Annex-11

HAZARD ASSESSMENT AND FORM FOR SUBMITTİNG HARMONISED CLASSIFICATION

PART 1

HUMAN HEALTH HAZARD ASSESSMENT

1.0 INTRODUCTION

1.0.1 The objective of the human health hazard assessment is to determine the classification of a substance and a Derived No-Effect Level (DNEL) in accordance with this By-law.

1.0.2 The human health hazard assessment shall consider the toxicokinetic profile (i.e. absorption, metabolism, distribution and elimination) of the substance and the following groups of effects:

(1) acute effects such as acute toxicity, irritation and corrosivity;
(2) sensitisation;
(3) repeated dose toxicity; and
(4) CMR effects (carcinogenity, germ cell mutagenicity and toxicity for reproduction).

Based on all the available information, other effects shall be considered when necessary.

1.0.3 The hazard assessment shall comprise the following four steps:

Step 1: Evaluation of non-human information.
Step 2: Evaluation of human information.
Step 3: Classification and Labelling.
Step 4: Derivation of DNELs.

1.0.4 The first three steps shall be undertaken for every effect for which information available, submitted under relevant headings of Part 4 of this Annex and summarised in the Safety Data Sheet under headings "**Hazards Identification"** and "**Toxicological Information"**.

1.0.5 For any effect for which no relevant information is available, the relevant section shall contain the sentence: 'This information is not available'. The justification, including reference to any literature search carried out, shall be included in the technical dossier.

1.1 STEP 1: EVALUATION OF NON-HUMAN INFORMATION

1.1.1 The evaluation of non-human information shall comprise:
— the hazard identification for the effect based on all available non- human information,
— the establishment of the quantitative dose (concentration)-response (effect) relationship.

1.1.2 When it is not possible to establish the quantitative dose (concentration)- response (effect) relationship, then this should be justified and a semi- quantitative or qualitative analysis shall be included. For instance, for acute effects it is usually not

possible to establish the quantitative dose (concentration)-response (effect) relationship on the basis of the results of a test conducted in accordance with The By-law on Test Methods or internationally recognized scientific principles or tests done with internationally verified procedures. In such cases it suffices to determine whether and to which degree the substance has an inherent capacity to cause the effect.

1.1.3 All non-human information used to assess a particular effect on humans and to establish the dose (concentration) – response (effect) relationship, shall be briefly presented, if possible in the form of a table or tables, distinguishing between in vitro, in vivo and other information. The relevant test results (e.g. ATE, LD50, NO(A)EL or LO(A)EL) and test conditions (e.g. test duration, route of administration) and other relevant information shall be presented, in internationally recognised units of measurement for that effect.

1.1.4 If one study is available then a robust study summary should be prepared for that study. If there are several studies addressing the same effect, then, having taken into account possible variables (e.g. conduct, adequacy, relevance of test species, quality of results, etc.), normally the study or studies giving rise to the highest concern shall be used to establish the DNELs and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust summaries will be required of all key data used in the hazard assessment. If the study or studies giving rise to the highest concern are not used, then this shall be fully justified and included as part of the technical dossier, not only for the study being used but also for all studies demonstrating a higher concern than the study being used. It is important irrespective of whether hazards have been identified or not that the validity of the study be considered.

1.2 STEP 2: EVALUATION OF HUMAN INFORMATION

If no human information is available, this part shall contain the statement: 'No human information is available'. However, if human information is available, it shall be presented, if possible in the form of a table.

1.3 STEP 3: CLASSIFICATION AND LABELLING

1.3.1 The appropriate classification developed in accordance with the criteria in this By-law shall be presented and justified. Where applicable, Specific Concentration limits resulting from the application of Article 12 of this By-law and Articles 14 and 16 of By-law on the Classification, Packaging and Labelling of Dangerous Substances and Preparations shall be presented and, if they are not included in Part 3 of Annex VI to this By-law, justified.

