ANNEX-9

GENERAL PROVISIONS FOR ADAPTATION OF THE STANDARD TESTING REGIMES

Tables which include the information for substances manufactured or imported according to the tonnage bands are given below:

— Table 1 for one tonne or more and less than 10 tonnes manufactured or imported substances;

— Table 1 and 2 for 10 tonnes or more and less than 100 tonnes manufactured or imported substances;

— Table 1,2 and 3 for 100 tonnes or more and less than 1000 tonnes manufactured or imported substances;

— Table 1,2,3 and 4 for 1000 tonnes or more manufactured or imported substances.

In addition to the specific rules set out in column 2 of Table 1 to 4, the standard testing regime in accordance with the general rules set out in Section 1 of this Annex.

SECTION ONE
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 the By-law on Principles of Good Laboratory Practices or the internationally recognised test methods

Data shall be considered to be equivalent to data generated by the corresponding test methods which are internationally recognised or given in the By-law on Principles of Good Laboratory Practices.

(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 the By-law on Principles of Good Laboratory Practices or the internationally recognised test methods

Data shall be considered to be equivalent to data generated by the corresponding test

methods which are internationally recognised or given in the By-law on Principles of Good Laboratory Practices 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 internationally recognised test methods or to the By-law on Principles of Good Laboratory Practices;

(3) exposure duration comparable to or longer than the corresponding test methods referred to internationally recognised test methods or to the By-law on Principles of Good Laboratory Practices if exposure duration is a relevant parameter; and

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

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.

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 the By-law on Principles of Good Laboratory Practices or from an internationally recognised test method as being

equivalent, leading to the conclusion that a substance has or has not a particular dangerous property.

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.

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.

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. Depending on the potential risk, immediate confirmation of the relevant institution requiring testing beyond the information foreseen in Table 1 to 4 for the respective tonnage level is necessary. 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.

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.

1.5. Grouping of substances and read-across approach

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.

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 the By-law on Principles of Good Laboratory Practices or to internationally recognised test methods,

— cover an exposure duration comparable to or longer than the corresponding test method referred to the By-law on Principles of Good Laboratory Practices or to internationally recognised test methods if exposure duration is a relevant parameter, and

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

Table 1.

Standard Information Requirements for Substances Manufactured Or Imported in Quantities of One Tonne or More and Less Than 10 Tonnes

1. Data on physical-chemical properties of substances	
COLUMN 1	COLUMN 2

STANDARD INFORMATION REQUIRED	SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1
1.1. State of the substance at 20 °C and 101,3 kPa	
1.2. Melting/freezing point	1.2. The study does not need to be conducted below a lower limit of - 20 °C.
1.3. Boiling point	1.3. The study does not need to be conducted: — for gases, or — for solids which either melt above 300 °C or decompose before boiling. In such cases the boiling point under reduced pressure may be estimated or measured, or — for substances which decompose before boiling (e.g. auto-oxidation, rearrangement, degradation, decompo- sition, etc.).
1.4. Relative density	1.4. The study does not need to be conducted if: — the substance is only stable in solution in a particular solvent and the solution density is similar to that of the solvent. In such cases, an indication of whether the solution density is higher or lower than the solvent density is sufficient, or — the substance is a gas. In this case, an estimation based on calculation shall be made from its molecular weight and the Ideal Gas Laws.
1.5. Vapour pressure	1.5. The study does not need to be conducted if the melting point is above 300 °C. If the melting point is between 200 °C and 300 °C, a limit value based on measurement or a recognised calculation method is sufficient.
1.6. Surface tension	1.6. The study need only be conducted if: — based on structure, surface activity is expected or can be predicted, or — surface activity is a desired property of the material. If the water solubility is below 1 mg/l at 20 °C the test does not need to be conducted.
1.7. Water solubility	1.7. The study does not need to be conducted if:

