ANNEX IX

STANDARD INFORMATION REQUIREMENTS FOR SUBSTANCES MANUFACTURED OR IMPORTED IN QUANTITIES OF 100 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)(ç).

Column 1 of this Annex establishes the standard information required for all substances manufactured or imported in quantities of 100 tonnes or more in accordance with Article 13(1)(ç). Accordingly, the information required in column 1 of this Annex is additional to that required in column 1 of Annexes VII and VIII. 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.

7. INFORMATION ON THE PHYSICOCHEMICAL PROPERTIES OF THE SUBSTANCE	
COLUMN 1 **STANDARD INFORMATION REQUIRED**	**COLUMN 2** **SPECIFIC RULES FOR ADAPTATIION FROM COLUMN 1**
7.15. Stability in organic solvents and identity of relevant degradation products Only required if stability of the substance is considered to be critical.	7.15. The study does not need to be conducted if the substance is inorganic.

7.16. Dissociation constant	7.16. 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.
7.17. Viscocity	
8. TOXICOLOGICAL INFORMATION	
COLUMN 1 **STANDARD INFORMATION REQUIRED**	**COLUMN 2** **SPECIFIC RULES FOR ADAPTATIION FROM COLUMN 1**
	8.4. If there is a positive result in any of the in vitro genotoxicity studies in Annex VII or VIII and there are no results available from an in vivo study already, an appropriate in vivo somatic cell genotoxicity study shall be proposed by the registrant. 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. Repeated döşe 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, unless already provided as part of Annex VIII requirements or if tests according to Section 8.6.2 of this Annex is proposed. In this case, Section 3 of Annex XI shall not apply. 8.6.2. 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.	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 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. 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 by the registrant or may be required by the Ministry in accordance with Articles 36 or 37 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 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 to humans may be expected).
8.7. Reproductive toxicity	8.7. 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. 8.7.2. 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.

8.7.2. Pre-natal developmental toxicity study, one species, most appropriate route of administration, having regard to the likely route of human exposure (B.31 of the By-law on Determination of Physico-Chemical, Toxicological and Ecotoxicological Properties of Substances and Mixtures or OECD 414).	
8.7.3. Extended One- Generation Reproductive Toxicity Study (B.56 of the 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, 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 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: — 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 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. Çalışma tek tür üzerinde gerçekleştirilir. 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.

9. ECOTOXICOLOGICAL INFORMATION	
9.1. Aquatic toxicity 9.1.5. Long-term toxicity testing on invertebrates (preferred species Daphnia), (unless already provided as part of Annex VII requirements) 9.1.6. Long-term toxicity testing on fish, (unless already provided as part of Annex VIII requirements) The information shall be provided for one of the Sections 9.1.6.1, 9.1.6.2 or 9.1.6.3. 9.1.6.1. Fish early-life stage (FELS) toxicity test 9.1.6.2. Fish short-term toxicity test on embryo and sac- fry stages 9.1.6.3. Fish, juvenile growth test	9.1. Long-term toxicity testing shall be proposed by the registrant if the chemical safety assessment according to Annex I indicates the need to investigate further the effects on aquatic organisms. The choice of the appropriate test(s) depends on the results of the chemical safety assessment.
9.2. Degradation	9.2. Further biotic degradation testing shall be proposed by the registrant 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).

9.2.1. Biotic	9.2.1.2. The study need not be conducted if: — the substances is highly insoluble in water, or — the substance is readily biodegradable.
9.2.1.2. Simulation testing on ultimate degradation in surface water	
9.2.1.3. Soil simulation testing (for substances with a high potential for adsorption to soil)	9.2.1.3. The study need not be conducted: — if the substance is readily biodegradable, or — if direct and indirect exposure of soil is unlikely.
9.2.1.4. Sediment simulation testing (for substances with a high potential for adsorption to sediment)	9.2.1.4. The study need not be conducted: — if the substance is readily biodegradable, or — if direct and indirect exposure of sediment is unlikely.
9.2.3. Identification of degradation products	9.2.3. Unless the substance is readily biodegradable
9.3. Fate and behaviour in the environment	

9.3.2. Bioaccumulation in aquatic species, preferably fish	9.3.2. 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.
9.3.3. Further information on adsorption/desorption depending on the results of the study required in Annex VIII	9.3.3. 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 coefficient), or — the substance and its degradation products decompose rapidly.
9.4. Effects on terrestrial organisms	9.4. 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 equilibrium 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 registrant shall consider long-term toxicity testing instead of short-term.

9.4.1. Short-term toxicity to invertebrates 9.4.2. Effects on soil microorganisms 9.4.3. Short-term toxicity to plants	

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.