ANNEX X

STANDARD INFORMATION REQUIREMENTS FOR SUBSTANCES MANUFACTURED OR IMPORTED IN QUANTITIES OF 1 000 TONNES OR MORE

At the level of this Annex, the registrant must submit a proposal and a time schedule for fulfilling the information requirements of this Annex in accordance with Article 13(1)(d).

Column 1 of this Annex establishes the standard information required for all substances manufactured or imported in quantities of 1 000 tonnes or more in accordance with Article 13(1)(d). Accordingly, the information required in column 1 of this Annex is additional to that required in column 1 of Annexes VII, VIII and IX. Any other relevant physicochemical, toxicological and ecotoxicological information that is available shall be provided. Column 2 of this Annex lists specific rules according to which the registrant may propose to omit the required standard information, replace it by other information, provide it at a later stage or adapt it in another way. If the conditions are met under which column 2 of this Annex allows an adaptation to be proposed, the registrant shall clearly state this fact and the reasons for proposing each adaptation under the appropriate headings in the registration dossier.

In addition to these specific rules, a registrant may propose to adapt the required standard information set out in column 1 of this Annex according to the general rules contained in Annex XI. In this case as well, he shall clearly state the reasons for any decision to propose adaptations to the standard information under the appropriate headings in the registration dossier referring to the appropriate specific rule(s) in column 2 or in Annex XI.

Before new tests are carried out to determine the properties listed in this Annex, all available in vitro data, in vivo data, historical human data, data from valid (Q)SARs and data from structurally related substances (read-across approach) shall be assessed first. In vivo testing with corrosive substances at concentration/dose levels causing corrosivity shall be avoided. Prior to testing, further guidance on testing strategies should be consulted in addition to this Annex.

When, for certain endpoints, it is proposed not to provide information for other reasons than those mentioned in column 2 of this Annex or in Annex XI, this fact and the reasons shall also be clearly stated.

8. TOXICOLOGICAL INFORMATION	
COLUMN 1 **STANDARD INFORMATION REQUIRED**	**COLUMN 2** **SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1**
	8.4. If there is a positive result in any of the in vitro genotoxicity studies in Annexes VII or VIII, a second in vivo somatic cell test may be necessary, depending on the quality and relevance of all the available data.

	If there is a positive result from an in vivo somatic cell study available, the potential for germ cell mutagenicity should be considered on the basis of all available data, including toxicokinetic evidence. If no clear conclusions about germ cell mutagenicity can be made, additional investigations shall be considered.
	8.6.3. A long-term repeated toxicity study (≥ 12 months) may be proposed by the registrant or required by the Ministry in accordance with Articles 36 or 37 if the frequency and duration of human exposure indicates that a longer term study is appropriate and one of the following conditions is met: — serious or severe toxicity effects of particular concern were observed in the 28-day or 90-day study for which the available evidence is inadequate for toxicological evaluation or risk characterisation, or — effects shown in substances with a clear relationship in molecular structure with the substance being studied were not detected in the 28-day or 90-day study, or — the substance may have a dangerous property that cannot be detected in a 90-day study.
	8.6.4. Further studies shall be proposed by the registrant or may be required by the Ministry in accordance with Articles 36 or 37 in case of: — toxicity of particular concern (e.g. serious/severe effects), or — indications of an effect for which the available evidence is inadequate for toxicological evaluation and/or risk characterisation. In such cases it may also be

	more appropriate to perform specific toxicological studies that are designed to investigate these effects (e.g. immunotoxicity, neurotoxicity), or — particular concern regarding exposure (e.g. use in consumer products leading to exposure levels which are close to the dose levels at which toxicity is observed).
8.7. Reproductive toxicity	8.7. The studies need not 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 — the substance is of low toxicological activity (no evidence of 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. M3 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. 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 Ministry in accordance with Article 36 or 37, 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:

8.7.2. Developmental toxicity study, one species, most appropriate route of administration, having regard to the likely route of human exposure (OECD 414).	— 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.
8.7.3. Extended One- Generation Reproductive Toxicity Study (B.56 of By-law on Determination of Physico-Chemical, Toxicological and Ecotoxicological Properties of Substances and Mixtures 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, unless already provided as part of Annex IX requirements.	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 Ministry in accordance with Article 36 or 37, 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 13 March 2015 shall be considered appropriate to address this standard information requirement.
8.9.1. Carcinogenicity study	8.9.1. A carcinogenicity study may be proposed by the registrant or may be required by the Ministry in accordance with Articles 36 or 37 if: — the substance has a widespread dispersive use or there is evidence of frequent or long-term human exposure, and — the substance is classified as germ cell mutagen category 2 or there is evidence from the repeated dose study(ies) that the substance is able to induce hyperplasia and/or pre-neoplastic lesions. If the substance is classified as germ cell mutagen category 1A or 1B, the default presumption would be that a genotoxic mechanism for carcinogenicity is likely. In

	these cases, a carcinogenicity test will normally not be required.
9. ECOTOXICOLOGICAL INFORMATION	
9.2. Degradation 9.2.1. Biotic	9.2. Further biotic degradation testing shall be proposed if the chemical safety assessment according to Annex I indicates the need to investigate further the degradation of the substance and its degradation products. The choice of the appropriate test(s) depends on the results of the chemical safety assessment and may include simulation testing in appropriate media (e.g. water, sediment or soil).
9.3. Fate and behaviour in the environment	9.3.4. Further testing shall be proposed by the registrant or may be required by the Ministry

9.3.4. Further information on the environmental fate and behaviour of the substance and/or degradation products	in accordance with Articles 36 or 37 if the chemical safety assessment according to Annex I indicates the need to investigate further the fate and behaviour of the substance. The choice of the appropriate test(s) depends on the results of the chemical safety assessment.
9.4. Effects on terrestrial organisms 9.4.4. Long-term toxicity testing on invertebrates, unless already provided as part of Annex IX requirements. 9.4.6. Long-term toxicity testing on plants, unless already provided as part of Annex IX requirements.	9.4. Long-term toxicity testing shall be proposed by the registrant if the results of the chemical safety assessment according to Annex I indicates the need to investigate further the effects of the substance and/or degradation products on terrestrial organisms. The choice of the appropriate test(s) depends on 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.
9.5.1. Long-term toxicity to sediment organisms	9.5.1 Long-term toxicity testing shall be proposed by the registrant if the results of the chemical safety assessment indicates the need to investigate further the effects of the substance and/or relevant degradation products on sediment organisms. The choice of the appropriate test(s) depends on the results of the chemical safety assessment.
9.6.1. Long-term or reproductive toxicity to birds	9.6.1. Any need for testing should be carefully considered taking into account the large mammalian dataset that is usually available at this tonnage level.

10. METHODS OF DETECTION AND ANALYSIS

Description of the analytical methods shall be provided on request, for the relevant compartments for which studies were performed using the analytical method concerned. If the analytical methods are not available this shall be justified.