	— the substance is hydrolytically unstable at pH 4, 7 and 9 (half-life less than 12 hours), or — the substance is readily oxidisable in water. If the substance appears 'insoluble' in water, a limit test up to the detection limit of the analytical method shall be performed.
1.8. Partition coefficient n-octanol/water	1.8. The study does not need to be conducted if the substance is inorganic. If the test cannot be performed (e.g. the substance decomposes, has a high surface activity, reacts violently during the performance of the test or does not dissolve in water or in octanol, or it is not possible to obtain a suf- ficiently pure substance), a calculated value for log P as well as details of the calculation method shall be provided.
1.9. Flash-point	1.9. The study does not need to be conducted if: — the substance is inorganic, or — the substance only contains volatile organic components with flash-points above 100 °C for aqueous solutions, or — the estimated flash-point is above 200 °C, or — the flash-point can be accurately predicted by interpo- lation from existing characterised materials.
1.10. Flammability	1.10. The study does not need to be conducted: — if the substance is a solid which possesses explosive or pyrophoric properties. These properties should always be considered before considering flammability, or — for gases, if the concentration of the flammable gas in a mixture with inert gases is so low that, when mixed with air, the concentration is all time below the lower limit, or — for substances which spontaneously ignite when in contact with air.

1.11. Explosive properties	1.11. The study does not need to be conducted if: — there are no chemical groups associated with explosive properties present in the molecule, or — the substance contains chemical groups associated with explosive properties which include oxygen and the calculated oxygen balance is less than -200, or — the organic substance or a homogenous mixture of organic substances contains chemical groups associated with explosive properties, but the exothermic decompo- sition energy is less than 500 J/g and the onset of exothermic decomposition is below 500 °C, or — for mixtures of inorganic oxidising substances (UN Division 5.1) with organic materials, the concentration of the inorganic oxidising substance is: — less than 15 %, by mass, if assigned to UN Packaging Group I (high hazard) or II (medium hazard), — less than 30 %, by mass, if assigned to UN Packaging Group III (low hazard). Note: Neither a test for propagation of detonation nor a test for sensitivity to detonative shock is required if the exothermic decomposition energy of organic materials is less than 800 J/g.
1.12. Self-ignition temperature	1.12. The study does not need to be conducted: — if the substance is explosive or ignites spontaneously with air at room temperature, or — for liquids non flammable in air, e.g. no flash point up to 200 °C, or — for gases having no flammable range, or

	- — for solids, if the substance has a melting point ≤ 160 °C, or if preliminary results exclude self-heating of the substance up to 400 °C.
1.13. Oxidising properties	1.13. The study does not need to be conducted if: — the substance is explosive, or — the substance is highly flammable, or — the substance is an organic peroxide, or — the substance is incapable of reacting exothermically with combustible materials, for example on the basis of the chemical structure (e.g. organic substances not containing oxygen or halogen atoms and these elements are not chemically bonded to nitrogen or oxygen, or inorganic substances not containing oxygen or halogen atoms). The full test does not need to be conducted for solids if the preliminary test clearly indicates that the test substance has oxidising properties. Note that as there is no test method to determine the oxidising properties of gaseous mixtures, the evaluation of these properties must be realised by an estimation method based on the comparison of the oxidising potential of gases in a mixture with that of the oxidising potential of oxygen in air.
1.14. Granulometry	1.14. The study does not need to be conducted if the substance is marketed or used in a non solid or granular form.
2. Data on toxicological properties of substances	
2.1. Skin irritation or skin corrosion The assessment of this endpoint shall comprise the following consecutive steps: (1)an assessment of the available human and animal data, (2)an assessment of the acid or alkaline reserve, (3)in vitro study for skin corrosion, (4)in vitro study for skin irritation.	2.1. Steps 3 and 4 do not need to be conducted if: the available information indicates that the criteria are met for classification as corrosive to the skin or irritating to eyes, orthe substance is flammable in air at room temperature, or the substance is classified as very toxic in contact with skin, oran acute toxicity study by the dermal route does not indicate skin irritation up to the limit dose level (2000 mg/kg body weight).
2.2. Eye irritation The assessment of this endpoint shall comprise the following consecutive steps:	2.2. Step 3 does not need to be conducted if:

