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ANNEX VI

COMMON PRINCIPLES FOR THE EVALUATION OF DOSSIERS FOR BIOCIDAL PRODUCTS

ASSESSMENT

General principles

13. The data submitted in support of an application for authorisation of a biocidal product shall be validated by the evaluating or receiving competent authority in accordance with the relevant articles of the Regulation. After validation of these data the competent authorities shall utilise them by carrying out a risk assessment based on the proposed use. Information submitted in the framework of Regulation (EC) No 1907/2006 shall be taken into account where appropriate.
14. A risk assessment on the active substance present in the biocidal product shall always be carried out. If there are, in addition, any substances of concern present in the biocidal product then a risk assessment shall be carried out for each of these. The risk assessment shall cover the proposed normal use of the biocidal product, together with a realistic worst-case scenario including any relevant production and disposal issue. The assessment shall also take account of how any 'treated articles' treated with or containing the product may be used and disposed of. Active substances that are generated in-situ and the associated precursors shall also be considered.
15. In carrying out the assessment, the possibility of cumulative or synergistic effects shall also be taken into account. The Agency shall, in collaboration with the Commission, Member States and interested parties, develop and provide further guidance on the scientific definitions and methodologies for the assessment of cumulative and synergistic effects.
16. For each active substance and each substance of concern present in the biocidal product, the risk assessment shall entail hazard identification and the establishment of appropriate reference values for dose or effect concentrations such as NOAEL or Predicted No Effect Concentrations (PNEC), where possible. It shall also include, as appropriate, a dose (concentration) — response (effect) assessment, together with an exposure assessment and a risk characterisation.
17. The results arrived at from a comparison of the exposure to the appropriate reference values for each of the active substances and for any substances of concern shall be integrated to produce an overall risk assessment for the biocidal product. Where quantitative results are not available the results of the qualitative assessments shall be integrated in a similar manner.
18. The risk assessment shall determine:
 - (a) the hazards due to the physico-chemical properties,
 - (b) the risk to humans and animals,
 - (c) the risk to the environment,
 - (d) the measures necessary to protect humans, animals and the environment, both during the proposed normal use of the biocidal product and in a realistic worst-case situation.
19. In certain cases it may be concluded that further data are required before a risk assessment can be finalised. Any such additional data requested shall be the minimum necessary to complete such a risk assessment.

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20. The information provided on the biocidal product family shall permit the evaluating body to reach a decision on whether all the products within the biocidal product family comply with the criteria under Article 19(1)(b).
21. Where relevant the technical equivalence for every active substance contained in the biocidal product shall be established with reference to active substances already included in the list of approved active substances.

Effects on human and animal health

Effects on human health

22. The risk assessment shall take account of the following potential effects arising from the use of the biocidal product and the populations liable to exposure.
23. The effects previously mentioned result from the properties of the active substance and any substance of concern present. They are:
- acute toxicity,
 - irritation,
 - corrosivity,
 - sensitisation,
 - repeated dose toxicity,
 - mutagenicity,
 - carcinogenicity,
 - reproductive toxicity,
 - neurotoxicity,
 - immunotoxicity,
 - disruption of the endocrine system,
 - any other special properties of the active substance or substance of concern,
 - other effects due to physico-chemical properties.
24. The populations previously mentioned are:
- professional users,
 - non-professional users,
 - humans exposed directly or indirectly via the environment.

In considering these populations, particular attention should be given to the need to protect vulnerable groups within these populations.

25. The hazard identification shall address the properties and potential adverse effects of the active substance and any substances of concern present in the biocidal product.
26. The evaluating body shall apply points 27 to 30 when carrying out a dose (concentration) - response (effect) assessment on an active substance or a substance of concern present in a biocidal product.
27. For repeated dose toxicity and reproductive toxicity the dose-response relationship shall be assessed for each active substance or substance of concern and, where possible, a NOAEL identified. If it is not possible to identify a NOAEL, the lowest-observed-adverse-effect level (LOAEL) shall be identified. Where appropriate, other dose-effect descriptors may be used as reference values.
28. For acute toxicity, corrosivity and irritation, it is not usually possible to derive a NOAEL or LOAEL on the basis of tests conducted in accordance with the

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requirements of this Regulation. For acute toxicity, the LD₅₀ (median lethal dose) or LC₅₀ (median lethal concentration) value or another appropriate dose-effect descriptor shall be derived. For the other effects it shall be sufficient to determine whether the active substance or substance of concern has an inherent capacity to cause such effects during use of the biocidal product.

