developmental immunotoxicity instead of cohorts 2A/2B (developmental neurotoxicity) and/or cohort 3 (developmental immunotoxicity) of the Extended One-Generation Reproductive Toxicity Study may be proposed by the registrant in order to clarify the concern on developmental toxicity. Two-generation reproductive toxicity studies (B.35, OECD TG 416) that were initiated before [date of the entry into force of this Regulation] shall be considered appropriate to address this standard information requirement. The study shall be performed on one species. The need to perform a study at this tonnage level or the next on a second strain or a second species may be considered and a decision should be based on the outcome of the first test and all other relevant available data."

(3) In Annex X, in the table setting out the toxicological information, in column 1 (Standard Information Requirement) and column 2 (Specific Rules for Adaptation from Column 1) point 8.7.3. is replaced by the following:

"COLUMN 1 STANDARD INFORMATION REQUIRED	COLUMN 2 SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1
8.7.3. Extended One-Generation Reproductive Toxicity Study (B.56 of the Commission Regulation on test methods as specified in Article 13(3) or OECD 443), basic test design (cohorts 1A and 1B without extension to include a F2 generation), one species, most	"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 in accordance with Articles 40 or 41, if: (a) the substance has uses leading to significant exposure of consumers or professionals, taking into account, *inter alia*, consumer exposure from articles, and (b) any of the following conditions are met: - the substance displays genotoxic effects in somatic cell

appropriate route of administration, having regard to the likely route of human exposure, unless already provided as part of Annex IX requirements.	mutagenicity tests in vivo which could lead to classifying it as Mutagen Category 2, or - there are indications that the internal dose for the substance and/or any of its metabolites will reach a steady state in the test animals only after an extended exposure, or - there are indications of one or more relevant modes of action related to endocrine disruption from available in vivo studies or non-animal approaches. 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 accordance with Articles 40 or 41, in case of particular concerns on (developmental) neurotoxicity or (developmental) immunotoxicity justified by any of the following: - existing information on the substance itself derived from relevant available in vivo or non-animal approaches (e.g. abnormalities of the CNS, evidence of adverse effects on the nervous or immune system in studies on adult animals or animals exposed prenatally), or - specific mechanisms/modes of action of the substance with an association to (developmental) neurotoxicity and/or (developmental) immunotoxicity (e.g. cholinesterase inhibition or relevant changes in thyroidal hormone levels associated to adverse effects), or - existing information on effects caused by substances structurally analogous to the substance being studied, suggesting such effects or mechanisms/modes of action. Other studies on developmental neurotoxicity and/or developmental immunotoxicity instead of cohorts 2A/2B (developmental neurotoxicity) and/or cohort 3 (developmental immunotoxicity) of the Extended One-Generation Reproductive Toxicity Study may be proposed by the registrant in order to clarify the concern on developmental toxicity. Two-generation reproductive toxicity studies (B.35, OECD TG 416) that were initiated before [date of the entry into force of this Regulation] shall be considered appropriate to address this standard information requirement."