

Annex IV – Exemptions from Registration under REACH

Criteria Document – DRAFT (version 2007.10.15)

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1 INTRODUCTION

One of the main purposes of Regulation (EC) No 1907/2006 of the European Parliament and the Council of 18 December 2006 (REACH) is to ensure a high level of protection of human health and the environment. REACH is based on the principle that manufacturers, importers and downstream users shall ensure that the manufacture, placing on the market and use of substances shall not adversely affect human health or the environment. As part of the registration procedure, the registrant is required to document that substances can be used in a safe manner, with regard to human health and the environment.

Annex IV of REACH identifies substances that are exempted from the registration, evaluation and downstream user provisions of REACH *on the basis that sufficient information is known about these substances so that they are considered to cause minimum risk because of their intrinsic properties* (Article 2(7)(a)).

The current Annex IV of REACH essentially reproduces the list of substances exempted from the obligation to register under the present Existing Substances Regulation (Regulation (EEC) No 793/93). This list has not been revised since then, except with the addition of one substance, Cellulose Pulp, during the progress of the Regulation through the regulatory process.

According to REACH (Article 138(4)), the Commission is to carry out a review of Annex IV by 1 June 2008, in order to consider whether additional substances should be added to the Annex and whether substances currently in the Annex meet the basic criterion that “sufficient information is known about these substances so that they are considered to cause minimum risk because of their intrinsic properties”.

This review requires definition of the core requirements of “sufficient information” and “minimum risk” and the development of additional criteria for the evaluation of this information and the potential risk of substances to be included, or already included, in the Annex. Once the Commission, together with an advisory group of Member States and other stakeholders, have agreed on these criteria, the minimum data-set required and a format for adding or removing substances from Annex IV, the intent is to review each current entry and proposed new entry to see if it meets the criteria for inclusion in Annex IV, documenting the conclusion for the entry, and proposing addition to, or deletion from, the list as appropriate.

This document provides a proposal for the assessment of whether substances should be included in Annex IV (section 2), the information and documentation requirements when making a submission requesting the addition of an additional

substance to the current Annex IV (sections 3 and 4), and the subsequent review process (section 5).

For the purposes of this review,

- “Sufficient information” means: the information specified in section 3 which is considered to be necessary to confirm the “minimum risk because of intrinsic properties” posed by a substance.
- “Minimum risk because of intrinsic properties” means: that negligible risk can be assumed on the basis of the intrinsic properties of the substance.

It is important to note that the principle of “minimum risk because of intrinsic properties” is clearly different from the approach applied in registration under REACH. The proposed criteria for minimum risk should apply at all tonnage levels and need to be independent of the specific uses of the substance and the resulting exposure of humans and the environment as all future uses cannot possibly be predicted. Consequently, the rules described in Annex XI section 3 do not apply as they are based on an exposure assessment of a known use of the substance. Likewise, the tonnage of substances is not considered as the future level of manufacture and import of a substance cannot be predicted. The information requirements and associated criteria are therefore the same regardless of the tonnage currently manufactured in, or imported into, the EU.

In developing the document, the following principles were followed:

- A concrete description of what constitutes a “minimum risk because of intrinsic properties” needed to be developed.
- Based on the description of “minimum risk because of intrinsic properties” information requirements were defined.

2 CRITERIA FOR DETERMINING MINIMUM RISK BECAUSE OF INTRINSIC PROPERTIES

As following Article 2.7(a) minimum risk in this exercise is based on intrinsic properties, use and exposure information will not be included. Using only information on intrinsic properties of the substance leads to a more uncertain determination of the magnitude of risk. Due to this inherent uncertainty and the need to include only substances which pose a minimum risk, strict hazard-based criteria needed to be developed. Such criteria are proposed below. Minimum risk because of intrinsic properties can only be concluded if all criteria for physicochemical properties, toxicological properties and ecotoxicological properties mentioned in sections 2.1 to 2.3 are met.

