ANNEX VIII

STANDARD INFORMATION REQUIREMENTS FOR SUBSTANCES MANUFACTURED OR IMPORTED IN QUANTITIES OF 10 TONNES OR MORE

Column 1 of this Annex establishes the standard information required for all substances manufactured or imported in quantities of 10 tonnes or more in accordance with Article 13(1)(c). Accordingly, the information required in column 1 of this Annex is additional to that required in column 1 of Annex VII. 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 required standard information may be omitted, replaced by other information, provided at a different stage or adapted in another way. If the conditions are met under which column 2 of this Annex allows adaptations, the registrant shall clearly state this fact and the reasons for each adaptation under the appropriate headings in the registration dossier.

In addition to these specific rules, a registrant may 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 adapt 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, information is not provided 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**
8.1. Skin corrosion/ irritation	8.1. An in vivo study for skin corrosion/irritation shall be considered only if the in vitro studies under points 8.1.1 and 8.1.2 in Annex VII are not applicable, or the results of these studies are not adequate for classification and risk assessment. The study does not need to be conducted if:

	— the substance is a strong acid (pH ≤ 2,0) or base (pH ≥ 11,5), or — the substance is spontaneously flammable in air or in contact with water or moisture at room temperature, or — the substance is classified as acute toxicity by the dermal route (Category 1), or — an acute toxicity study by the dermal route does not indicate skin irritation up to the limit dose level (2 000 mg/kg body weight).
8.2. Serious eye damage/eye irritation	8.2. An in vivo study for eye corrosion/irritation shall be considered only if the in vitro study(ies) under point 8.2.1 in Annex VII are not applicable, or the results obtained from these study(ies) are not adequate for classification and risk assessment. The study does not need to be conducted if: — the substance is classified as skin corrosion, or — the substance is a strong acid (pH ≤ 2,0) or base (pH ≥ 11,5), or — the substance is spontaneously flammable in air or in contact with water or moisture at room temperature.
8.4. Mutagenicity 8.4.2. In vitro cytogenicity study in mammalian cells or in vitro micronucleus study	8.4.2. The study does not usually need to be conducted — if adequate data from an in vivo cytogenicity test are available, or — the substance is known to be carcinogenic category 1A or 1B or germ cell mutagenic category 1A, 1B or 2.
8.4.3. In vitro gene mutation study in mammalian cells, if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2.	8.4.3. The study does not usually need to be conducted if adequate data from a reliable in vivo mammalian gene mutation test are available.

	8.4. Appropriate in vivo mutagenicity studies shall be considered in case of a positive result in any of the genotoxicity studies in Annex VII or VIII.
8.5. Acute toxicity	8.5. The study/ies do(es) not generally need to be conducted if: — the substance is classified as skin corrosion.
8.5.2. By inhalation	In addition to the oral route (Annex VII, 8.5.1.), for substances other than gases, the information mentioned under 8.5.2 to 8.5.3 shall be provided for at least one other route. The choice for the second route will depend on the nature of the substance and the likely route of human exposure. If there is only one route of exposure, information for only that route needs to be provided. 8.5.2. Testing by the inhalation route is appropriate if exposure of humans via inhalation is likely taking into account the vapour pressure of the substance and/or the possibility of exposure to aerosols, particles or droplets of an inhalable size.
8.5.3. By dermal route	8.5.3. Testing by the dermal route is appropriate if: (1) inhalation of the substance is unlikely; and (2) skin contact in production and/or use is likely; and (3) the physicochemical and toxicological properties suggest potential for a significant rate of absorption through the skin. Testing by the dermal route does not need to be conducted if: — the substance does not meet the criteria for classification as acute toxicity or STOT SE by the oral route and