29. For mutagenicity and carcinogenicity, a non-threshold assessment should be carried out if the active substance or substance of concern is genotoxic and carcinogenic. If the active substance or a substance of concern is not genotoxic a threshold assessment shall be carried out.
30. With respect to skin sensitisation and respiratory sensitisation, in so far as there is no consensus on the possibility of identifying a dose/concentration below which adverse effects are unlikely to occur, particularly in a subject already sensitised to a given substance, it shall be sufficient to evaluate whether the active substance or substance of concern has an inherent capacity to cause such effects as a result of the use of the biocidal product.
31. When carrying out the risk assessment special consideration shall be given to toxicity data derived from observations of human exposure where such data are available, e.g. information gained from manufacture, from poison centres or epidemiology surveys.
32. An exposure assessment shall be carried out for each of the human populations (professional users, non-professional users and humans exposed directly or indirectly via the environment), for which exposure to a biocidal product occurs or can reasonably be foreseen, with particular attention paid to the pathways of exposure relevant for vulnerable groups. The objective of the assessment shall be to make a quantitative or qualitative estimate of the dose/concentration of each active substance or substance of concern, including relevant metabolites and degradation products to which a population is, or may be exposed during use of the biocidal product and articles treated with that product.
33. The exposure assessment shall be based on the information in the technical dossier provided in conformity with Articles 6 and 21 and on any other available and relevant information. Particular account shall be taken, as appropriate, of:
 - adequately measured exposure data,
 - the form in which the biocidal product is marketed,
 - the type of biocidal product,
 - the application method and application rate,
 - the physico-chemical properties of the biocidal product,
 - the likely routes of exposure and potential for absorption,
 - the frequency and duration of exposure,
 - maximum residue levels,
 - the type and size of specific exposed populations, where such information is available.
34. When conducting the exposure assessment, special consideration shall be given to adequately measured, representative exposure data where such data are available. Where calculation methods are used for the estimation of exposure levels, adequate models shall be applied.

These models shall:

- make a best possible estimation of all relevant processes taking into account realistic parameters and assumptions,

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- be subjected to an analysis taking into account possible elements of uncertainty,
- be reliably validated with measurements carried out under circumstances relevant for the use of the model,
- be relevant to the conditions in the area of use.

Relevant monitoring data from substances with analogous use and exposure patterns or analogous properties shall also be considered.

35. Where, for any of the effects set out in point 23 a reference value has been identified, the risk characterisation shall entail comparison of the reference value with the evaluation of the dose/concentration to which the population will be exposed. Where a reference value cannot be established a qualitative approach shall be used.

Assessment factors account for the extrapolation from animal toxicity to the exposed human population. The setting of an overall assessment factor considers the degree of uncertainty in inter-species and intra-species extrapolation. In the absence of suitable chemical-specific data, a default assessment factor of 100 is applied to the relevant reference value. Additional elements can also be considered for assessment factors, including toxicokinetics and toxicodynamics, the nature and severity of the effect, human (sub-)populations, exposure deviations between study results and human exposure with regard to frequency and duration, study duration extrapolation (e.g. sub-chronic to chronic), dose-response relationship and the overall quality of the toxicity data package.

Effects on animal health

36. Using the same relevant principles as described in the section dealing with effects on humans, the evaluating body shall consider the risks posed to animals from the biocidal product.

Effects on the environment

37. The risk assessment shall take account of any adverse effects arising in any of the three environmental compartments — air, soil and water (including sediment) — and of the biota, following the use of the biocidal product.
38. The hazard identification shall address the properties and potential adverse effects of the active substance and any substances of concern present in the biocidal product.
39. A dose (concentration) — response (effect) assessment shall be carried out in order to predict the concentration below which adverse effects in the environmental compartment of concern are not expected to occur. This shall be carried out for the active substance and for any substance of concern present in the biocidal product. This concentration is known as PNEC. However, in some cases, it may not be possible to establish a PNEC and a qualitative estimation of the dose (concentration) — response (effect) then has to be made.
40. The PNEC shall be determined from the data on effects on organisms and ecotoxicity studies submitted in accordance with requirements of Articles 6 and 20. It shall be calculated by applying an assessment factor to the reference values resulting from tests on organisms, e.g. LD₅₀ (median lethal dose), LC₅₀ (median lethal concentration), EC₅₀ (median effective concentration), IC₅₀ (concentration causing 50 % inhibition of a given parameter, e.g. growth), NOEL(C) (no-observed-effect level (concentration)), or LOEL(C) (lowest-observed-effect level (concentration)). Where appropriate, other dose-effect descriptors may be used as reference values.
41. An assessment factor is an expression of the degree of uncertainty in extrapolation from test data on a limited number of species to the real environment. Therefore, in

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general, the more extensive the data and the longer the duration of the tests, the smaller the degree of uncertainty and the size of the assessment factor.