(1)an assessment of the available human and animal data, (2)an assessment of the acid or alkaline reserve, (3)in vitro study for eye irritation.	— the available information indicates that the criteria are met for classification as corrosive to the skin or irritating to eyes, or — the substance is flammable in air at room temperature;
2.3. Skin sensitisation The assessment of this endpoint shall comprise the following conse- cutive steps: (1) an assessment of the available human, animal and alternative data, (2) In vivo testing.	2.3. Step 2 does not need to be conducted if: — the available information indicates that the substance should be classified for skin sensitisation or corrosivity, or — the substance is a strong acid (pH ≤ 2,0) or base (pH ≥ 11,5), or — the substance is flammable in air at room temperature. The Murine Local Lymph Node Assay (LLNA) is the firstchoice method for in vivo testing. Only in exceptional circumstances should another test be used. Justification for the use of another test shall be provided.
2.4. Mutagenicity 2.4.1. In vitro gene mutation study in bacteria	2.4. Further mutagenicity studies shall be considered in case of a positive result.
2.5. Acute toxicity 2.5.1. By oral route	2.5. The study/ies do(es) not generally need to be conducted if: — the substance is classified as corrosive to the skin. The study need not be conducted if a study on acute toxicity by the inhalation route (2.5.2) is available.
3. Data on ecotoxicological properties of substances	
3.1. Aquatic toxicity 3.1.1. Short-term toxicity testing on inverte- brates (preferred species Daphnia) The classifier may consider long-term toxicity testing instead of short- term.	3.1.1. 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, -a long-term aquatic toxicity study on invertebrates is available, or - adequate information for environmental classification and labelling is available. The long-term aquatic toxicity study on Daphnia (Table 3,

3.1.2. Growth inhibition study aquatic plants (algae preferred)	Section 3.1.5), shall be considered if the substance is poorly water soluble. 3.1.2. The study does not need to be conducted if there are miti- gating 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.
3.2. Degradation 3.2.1. Biotic 3.2.1.1. Ready biodegradability	 3.2.1.1. The study does not need to be conducted if the substance is inorganic.

Any other relevant physicochemical, toxicological and ecotoxicological information that is available shall be provided. Only physicochemical properties should be given for substances which not meets the criteria given below:

a) substances for which it is predicted to meet the criteria for category 1A or 1B classification in the hazard classes carcinogenicity, germ cell mutagenicity or reproductive toxicity or

1.PBT Substances

1.1.Persistenc criterion

- the degradation half-life in marine water is higher than 60 days;
- the degradation half-life in fresh or estuarine water is higher than 40 days;
- the degradation half-life in marine sediment is higher than 180 days;
- the degradation half-life in fresh or estuarine water sediment is higher than 120 days;
- the degradation half-life in soil is higher than 120 days.

1.2. Bioaccumulation criterion

A substance whose bioconcentration factor in aquatic species is higher than 2 000.

1.3. Toxicity criterion

- the long-term no-observed effect concentration (NOEC) or EC10 for marine or freshwater organisms is less than 0,01 mg/l;
- the substance meets the criteria for classification as carcinogenic (category 1A or 1B), germ cell mutagenic (category 1A or 1B), or toxic for reproduction (category 1A, 1B, or 2) according to this By-Law ;
- there is other evidence of chronic toxicity, as identified by the substance meeting the criteria for classification: specific target organ toxicity after repeated exposure (STOT RE category 1 or 2) according to this By-Law.

2. vPvB Substances

2.1. Persistence criterion

- the degradation half-life in marine, fresh or estuarine water is higher than 60 days;

- the degradation half-life in marine, fresh or estuarine water sediment is higher than 180 days;
- the degradation half-life in soil is higher than 180 days.

2.2. Bioaccumulation criterion

A substance whose bioconcentration factor in aquatic species is higher than 5 000.

b) substances with dispersive or diffuse use(s) particularly where such substances are used in consumer or incorporated into consumer articles; and (for which it is predicted (i.e. by application of (Q)SARs or other evidence) that they are likely to meet the classification criteria for any health or environmental hazard classes or differentiations under this By-Law.

Table 2.