The assessment should always include a statement as to whether the substance fulfils or does not fulfil the criteria given in this By-law for classification in the hazard class carcinogenicity category 1A or 1B, in the hazard class germ cell mutagenicity category 1A or 1B or in the hazard class reproductive toxicity category 1A or 1B.

1.3.2 If the information is inadequate to decide whether a substance should be classified for a particular hazard class or category, the registrant shall indicate and justify the action or decision he has taken as a result.

1.4 STEP 4: IDENTIFICATION OF DNEL(s)

1.4.1 Based on the outcomes of steps 1 and 2, DNELs shall be established for the substance, reflecting the likely route, duration and frequency of exposure. For some hazard classes, especially germ cell mutagenicity and carcinogenicity, the available information may not enable a toxicological threshold, and therefore a DNEL, to be established. If justified by the exposure scenario, a single DNEL may be sufficient. However, taking into account the available information and the exposure scenario in Section 9 of the Chemical Safety Report it may be necessary to identify different DNELs for each relevant human population (e.g. workers, consumers and humans liable to exposure indirectly via the environment) and possibly for certain vulnerable sub-populations (e.g. children, pregnant women) and for different routes of exposure. A full justification shall be given specifying, inter alia, the choice of the information used, the route of exposure (oral, dermal, inhalation) and the duration and frequency of exposure to the substance for which the DNEL is valid. If more than one route of exposure is likely to occur, then a DNEL shall be established for each route of exposure and for the exposure from all routes combined.

When establishing the DNEL, the following factors shall be taken into account:

- the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;
- the nature and severity of the effect;
- the sensitivity of the human population to which the quantitative and/or qualitative information on exposure applies.

1.4.2 If it is not possible to identify a DNEL, then this shall be clearly stated and fully justified.

PART 2

PHYSICOCHEMICAL HAZARD ASSESSMENT

2.0 GİRİŞ

2.0.1 The objective of the hazard assessment for physicochemical properties shall be to determine the classification of a substance in accordance with this By-law.

2.0.2 As a minimum, the potential effects to human health shall be assessed for the following physicochemical properties:
— explosivity,
— flammability,
— oxidising potential.

If the information is inadequate to decide whether a substance should be classified for a particular hazard class or category, the registrant shall indicate and justify the action or decision he has taken as a result.

2.0.3 The assessment of each effect shall be presented relevant headings of Part 4 of this Annex and summarised in the Safety Data Sheet under headings "**Hazards Identification"** and "**Physical and Chemical Properties"**.

2.0.4 For every physicochemical property, the assessment shall entail an evaluation of the inherent capacity of the substance to cause the effect resulting from the manufacture and identified uses.

2.0.5 The appropriate classification developed in accordance with the criteria in this By-law shall be presented and justified.

PART 3

ENVIRONMENTAL HAZARD ASSESSMENT

3.0 GİRİŞ

3.0.1 The objective of the environmental hazard assessment shall be to determine the classification and labelling and Predicted No-Effect Concentration (PNEC) of a substance in accordance with this By-law.

3.0.2 The environmental hazard assessment shall consider the potential effects on the environment, comprising the:
(1) aquatic (including sediment),
(2) terrestrial and
(3) atmospheric compartments, including the potential effects that may occur
(4) via food-chain accumulation.
(5) The potential effects on the microbiological activity of sewage treatment systems shall be considered.

The assessment of the effects on each of these five environmental spheres shall be presented relevant headings of Part 4 of this Annex and summarised in the Safety Data Sheet under headings "**Hazards Identification"** and "**Ecological Information"**.

3.0.3 For any environmental sphere, for which no effect information is available, the relevant heading of Part 4 of this Annex shall contain the sentence: 'This information is not available'. The justification, including reference to any literature research carried out, shall be included in the technical dossier. For any environmental sphere for which information is available, but the manufacturer or importer believes that it is not necessary to conduct the hazard assessment, the manufacturer or importer shall present a justification, with reference to pertinent information, under the relevant heading of Part 4 of this Annex and summarise in the Safety Data Sheet under heading "**Ecological Information".**

3.0.4 The hazard assessment shall comprise the following three steps:
Step 1: Evaluation of information.
Step 2: Classification and Labelling.
Step 3: Derivation of the PNEC.