42. For each environmental compartment, an exposure assessment shall be carried out in order to predict the likely concentration of each active substance or substance of concern present in the biocidal product. This concentration is known as the predicted environmental concentration (PEC). However, in some cases it may not be possible to establish a PEC and a qualitative estimate of exposure then has to be made.
43. A PEC, or where necessary a qualitative estimate of exposure, need only be determined for the environmental compartments to which emissions, discharges, disposal or distributions (including any relevant contribution from articles treated with biocidal products) are known or are reasonably foreseeable.
44. The PEC, or the qualitative estimation of exposure, shall be determined taking account of, in particular and where appropriate:
 - adequately measured exposure data,
 - the form in which the product is marketed,
 - the type of biocidal product,
 - the application method and application rate,
 - the physico-chemical properties,
 - breakdown/transformation products,
 - likely pathways to environmental compartments and potential for adsorption/desorption and degradation,
 - the frequency and duration of exposure,
 - long range environmental transportation.
45. When conducting the exposure assessment, special consideration shall be given to adequately measured, representative exposure data where such data are available. Where calculation methods are used for the estimation of exposure levels, adequate models shall be applied. The characteristics of these models shall be as listed in point 34. Where appropriate, on a case-by-case basis, relevant monitoring data from substances with analogous use and exposure patterns or analogous properties should also be considered.
46. For any given environmental compartment, the risk characterisation shall, as far as possible, entail comparison of the PEC with the PNEC so that a PEC/PNEC ratio may be derived.
47. If it has not been possible to derive a PEC/PNEC ratio, the risk characterisation shall entail a qualitative evaluation of the likelihood that an effect is occurring under the current conditions of exposure or will occur under the expected conditions of exposure.
48. The evaluating body shall conclude that the biocidal product does not comply with criterion (iv) under point (b) of Article 19(1) if it contains any substance of concern or relevant metabolites or breakdown or reaction products fulfilling the criteria for being PBT or vPvB in accordance with Annex XIII to Regulation (EC) No 1907/2006, or if it has endocrine-disrupting properties unless it is scientifically demonstrated that under relevant field conditions there is no unacceptable effect.

Effects on target organisms

49. An assessment shall be made to demonstrate that the biocidal product does not cause unnecessary suffering in its effect on target vertebrates. This shall include an

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evaluation of the mechanism by which the effect is obtained and the observed effects on the behaviour and health of the target vertebrates; where the intended effect is to kill the target vertebrate, the time necessary to obtain the death of the target vertebrate and the conditions under which death occurs shall be evaluated.

50. The evaluating body shall, where relevant, evaluate the possibility of the development by the target organism of resistance or cross-resistance to an active substance in the biocidal product.

Efficacy

51. Data submitted by the applicant shall be sufficient to substantiate the efficacy claims for the product. Data submitted by the applicant or held by the evaluating body must be able to demonstrate the efficacy of the biocidal product against the target organism when used normally in accordance with the conditions of authorisation.
52. Testing should be carried out according to Union guidelines where these are available and applicable. Where appropriate, other methods from the list below can be used. If relevant acceptable field data exist, these can be used.
- ISO, CEN or other international standard method
 - national standard method
 - industry standard method (if accepted by the evaluating body)
 - individual producer standard method (if accepted by the evaluating body)
 - data from the actual development of the biocidal product (if accepted by the evaluating body).

Summary

53. In each of the areas where risk assessments have been carried out, the evaluating body shall combine the results for the active substance together with the results for any substance of concern to produce an overall assessment for the biocidal product itself. This shall also take account of any cumulative or synergistic effects.
54. For biocidal product containing more than one active substance, any adverse effects shall also be considered together to produce an overall assessment for the biocidal product itself.

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