2.1 Physicochemical properties

All the following criteria must be met:

1. The data specified in section 3 on Information requirements must be provided.
2. The substance does not meet the criteria for classification as dangerous in accordance with Directive 67/548/EEC.
3. The substance does not meet any of the criteria laid out in Appendix IA of this document for the following endpoints (a. to n.):
 - a. **Explosive**, in Divisions 1.1, 1.2, 1.3, 1.4 and 1.5;
 - b. **Flammable gas**, Category 1 or Category 2;
 - c. **Flammable liquid**, Category 1, Category 2, Category 3 or Category 4;
 - d. **Flammable solid**, Category 1 or Category 2;
 - e. **Oxidising gas**, Category 1;
 - f. **Oxidising liquid**, Category 1, Category 2 or Category 3;
 - g. **Oxidising solid**, Category 1, Category 2 or Category 3;
 - h. **Corrosive to metals**, Category 1;
 - i. **Self-reactive substance**, Types A to F;
 - j. **Pyrophoric liquid**, Category 1;
 - k. **Pyrophoric solid**, Category 1;
 - l. **Self-heating substance**, Category 1 or Category 2;
 - m. **Substance which in contact with water emits flammable gas**, Category 1, Category 2 or category 3;
 - n. **Organic peroxide**, of Type A to G.

2.2 Toxicological properties

All the following criteria must be met:

1. The data specified in section 3 on Information Requirements must be provided.
2. The substance does not meet the criteria for classification as dangerous in accordance with Directive 67/548/EEC.
3. The substance does not meet the criteria for a substance of very high concern (SVHC) in accordance with Article 57 of REACH.
4. The intrinsic properties of the substance are well below the criteria for classification as dangerous in accordance with Directive 67/548/EEC (using all available data for all relevant toxicological endpoints). This is demonstrated by an absence of ‘*significant toxicological effects*’ in the relevant toxicological studies.
5. Absence of “*significant toxicological effects*” means:
 - a. Acute oral toxicity: no evident toxicity¹ at dose levels < 2000 mg/kg. Additionally the LD₀ must be > 5000 mg/kg where the substance has been tested at this level;
 - b. Acute dermal toxicity: no evident toxicity² at dose levels < 2000 mg/kg. Additionally the LD₀ must be > 5000 mg/kg where the substance has been tested at this level;
 - c. Acute inhalational toxicity: no evident toxicity² at an exposure level of 20 mg/litre/4h for gases or vapours and 5 mg/litre/4h for aerosols or particulates. Additionally the LD₀ must be > 50 mg/litre/4h for gases or vapours and > 12.5 mg/litre/4h for aerosols or particulates where the substance has been tested at this level;
 - d. Skin irritation: the substance does not meet the criteria for (a) assignation of the Risk Phrase R66 in Annex VI of Directive 67/548/EEC or (b) mild skin irritation according to the criteria laid down in Annex 1B of this document;
 - e. Eye irritation: the substance does not meet the criteria for “mildly irritating to eyes” according to the criteria laid down in Annex 1B of this document;

¹ Comprising: an absence of clinical signs of toxicity during the post-dosing observation period, no treatment-related body weight changes, no macroscopic findings at autopsy and no microscopic findings in cases where histopathological investigations have been undertaken.

- f. Sensitisation: no evidence of sensitisation potential from structural alerts, in animal tests (no evidence of a positive response in any animal tested) and no human evidence of sensitisation potential (no human cases of sensitisation reported);
- g. Repeated dose toxicity by the oral route: no evident toxicity² at <500 mg/kg/day (NOAEL) in the case of a 90-day study³. Results from longer-term (e.g. 2-year) studies should be evaluated by the applicant on a case-by-case basis using this criterion as a guide. For the purpose of reviewing current Annex IV entries, if only results from short-term studies (e.g. 28 day) are available, then these data should be evaluated on a case-by-case basis using this criterion as a guide;
- h. Repeated dose toxicity by the dermal route: no evident toxicity³ at <1000 mg/kg/day (NOAEL) in the case of a 90-day study⁴. Results from longer-term studies should be evaluated by the applicant on a case-by-case basis using this criterion as a guide. For the purpose of reviewing current Annex IV entries, if only results from short-term studies (e.g. 28 day) are available, then these data should be evaluated on a case-by-case basis using this criterion as a guide;
- i. Repeated dose toxicity by the inhalation route: no evident toxicity³ at <2.5 mg/litre/6h/day (NOAEL) in the case of a 90-day study.⁴ Results from longer-term studies should be evaluated by the applicant on a case-by-case basis using this criterion as a guide. For the purpose of reviewing current Annex IV entries, if only results from short-term studies (e.g. 28 day) are available, then these data should be evaluated on a case-by-case basis using this criterion as a guide;
- j. Carcinogenicity: no evidence of carcinogenic potential based on available data and application of relevant (Q)SAR models or other structural alerts;
- k. Mutagenicity: no evidence of mutagenic potential in vitro or in vivo nor from the application of relevant (Q)SAR models or other structural alerts;
- l. Reproductive toxicity: no evidence of reproductive toxicity at <1000 mg/kg/day by the oral route, at 2000 mg/kg/day by the dermal route or at 20 mg/litre/6h/day for gases or vapours or 5 mg/litre/6h/day for