3.1 STEP 1: EVALUATION OF INFORMATION

3.1.1 The evaluation of all available information shall comprise:
— the hazard identification based on all available information,

— the establishment of the quantitative dose (concentration)-response (effect) relationship.

3.1.2 When it is not possible to establish the quantitative dose (concentration)- response (effect) relationship, then this should be justified and a semi- quantitative or qualitative analysis shall be included.

3.1.3 All information used to assess the effects on a specific environmental sphere shall be briefly presented, if possible in the form of a table or tables. The relevant test results (e.g. LC50 or NOEC) and test conditions (e.g. test duration, route of administration) and other relevant information shall be presented, in internationally recognised units of measurement for that effect.

3.1.4 All information used to assess the environmental fate of the substance shall be briefly presented, if possible in the form of a table or tables. The relevant test results and test conditions and other relevant information shall be presented, in internationally recognised units of measurement for that effect.

3.1.5 If one study is available then a robust study summary should be prepared for that study. Where there is more than one study addressing the same effect, then the study or studies giving rise to the highest concern shall be used to draw a conclusion and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust summaries will be required of all key data used in the hazard assessment. If the study or studies giving rise to the highest concern are not used, then this shall be fully justified and included as part of the technical dossier, not only for the study being used but also for all studies reaching a higher concern than the study being used. For substances where all available studies indicate no hazards an overall assessment of the validity of all studies should be performed.

3.2 STEP 2: CLASSIFICATION AND LABELLING

3.2.1 The appropriate classification developed in accordance with the criteria in this By-law shall be presented and justified. Any M-factor resulting from the application of Article 12 of this By-law shall be presented and, if it is not included in Part 3 of Annex VI to this By-law, justified.

3.2.2 If the information is inadequate to decide whether a substance should be classified for a particular hazard class or category, the registrant shall indicate and justify the action or decision he has taken as a result.

3.3 STEP 3: IDENTIFICATION OF THE PNEC

3.3.1 Based on the available information, the PNEC for each environmental sphere shall be established. The PNEC may be calculated by applying an appropriate assessment factor to the effect values (e.g. LC50 or NOEC). An assessment factor expresses the difference between effects values derived for a limited number of species from laboratory tests and the PNEC for the environmental sphere.

3.3.2 If it is not possible to derive the PNEC, then this shall be clearly stated and fully justified.

PART 3
NOTIFICATION FORM FOR HARMONISED CLASSIFICATION

Form shall include the following parts:

1. IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

2. MANUFACTURE AND USES
2.1. Manufacture
2.2. Identified uses
2.3. Uses advised against

3. CLASSIFICATION AND LABELLING

4. ENVIRONMENTAL FATE PROPERTIES
4.1 Degradation
4.2. Environmental distribution
4.3. Bioaccumulation
4.4. Secondary poisoning

5. HUMAN HEALTH HAZARD ASSESSMENT
5.1. Toxicokinetics (absorption, metabolism, distribution and elimination)
5.2. Acute toxicity
5.3. Irritation
5.4. Corrosivity
5.5. Sensitisation
5.6 Repeated dose toxicity
5.7. Germ cell mutagenicity
5.8. Carcinogenicity
5.9. Toxicity for reproduction
5.10 Other effects
5.11. Derivation of DNEL(s)

6. HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICOCHEMICAL PROPERTIES
6.1. Explosivity
6.2. Flammability
6.3. Oxidising potential

7. ENVIRONMENTAL HAZARD ASSESSMENT
7.1. Aquatic compartment (including sediment)
7.2. Terrestrial compartment
7.3. Atmospheric compartment
7.4. Microbiological activity in sewage treatment systems

8. PBT AND vPvB ASSESSMENT