	— no systemic effects have been observed in in vivo studies with dermal exposure (e.g. skin irritation, skin sensitisation) or, in the absence of an in vivo study by the oral route, no systemic effects after dermal exposure are predicted on the basis of non-testing approaches (e.g. read across, QSAR studies).
8.6. Repeated dose toxicity 8.6.1. Short-term repeated dose toxicity study (28 days), one species, male and female, most appropriate route of administration, having regard to the likely route of human exposure.	8.6.1. The short-term toxicity study (28 days) does not need to be conducted if: — a reliable sub-chronic (90 days) or chronic toxicity study is available, provided that an appropriate species, dosage, solvent and route of administration were used, or — where a substance undergoes immediate disintegration and there are sufficient data on the cleavage products, or — relevant human exposure can be excluded in accordance with Annex XI Section 3. The appropriate route shall be chosen on the following basis: Testing by the dermal route is appropriate if: (1) inhalation of the substance is unlikely; and (2) skin contact in production and/or use is likely; and (3) the physicochemical and toxicological properties suggest potential for a significant rate of absorption through the skin. Testing by the inhalation route is appropriate if exposure of humans via inhalation is likely taking into account the vapour pressure of the substance and/or the possibility of exposure to aerosols, particles or droplets of an inhalable size. The sub-chronic toxicity study (90 days) (Annex IX, Section 8.6.2) shall be proposed by the

	registrant 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. Further studies shall be proposed by the registrant or may be required by the Agency in accordance with Article 40 or 41 in case of: — failure to identify a NOAEL in the 28 or the 90 days study, unless the reason for the failure to identify a NOAEL is absence of adverse toxic effects, or — toxicity of particular concern (e.g. serious/severe effects), or — indications of an effect for which the available evidence is inadequate for toxicological 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 — the route of exposure used in the initial repeated dose study was inappropriate in relation to the expected route of human exposure and route-to-route extrapolation cannot be made, 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 to humans may be expected), or — effects shown in substances with a clear relationship in molecular structure with the substance being studied, were not detected in the 28 or the 90 days study.

8.7. Reproductive toxicity 8.7.1. Screening for reproductive/ developmental toxicity, one species (OECD 421 or 422), if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from in vitro methods that the substance may be a developmental toxicant	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.
8.8. Toxicokinetics 8.8.1. Assessment of the toxicokinetic behaviour of the substance to the extent that can be derived from the relevant available information	

9. ECOTOXICOLOGICAL INFORMATION	
COLUMN 1 **STANDARD INFORMATION REQUIRED**	**COLUMN 2** **SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1**
9.1.3. Short-term toxicity testing on fish: the registrant may consider long-term toxicity testing instead of short-term.	9.1.3. The study does not need to be conducted if: — there are mitigating 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, or — a long-term aquatic toxicity study on fish is available. Long-term aquatic toxicity testing as described in Annex IX shall be considered if the chemical safety assessment according to Annex I indicates the need to investigate further effects on aquatic organisms. The choice of the appropriate test(s) will depend on the results of the chemical safety assessment.
9.1.4. Activated sludge respiration inhibition testing	9.1.4. The study does not need to be conducted if: — there is no emission to a sewage treatment plant, or — there are mitigating factors indicating that microbial toxicity is unlikely to occur, for instance the substance is highly insoluble in water, or — the substance is found to be readily biodegradable and the applied test concentrations are in the range of concentrations that can be expected in the influent of a sewage treatment plant. The study may be replaced by a nitrification inhibition test if available data show that the substance is likely to be an inhibitor of microbial growth or function, in particular nitrifying bacteria.

9.2. Degradation	9.2. Further degradation testing shall be considered if the chemical safety assessment according to Annex I indicates the need to investigate further the degradation of the substance. The choice of the appropriate test(s) will depend on the results of the chemical safety assessment.
9.2.1. Abiotic	
9.2.1.1. Hydrolysis as a function of pH.	9.2.2.1. The study does not need to be conducted if: — the substance is readily biodegradable, or — the substance is highly insoluble in water.
9.3. Fate and behaviour in the environment	
9.3.1. Adsorption/desorption screening	9.3.1. The study does not need to be conducted if: — based on the physicochemical properties the substance can be expected to have a low potential for adsorption (e.g. the substance has a low octanol water partition coefficient), or — the substance and its relevant degradation products decompose rapidly.