Standard Information Requirements for Substances Manufactured Or Imported in Quantities of 10Tonnes or More and Less Than 100 Tonnes

2. Data on toxicological properties of substances	
COLUMN 1 **STANDARD INFORMATION REQUIRED**	**COLUMN 2** **SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1**
2.1. Skin irritation 2.1.1. *In vivo skin irritation*	2.1.1. The study does not need to be conducted if: — the substance is classified as corrosive to the skin or as a skin irritant, or — the substance is a strong acid (pH ≤ 2,0) or base (pH ≥ 11,5), or — the substance is flammable in air at room temperature, or — the substance is classified as very toxic in contact with skin, 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).
2.2. Eye irritation 2.2.1. *In vivo eye irritation*	2.2.1. The study does not need to be conducted if: — the substance is classified as irritating to eyes with risk of serious damage to eyes, or — the substance is classified as corrosive to the skin and provided that the classifier classified the substance as eye irritant, or — the substance is a strong acid (pH ≤ 2,0) or base (pH ≥

	11,5), or — the substance is flammable in air at room temperature.
2.4. Mutagenicity 2.4.2. In vitro cytogenicity study in mammalian cells or in vitro micronucleus study	 2.4.2. 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 mutagenic category 1A, 1B or 2.
2.4.3. In vitro gene mutation study in mammalian cells, if a negative result in Table 1 Section 2.4.1. and Table 2 Section 2.4.2	2.4.3. The study does not usually need to be conducted if adequate data from a reliable in vivo mammalian gene mutation test are available. 2.4. Appropriate in vivo mutagenicity studies shall be considered in case of a positive result in any of the genotoxicity studies in Table 1 or Table 2
2.5. Acute toxicity 2.5.2. By inhalation 2.5.3. By dermal route	2.5. The study/ies do(es) not generally need to be conducted if: — the substance is classified as corrosive to the skin. In addition, for substances other than gases, the information mentioned under 2.5.2 to 2.5.3 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 need be provided. 2.5.2. 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. 2.5.3. 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.
2.6. Repeated dose toxicity 2.6.1. Short-term repeated döşe toxicity study (28 days), one species, male and female, most	 2.6.1. The short-term toxicity study (28 days) does not need to be conducted if:

appropriate route of administration, having regard to the likely route of human exposure.	— 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. 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) may be proposed by the notifier 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 bedetected 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 notifier or may be required by the relevant institution: — 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.
2.7. Reproductive toxicity 2.7.1. 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	2.7.1. 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, or — a pre-natal developmental toxicity study (Table 3, 2.7.2) or a two-generation reproductive toxicity study (Table 3, Section 2.7.3) 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 develop- mental 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 a pre- natal developmental toxicity study (Table 3, Section 2.7.2) or a two-generation reproductive toxicity study (Table 3, Section 2.7.3) may be proposed instead of the screening study.
2.8. Toxicokinetics 2.8.1. Assessment of the toxicokinetic behaviour of the substance to the extent that can be derived from the relevant available information	
3. Data on ecotoxicological properties of substances	
3.1.3. Short-term toxicity testing on fish: the long-term toxicity testing instead of short- term may considered .	3.1.3. 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 Table 3 shall be considered if the harmonized classification application indicates the need to investigate further effects on aquatic organisms. The long-term aquatic toxicity study on fish (Table 3, Section 3.1.6) shall be considered if the substance is poorly water soluble.
3.1.4. Activated sludge respiration inhibition testing	3.1.4. 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

3.2. Degradation 3.2.1. Abiotic 3.2.1.1. Hydrolysis as a function of pH.	and the applied test concentrations are in the range of concen- trations 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. 3.2.1.1. The study does not need to be conducted if: — the substance is readily biodegradable, or — the substance is highly insoluble in water.
3.3. Fate and behaviour in the environment 3.3.1. Adsorption/deso- rption screening	3.3.1. 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 coef- ficient), or — the substance and its relevant degradation products decompose rapidly.

The informations in the first column of this table, should be given in addition to the information in the first column of Table 1. Any other relevant physicochemical, toxicological and ecotoxicological information that is available shall be provided.

Table 3.