² Comprising: an absence of clinical signs of toxicity during the period of the study including behavioural changes, no treatment-related body weight or food consumption changes, no macroscopic findings at autopsy, no treatment-related effects on organ weights, clinical chemical or haematological parameters or urinalysis, no treatment-related microscopic findings.

³ The data set for application for an exemption from registration will normally include a 90-day study

aerosols or particulates (limit tests) by the inhalation route⁴, nor from the application of relevant (Q)SAR models or other structural alerts;

- m. Harm to breastfed babies: the substance should not interfere or be suspected to be able to interfere with lactation, nor should it be a substance which may be present in breast milk or be suspected to be able to pass over to breast milk;
 - n. Narcotic effects: the substance should not cause any signs of CNS depression even after prolonged or repeated exposure;
 - o. Danger of cumulative effects: the substance should not have been shown to accumulate in the human body or be suspected to have properties leading to such accumulation.
6. The substance must not meet any of the screening criteria for PBT or vPvB set out in the TGD for the CSA/CSR⁵ nor must it be on the PBT working group list.
 7. The substance shall not be identified or suspected to have endocrine activity from in vivo or in vitro tests, nor from the application of relevant (Q)SAR models or other structural alerts, which may raise any concern for endocrine-disrupting properties (DG Environment, ENV.D4./ETU/2005/0028r; http://ec.europa.eu/environment/endocrine/documents/final_report_2007.pdf)
 8. The substance shall not be listed in Annex II or Annex III of the Cosmetic Directive 76/768/EEC.

2.3 Ecotoxicological properties

All the following criteria must be met:

1. The data specified in section 3 on Information requirements must be provided.
2. The substance does not meet the criteria for classification as dangerous in accordance with Directive 67/548/EEC.
3. The substance does not meet the criteria for a substance of very high concern in accordance with Article 57 of REACH.
4. The intrinsic properties of the substance are well below the criteria for classification as dangerous in accordance with Directive 67/548/EEC (using all available data), i.e.:

⁴ There is currently limited scientific basis for the indicated figures for the dermal and inhalation routes.

⁵ The TGD for the CSA/CSR is not yet finalised and, thus, the best available draft TGD will be used.

- a. The substance shall have a very low potential to bioaccumulate in aquatic species, e.g. fish, i.e. experimentally determined bioconcentration factor is <10. For organic substances an alternative criteria of log Pow < 2.0 can be applied.
 - b. The substance shall be readily biodegradable (excluding inorganic substances)
 - c. The aquatic toxicity shall fulfil both of following criteria:
 - i. Acute, short-term EC/LC50 > 1,000 mg/L, or > water solubility, or no significant adverse effects recorded at 100 mg/l in acute, short-term aquatic toxicity tests *and* validated QSAR data showing acute effects (EC/LC50) > 1000 mg/l.
 - ii. Chronic long-term NOEC > 10 mg/L
5. The substance must not have adverse effects on terrestrial organisms, meaning that no adverse effects are reported in any of the tests required under Annex IX of the REACH Regulation at the maximum test concentrations prescribed by the respective OECD guidelines.
 6. The substance must not meet any of the screening criteria for PBT or vPvB set out in the TGD for the CSA/CSR⁶ nor must it be on the PBT working group list.
 7. The substance shall not be identified or suspected to have endocrine activity from in vivo or in vitro tests, nor from the application of relevant (Q)SAR models or other structural alerts, which may raise any concern for endocrine-disrupting properties (DG Environment, ENV.D4./ETU/2005/0028r; http://ec.europa.eu/environment/endocrine/documents/final_report_2007.pdf)
 8. The substance shall not present a risk to the ozone layer, i.e. the substance shall not be included in Annex I to EC 2037/2000.

