ANNEX XI

GENERAL RULES FOR ADAPTATION OF THE STANDARD TESTING REGIME SET OUT IN ANNEXES VII TO X

Annexes VII to X set out the information requirements for all substances manufactured or imported in quantities of:

— one tonne or more in accordance with Article 12(1)(a),

— 10 tonnes or more in accordance with Article 12(1)(c),

— 100 tonnes or more in accordance with Article 12(1)(d), and

— 1 000 tonnes or more in accordance with Article 12(1)(e).

In addition to the specific rules set out in column 2 of Annexes VII to X, a registrant may adapt the standard testing regime in accordance with the general rules set out in Section 1 of this Annex. Under dossier evaluation the Agency may assess these adaptations to the standard testing regime.

1. 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 GLP or the test methods referred to in Article 13(3)*

Data shall be considered to be equivalent to data generated by the corresponding test methods referred to in Article 13(3) if the following conditions are met:

(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 GLP or the test methods referred to in Article 13(3)*

Data shall be considered to be equivalent to data generated by the corresponding test methods referred to in Article 13(3) 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 in Article 13(3);

(3) exposure duration comparable to or longer than the corresponding test methods referred to in Article 13(3) 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 in Article 13(3) or from an international test method recognised by the Commission or the Agency 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.

The Agency in collaboration with the Commission, Member States and interested parties shall develop and provide guidance in assessing which (Q)SARs will meet these conditions and provide examples.

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. In this context, 'suitable' means sufficiently well developed according to internationally agreed test development criteria (e. g. the European Centre for the Validation of Alternative Methods (ECVAM)) criteria for the entry of a test into the prevalidation process). Depending on the potential risk, immediate confirmation requiring testing beyond the information foreseen in Annexes VII or VIII or proposed confirmation requiring testing beyond the information foreseen in Annexes IX or X for the respective tonnage level may be 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, unless testing is not required in accordance with Annexes VII to X or the other rules in this Annex.

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 Agency, after consulting with relevant stakeholders and other interested parties, shall issue guidance on technically and scientifically justified methodology for the grouping of substances sufficiently in advance of the first registration deadline for phase-in substances.

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 in Article 13(3),

— cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter, and

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

2. 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 in Article 13(3), more specifically on the technical limitations of a specific method, shall always be respected.

3. SUBSTANCE-TAILORED EXPOSURE-DRIVEN TESTING

3.1. Testing in accordance with Sections 8.6 and 8.7 of Annex VIII, Annex IX and Annex X may be omitted, based on the exposure scenario(s) developed in the Chemical Safety Report.

3.2. In all cases, adequate justification and documentation shall be provided. The justification shall be based on an exposure assessment in accordance with Section 5 of Annex I and be consistent with the criteria adopted pursuant to Section 3.3, and the specific conditions of use must be communicated through the chemical supply chain in accordance with Articles 31 or 32.

3.3. The Commission shall adopt the measures designed to amend non-essential elements of this Regulation by supplementing it, in accordance with the procedure referred to in Article 133(4), to set the criteria defining what constitutes adequate justification under Section 3.2 by 1 December 2008.