Standard Information Requirements for Substances Manufactured Or Imported in Quantities of 100Tonnes or More and Less Than 1000 Tonnes

1. Data on physicochemical properties of substances	
COLUMN 1 **STANDARD INFORMATION REQUIRED**	**COLUMN 2** **SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1**
1.15. Stability in organic solvents and identity of relevant degradation products only required if stability of the substance is considered to be	1.15. The study does not need to be conducted if the substance is inorganic.

critical.	
1.16. Dissociation constant	1.16. The study does not need to be conducted if: — the substance is hydrolytically unstable (half-life less than 12 hours) or is readily oxidisable in water, or — it is scientifically not possible to perform the test for instance if the analytical method is not sensitive enough.
1.17. Viscosity	
2. Data on toxicological properties of substances	
	2.4. If there is a positive result in any of the in vitro genotoxicity studies in Table I or Table II and there are no results available from an in vivo study already, an appropriate in vivo somatic cell genotoxicity study may be proposed. 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 toxi- cokinetic evidence. If no clear conclusions about germ cell mutagenicity can be made, additional investigations shall be considered.
2.6. Repeated dose toxicity 2.6.1. 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, unless already provided as part of Table 2 equirements or if tests according to Section 2.6.2 of this Table is proposed. 2.6.2. Sub-chronic toxicity study (90- day), one species, rodent, male and female, most appropriate route of administration, having regard to the likely route of human exposure.	2.6.2. 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 according to the criteria for classifying the substance as R48, 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, provided that an appropriate species and route of administration were used, or — a substance undergoes immediate disintegration

	and there are sufficient data on the cleavage products (both for systemic effects and effects at the site of uptake), or — the substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and no evidence of toxicity in a 28-day 'limit test', particularly if such a pattern is coupled with limited human exposure. The appropriate route shall be chosen on the following basis: Testing by the dermal route is appropriate if: (1) skin contact in production and/or use is likely; and (2) the physicochemical properties suggest a significant rate of absorption through the skin; and (3) one of the following conditions is met: — toxicity is observed in the acute dermal toxicity test at lower doses than in the oral toxicity test, or — systemic effects or other evidence of absorption is observed in skin and/or eye irritation studies, or — in vitro tests indicate significant dermal absorption, or — significant dermal toxicity or dermal penetration is recognised for structurally-related substances.Uygun yol aşağıdaki esaslar çerçevesinde seçilir:
	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. Further studies shall be proposed in case of: — failure to identify a NOAEL in 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 characteri sation. In such cases it may also be more appropriate to perform specific toxicological studies that are designed to investigate these effects (e.g. immunotoxicity, neuro- toxicity), 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).
2.7. Reproductive toxicity	2.7. The studies do 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 — 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. 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.
2.7.2. Pre-natal develop- mental toxicity study, one species most appropriate route of administration, having regard to the likely route of human exposure obtained from test methods done according to the By-law on Principles of Good Laboratory Practices or internationally recognised test methods or By-Law on Test Methods.	2.7.2. The study shall be initially performed on one species. A decision on the need to perform a study at this tonnage level or the next on a second species should be based on the outcome of the first test and all other relevant available data.
2.7.3. Two-generation reproductive toxicity study, one species, male and female,most appropriate route of administration, having regard to the likely route of human exposure, if the 28-day or 90-day study indicates adverse effects on reproductive organs or tissues.	2.7.3. The study shall be initially performed on one species. A decision on the need to perform a study at this tonnage level or the next on a second species should be based on the outcome of the first test and all other relevant available date.
3. Data on ecotoxicological properties of substances	
3.1. Aquatic toxicity 3.1.5. Long-term toxicity testing on inverte- brates (preferred species Daphnia), (unless already provided as part of Table 1 requirements) 3.1.6. Long-term toxicity testing onfish, (unless already provided as part of Table 2 requirements) The information shall be provided for one of the Sections 3.1.6.1, 3.1.6.2 or 3.1.6.3 of this Table. 3.1.6.1. Fish early-life stage (FELS) toxicity test 3.1.6.2. Fish short-term toxicit test on embryo and sac-fry stages 3.1.6.3. Fish,juvenile growth test	
3.2. Degradation 3.2.1. Biotic 3.2.1.2. . Simulation testing on ultimate degradation in surface water	3.2.1.2. The study need not be conducted if: — the substances is highly insoluble in water, or — the substance is readily biodegradable.
3.2.1.3. Soil simulation testing (for substances with a high potential for adsorption to	3.2.1.3. The study need not be conducted:

soil)	— if the substance is readily biodegradable, or — if direct and indirect exposure of soil is unlikely.
3.2.1.4. Sediment simulation testing (for substances with a high potential for adsorption to sediment)	3.2.1.4. The study need not be conducted: — if the substance is readily biodegradable, or — if direct and indirect exposure of sediment is unlikely.
3.2.3. Identification of degradation products	3.2.3. Unless the substance is readily biodegradable.
3.3. Fate and behaviour in the environment	
3.3.2. Bioaccumulation in aquatic species, preferably fish	3.3.2. The study need not be conducted if: the substance has a low potential for bioaccumulation (for instance a log Kow ≤ 3) and/or a low potential to cross biological membranes, or — direct and indirect exposure of the aquatic compartment is unlikely.
3.3.3. Further information on adsorption/desorption depending on the results of the study required in Table II	3.3.3. The study need not 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 coef- ficient), or — the substance and its degradation products decompose rapidly.
3.4. Effects on terrestrial organisms	3.4. These studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely. In the absence of toxicity data for soil organisms, the equi- librium partitioning method may be applied to assess the hazard to soil organisms. The choice of the appropriate tests depends on the outcome of the chemical safety assessment. In particular for substances that have a high potential to adsorb to soil or that are very persistent, the notifier may conduct long-term toxicity testing instead of short-term.
3.4.1. Short-term toxicity to invertebrates	

3.4.2. Effects on soil micro-organisms 3.4.3. Short-term toxicity to plants	
4. 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.

The informations in the first column of this table, should be given in addition to the information in the first column of Table 1 and Table 2. Any other relevant physicochemical, toxicological and ecotoxicological information that is available shall be provided.

Table 4.

Standard Information Requirements for Substances More Than 1000 Tonnes

2. Data on toxicological properties of substances	
COLUMN 1 **STANDARD INFORMATION REQUIRED**	**COLUMN 2** **SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1**
	2.4. If there is a positive result in any of the in vitro genotoxicity studies in Table I or II, 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 toxi- cokinetic evidence. If no clear conclusions about germ cell mutagenicity can be made, additional investigations shall be considered.
	2.6.3. A long-term repeated toxicity study (≥ 12 months) may be proposed 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.
	2.6.4. Further studies may be done 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 appro- priate 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). bulunması.
2.7. Reproductive toxicity 2.7.2. Developmental toxicity study, one species, most appropriate route of administration, having regard to the likely route of human exposure (OECD 414). 2.7.3. Two-generation reproductive toxicity study, one species, male and female, most appropriate route of administration, having regard to the likely route of human exposure, unless already provided as part of Table III requirements	2.7. 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. 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 develop- mental toxicity must be considered.
2.9.1. Carcinogenicity study	2.9.1. A carcinogenicity study may be conducted if: — the substance has a widespread dispersive use or there is evidence of frequent or long-term human exposure, — 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
3. Data on ecotoxicological properties of substances	
3.2. Degradation 3.2.1. Biotic	
3.3. Fate and behaviour in the environment 3.3.4. Further information on the environmental fate and behaviour of the substance and/ ordegradation products 3.4. Effects on terrestrial organisms 3.4.4. Long-term toxicity testing on inverte-brates, unless already provided as part of Table III requirements . 3.4.6. Long-term toxicity testing on plants, unless already provided as part of Table III requirements. 3.5.1. Long-term toxicity to sediment organisms	3.4. These studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely. 3.6.1. Any need for testing should be carefully

3.6.1. Long-term or reproductive toxicity to birds	considered taking into account the large mammalian.
4. Methods of detection and analysis	Long-term toxicity testing shall be provided on request 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.

The informations in the first column of this table, should be given in addition to the information in the first column of Table 1, Table 2 and Table 3. Any other relevant physicochemical, toxicological and ecotoxicological information that is available shall be provided.

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 internationally recognised test methods or to the By-law on Principles of Good Laboratory Practices, more specifically on the technical limitations of a specific method, shall always be respected.