3 INFORMATION REQUIREMENTS

The information required in a submission requesting the addition of a substance to Annex IV shall be sufficient for an evaluation of the fulfillment of the criteria for determining minimum risk because of intrinsic properties. The information shall consist of:

1. The information needed for identification of the substance (as defined in REACH Annex VI, section 2).

⁶ The TGD for the CSA/CSR is not yet finalised and, thus, the best available draft TGD will be used.

2. The standard information corresponding to the endpoints set out in Annex VII, Annex VIII, Annex IX and Annex X, subject to the following clarifications:
 - The specific rules for adaptation provided in column 2 of the Annexes apply, in relation to exceptions from the standard information requirements listed above *except* when these are based on exposure or risk considerations ;
 - Information is required on all the physicochemical properties of the substance according to the requirements in Annexes VII and IX with the clarification that information is not required for the endpoints 7.2 Melting/freezing point, 7.4 Relative density, 7.6 Surface tension, 7.15 Stability in organic solvents and identity of relevant degradation products, and 7.16 Dissociation constant;
 - Toxicological information is required sufficient to demonstrate that the criteria set out in section 2 of this document have been met and referring to requirements in Annexes VII-X, as appropriate (information according to Annex X is only required when such studies are available);
 - Ecotoxicological information sufficient to demonstrate that the criteria set out in section 2 of this document have been met and referring to requirements in Annexes VII-X, as appropriate, with the clarification that a minimum of one long-term toxicity study as described in endpoint 9.1 (Annex IX) for the most sensitive organism (crustacean or fish) is always required (information according to Annex X is only required when such studies are available).
3. All available test data and non-test data on the substance and its known metabolites. This includes the information in literature and databases and, when applicable, information obtained from (Q)SARs, grouping of substances or read-across approach, in vivo and in vitro testing, and epidemiological studies, cf. Annex XI section 1. If such information is used, in accordance with Annex XI, this must be fully justified and documented. In this context, available information from risk and hazard assessments performed under international, national and Community programmes or legislation as well as voluntary initiatives may be used to provide reliable information on intrinsic properties.
4. Robust study summaries, in accordance with the IUCLID 5 manual and the OECD HPV Chemicals Programme Manual shall be provided for a minimum of one key study per endpoint for physicochemical, toxicological and ecotoxicological properties. If the key study for any toxicological or ecotoxicological endpoint is not the study giving rise to

the highest concern, the use of the particular key study must be fully justified and robust study summaries shall be provided for the study or studies showing a higher effect than the key study. Full study reports need not be submitted but the applicant should be in legitimate possession of, or have permission to refer to, the full study report and be able to submit it to the European Commission or the contractor upon request. Evidence of such rights must be available on request (e.g. ownership, letter of access).

