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ANNEX IV

GENERAL RULES FOR THE ADAPTATION OF THE DATA REQUIREMENTS

This Annex sets out rules to be followed when the applicant proposes to adapt the data requirements set out in Annexes II and III in accordance with Article 6(2) and (3) or Article 21(1) and (2), without prejudice to the specific rules set out in Annex III on the use of the calculation methods for classification of mixtures to avoid testing on vertebrates.

The reasons for such adaptations to the data requirements must be clearly stated under the appropriate heading of the dossier referring to the specific rule(s) of this Annex.

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 relevant test methods.

Data shall be considered to be equivalent to data generated by the corresponding test methods if the following conditions are met:

- (1) adequacy of the data for the purpose of classification and labelling and risk assessment;
- (2) sufficient adequate and reliable documentation is provided to assess the equivalency 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 relevant test methods.

Data shall be considered to be equivalent to data generated by the corresponding test methods if the following conditions are met:

- (1) adequacy of the data for the purpose of classification and labelling and risk assessment;
- (2) adequate and reliable coverage of the key parameters/endpoints foreseen to be investigated in the corresponding test methods;
- (3) exposure duration comparable to or longer than the corresponding test methods if exposure duration is a relevant parameter;
- (4) adequate and reliable documentation of the study is provided; and
- (5) the study is performed using a system of quality assurance.

1.1.3. Historical human data

As a general rule, in accordance with Article 7(3) of Regulation (EC) No 1272/2008, tests on humans shall not be performed for the purposes of this Regulation. However, existing historical human data, such as epidemiological studies on exposed populations, accidental or occupational exposure data, biomonitoring studies, clinical studies and human volunteer studies performed in accordance with internationally accepted ethical standards shall be considered.

Data collected on humans shall not be used to lower the safety margins resulting from tests or studies on animals.

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The strength of the data for a specific human health effect depends, among other things, on the type of analysis and 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 does not have a particular dangerous property, while the information from each single source alone is considered insufficient to support this notion. There may be sufficient weight of evidence from the use of positive results of newly developed test methods, not yet included in the relevant test methods or from an international test method recognised by the Commission as being equivalent, leading to the conclusion that a substance has a particular dangerous property. However, if the newly developed test method has been approved by the Commission, but has not yet been published, its results may be taken into account even where this leads to the conclusion that a substance does not have a particular dangerous property.

Where consideration of all the available data provides sufficient weight of evidence for the presence or absence of a particular dangerous property:

- further testing on vertebrates for that property shall not be undertaken,
- further testing not involving vertebrates 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, but not the absence of a given dangerous property. Results of (Q)SARs may be used instead of testing when the following conditions are met:

- the 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,
- the results are adequate for the purpose of classification and labelling and risk assessment, and
- adequate and reliable documentation of the applied method is provided.

The Agency shall, in collaboration with the Commission, Member States and interested parties, develop and provide guidance on the use of (Q)SARs.

1.4. In vitro methods

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Results obtained from suitable *in vitro* methods may indicate the presence of a given 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.

Where such *in vitro* tests are positive, it is necessary to confirm the dangerous property by adequate *in vivo* tests. However, 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 risk assessment; and
- (3) adequate and reliable documentation of the applied method is provided.

In the case of negative results, these exemptions do not apply. A confirmation test may be requested on a case-by-case basis.

1.5. Grouping of substances and read-across approach

Substances whose physico-chemical, toxicological and ecotoxicological properties are 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 physico-chemical properties, human and animal 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 indicating the presence of dangerous properties;
- (2) common precursors and/or the likelihood of common breakdown products via physical and biological processes, which result in structurally similar chemicals and indicates the presence of dangerous properties; 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 shall:

- be adequate for the purpose of classification and labelling and risk assessment,
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method, and
- cover an exposure duration comparable to or longer than the corresponding test method if exposure duration is a relevant parameter.

In all cases, adequate and reliable documentation of the applied method shall be provided.

The Agency shall, in collaboration with the Commission, Member States and interested parties, develop and provide guidance on technically and scientifically justified methodology for the grouping of substances.

2. TESTING IS TECHNICALLY NOT POSSIBLE

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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 relevant test methods, more specifically on the technical limitations of a specific method, shall always be respected.

3. PRODUCT-TAILORED EXPOSURE-DRIVEN TESTING

- 3.1. Testing in accordance with some endpoints in Sections 8 and 9 of Annexes II and III, notwithstanding Article 6(2), may be omitted based on exposure considerations, where exposure data in accordance with Annex II or III are available.

In that case, the following conditions shall be met:

- An exposure assessment shall be performed, covering primary and secondary exposure under realistic worst case for all intended uses of the biocidal product that contains the active substance for which approval is applied, or of the biocidal product for which the authorisation is sought.
- If a new exposure scenario is introduced at a later stage, during the product authorisation process, additional data shall be submitted to assess whether the justification for data adaptation still applies.
- The reasons why the outcome of the exposure assessment justifies waiving of data requirements shall be clearly and transparently explained.

However, testing cannot be omitted for non-threshold effects. As a consequence, certain core data shall always be obligatory, e.g. genotoxicity testing.

If relevant, the Agency shall, in collaboration with the Commission, Member States and interested parties, develop and provide further guidance on the criteria established in accordance with Article 6(4) and Article 21(3).

- 3.2. In all cases, adequate justification and documentation shall be provided. The justification shall be based on an exposure assessment, in accordance with the relevant Technical Notes for Guidance where available.

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