5. When the results submitted are not in accordance with publicly available sources (i.e. ESIS, IUCLID,...), the applicant must present scientific judgement which justifies that the key studies in the submission are superior to the publicly available studies showing different results; as a minimum the applicant is requested to review the information in the IUCLID database.
6. The information submitted shall be sufficient to enable a conclusion to be reached on the intrinsic hazard of the substance, for each relevant endpoint. The information shall be presented clearly and succinctly.
7. If the general rules for adaptation of the standard testing regime as described in Annex XI, sections 1 and 2, have been applied, their use must be fully justified. As previously indicated the rules described in Annex XI section 3 do not apply as they are based on an exposure assessment and, thus, a known use of the substance; consequently exposure resulting from unknown future uses cannot be addressed.
8. Commonly known substances, where there is clear scientific evidence that prolonged daily and continuous human and environmental exposure does not lead to more than minimum risk may be evaluated case-by-case as the information required in Annexes VII to X would not add useful data to the already available information. This approach could be warranted for substances such as sugar which can be considered to constitute a minimum risk even though a full dataset may not be available. Waiving of standard information requirements for such substances may refer to Annex XI, particularly sections 1.1 (Use of existing data) and 1.2 (Weight of evidence). Minimum risk can, however, not be concluded based alone on a Community risk assessment not resulting in risk management measures being recommended.
9. If grouping of substances and the read-across approach are applied, in accordance with Annex XI section 1.5, this must be fully justified and documented. This means that unambiguous identification of the substances included in the grouping and information on the endpoints where the approach is applied must be clearly provided.

10. Information need not be provided if testing is not technically possible due to the intrinsic physicochemical properties of a substance, cf. Annex XI section 2. If waiving of the requirement for information is applied for this reason in accordance with Annex XI, it must be fully justified and documented.

4 DOCUMENTATION REQUIREMENTS

The following documentation requirements must be met:

1. Submissions to be considered for the inclusion of an additional substance in Annex IV shall consist of a dossier including:
 - An overall conclusion from the applicant on whether the substance meets the criteria laid down in this document, with justification;
 - A conclusion (descriptive and numerical) per endpoint based on consideration of the information required; and
 - The information specified in section 3 on 'Information requirements' and a completed format in accordance with the instructions in Appendix 2.
2. The information in the dossier must be clearly presented in accordance with these instructions, the information requirements and in English only. Any submission with an incomplete or unclear dossier will be rejected without further consideration.
3. If there is publicly available information on the substance or known metabolites of the substance, not addressed in the submission, which leads to any doubt on the potential risk of the substance, then the submission will be rejected without further consideration.
4. If robust study summaries or other relevant information, e.g. (Q)SAR results with clear justification, are not presented in a clear manner for all key studies, then the submission will be rejected without further consideration.
5. Submissions to be considered for deletion of a substance in the existing Annex IV shall include a dossier containing a conclusion that the substance does meet the criteria laid down in this document. Documentation and justification shall be provided by completion of the relevant sections of the format (Appendix 2).

5. PROCESS

5.1 Submissions seeking the addition to or deletion of a substance from the existing Annex IV

Submissions seeking the addition or deletion of an entry to Annex IV shall be submitted by 30 November 2007 to the national competent authority of the country in which the applicant is based or to one of the following industry associations (CEFIC, CONCAWE, REACH Alliance).

Only one proposal for each substance should be submitted to the Member States and industry associations (see above). Due to limited resources and the short timescales involved in the review Member States and stakeholders should co-ordinate their efforts to achieve this end. Multiple proposals for a substance will be assessed separately rather than jointly due to resource constraints (also see point 4.3 above).

The Member State or industry association to whom the submission was made will screen the proposals against the agreed criteria and, if satisfied that the criteria and information requirements are fulfilled, forward the submission to the contractor and the Commission⁷. If a submission does not meet the information requirements or criteria it may be rejected by the Member State or industry association. Such rejection shall be communicated to the applicant and the Commission⁸ with a brief justification for such rejection following a standard format to be developed by the contractor. If an incomplete submission is not rejected by the Member State or industry association then an explanation of why the submission does not meet the criteria should be forwarded by the MS or industry association concerned to the Commission.

If one of the criteria is not met the submission to be considered for the inclusion of an additional substance in Annex IV will be rejected by the contractor without further consideration of other criteria.

The contractor will evaluate the proposals submitted to it by Member States and the industry associations and forward a summary and conclusion on either addition to, or deletion from, Annex IV to the Commission.

The strict deadline for the Member States or industry associations to forward submissions satisfying the requirements set out in this document to the contractor and the Commission shall be 10 January 2008.

⁷ AnnexIV@dhigroup.com mentioning in the subject line: "Proposal for inclusion in/deletion from Annex IV" as well as to ENV-reach-review-annex-IV@ec.europa.eu and Anja.Klauk@ec.europa.eu

⁸ ENV-reach-review-annex-IV@ec.europa.eu and Anja.Klauk@ec.europa.eu, mentioning in the subject line: "Rejected proposal for inclusion in/deletion from Annex IV"

5.2 Evaluations of substances already in Annex IV

The existing entries of Annex IV will be reviewed to see if they meet the developed criteria. The following approach will be applied:

- The contractor will collect data according to the information requirements for inclusion in Annex IV (see above) from easily accessible data sources, i.e. ECOTOX, GESAMP, IUCLID and HSDB. The developed format for submissions will be used as far as possible.
- The contractor will group substances in Annex IV, where possible, so that read-across principles can be used for all substances belonging to the same group. The following grouping could be applied:
 1. Sugars (e.g. glucose, L-sorbose)
 2. Saturated aliphatic monocarboxylic acids (e.g. lauric acid, palmitic acid, stearic acid)
 3. Fatty acids (e.g. C6-12, C12-14, C12-18, C16-18 saturated fatty acids and/or unsaturated fatty acids)
 4. Vegetable oils (e.g. sunflower oil, soybean oil, stafflower oil, linseed oil, corn oil)
 5. Glycerides (e.g. C10-18, C12-14, C16-18 and C18 unsaturated, C16-18 and mono and di-C18 unsaturated)
 6. Unsaturated aliphatic acids and their salts (e.g. oleic acid and potassium oleate, stearic acid and sodium stearate, calcium distearate)
 7. Esters (e.g. D-glucitol monostearate from D-glucitol and stearic acid)
- The contractor will check whether the entries fulfil the data requirements and the criteria above. Bearing in mind the historical evidence on substances in Annex IV, the **burden of proof is directed at identifying evidence of human health or environmental effects** according to the above criteria. This is as opposed to proposals for additions to Annex IV, where the burden of proof is directed at demonstrating compliance with the criteria and information requirements described in section 2 of this document.
- Should the contractor find indications in the information assessed leading to the conclusion that a substance does not fulfil the criteria the relevant industry association(s) shall be informed. They will be given the opportunity to dispute this by sending information showing that the substance in question does fulfil the criteria for inclusion in Annex IV.
- The contractor will prepare summaries of the review of the existing entries of Annex IV.

APPENDIX IA

Criteria⁹ for identification of hazardous physicochemical properties

1. **Explosive.** A substance shall **not** meet the criteria for any one of the divisions 1.1, 1.2, 1.3, 1.4 and 1.5, based on Test Series 2 to 8 in part I of the UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria according to the following description and the results of the tests laid down in Table 1 below:
 - (a) Division 1.1 Substances, mixtures and articles which have a mass explosion hazard (a mass explosion is one which affects almost the entire quantity present virtually instantaneously);
 - (b) Division 1.2 Substances, mixtures and articles which have a projection hazard but not a mass explosion hazard;
 - (c) Division 1.3 Substances, mixtures and articles which have a fire hazard and either a minor blast hazard or a minor projection hazard or both, but not a mass explosion hazard:
 - (i) combustion of which gives rise to considerable radiant heat; or
 - (ii) which burn one after another, producing minor blast or projection effects or both;
 - (d) Division 1.4 Substances, mixtures and articles which present no significant hazard:
 - Substances, mixtures and articles which present only a small hazard in the event of ignition or initiation. The effects are largely confined to the package and no projection of fragments of appreciable size or range is to be expected. An external fire shall not cause virtually instantaneous explosion of almost the entire contents of the package;
 - (e) Division 1.5 Very insensitive substances or mixtures which have a mass explosion hazard:

⁹ These criteria are established via the ADR, “**European Agreement Concerning the International Carriage of Dangerous Goods by Road**” 2007, which is the legislation applicable to transport of dangerous goods in the European Community and in internationally in all countries that are signatories to the ADR. The ADR is enacted under the auspices of the United Nations Economic Commission for Europe http://www.unece.org/trans/danger/publi/adr/adr_e.html. Further information on the criteria and on the test methods to be applied can be obtained from the ADR and/or the UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria

- Substances and mixtures which have a mass explosion hazard but are so insensitive that there is very little probability of initiation or of transition from burning to detonation under normal conditions.

Table 1
Tests necessary to apply the criteria for explosives

Category	Criteria
Unstable explosives or explosives of Division 1.1 to 1.6	<p>For explosives of Divisions 1.1 to 1.5, the following are the core set of tests that need to be performed:</p> <p>Explosibility: according to UN Test Series 2 (section 12 of the <i>UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria</i>). Intentional explosives¹⁰ shall not be subject to UN Test Series 2.</p> <p>Sensitiveness: according to UN Test Series 3 (section 13 of the <i>UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria</i>).</p> <p>Thermostability: according to UN Test 3(c) (Sub-section 13.6.1 of the <i>UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria</i>).</p> <p>Further tests are necessary to allocate the correct Division.</p>

2. **Flammable gas.** A substance shall **not** meet the criteria for classification as a flammable gas, Category 1 or Category 2, laid out in Table 2 below,

Table 2
Criteria for flammable gases

Category	Criteria
1	<p>Gases, which at 20°C and a standard pressure of 101.3 kPa:</p> <p>(a) are ignitable when in a mixture of 13% or less by volume in air; or</p> <p>(b) have a flammable range with air of at least 12 percentage points regardless of the lower flammable limit.</p>
2	<p>Gases, other than those of Category 1, which, at 20°C and a standard pressure of 101.3 kPa, have a flammable range while mixed in air.</p>

Note 1:

Ammonia and methyl bromide are regarded as flammable gases (special cases).

3. **Flammable liquid.** A substance shall **not** meet the criteria for a flammable liquid, Category 1, Category 2, Category 3 or Category 4, laid out in Table 3 below.

¹⁰ This comprises substances, mixtures and articles which are manufactured with a view to producing a practical, explosive or pyrotechnic effect.

Table 3
Criteria for flammable liquids

Category	Criteria
1	Flash point < 23°C and initial boiling point ≤ 35°C
2	Flash point < 23°C and initial boiling point > 35°C
3	Flash point ≥ 23°C and ≤ 60°C ¹¹
4	Flash point > 60 °C and ≤ 93 °C

4. **Flammable solid.** A substance shall **not** meet the criteria for a Category 1 or Category 2 flammable solid, laid out in Table 4 below.

Table 4
Criteria for flammable solids

Category	Criteria
1	Burning rate test Substances other than metal powders: (a) wetted zone does not stop fire and (b) burning time < 45 seconds or burning rate > 2.2 mm/s <i>Metal powders</i> burning time ≤ 5 minutes
2	Burning rate test Substances other than metal powders: (a) wetted zone stops the fire for at least 4 minutes and (b) burning time < 45 seconds or burning rate > 2.2 mm/s <i>Metal powders</i> burning time > 5 minutes and ≤ 10 minutes

5. **Oxidising gas.** A substance shall **not** meet the criteria for a Category 1 oxidising gas, laid out in Table 5 below.

Table 5
Criteria for oxidising gases

Category	Criteria
1	Any gas which may, generally by providing oxygen, cause or contribute to the combustion of other material more than air does.

¹¹ Gas oils, diesel and light heating oils in the flash point range of 55°C to 75°C may be regarded as Category 3 for transport.

6. **Oxidising liquid.** A substance shall **not** meet the criteria for a Category 1, Category 2 or Category 3 oxidising liquid, laid out in Table 6 below.

Table 6
Criteria for oxidising liquids

Category	Criteria
1	Any substance or mixture which, in the 1:1 mixture, by mass, of substance and cellulose tested, spontaneously ignites; or the mean pressure rise time of a 1:1 mixture, by mass, of substance and cellulose is less than that of a 1:1 mixture, by mass, of 50% perchloric acid and cellulose
2	Any substance or mixture which, in the 1:1 mixture, by mass, of substance and cellulose tested, exhibits a mean pressure rise time less than or equal to the mean pressure rise time of a 1:1 mixture, by mass, of 40% aqueous sodium chlorate solution and cellulose; and the criteria for Category 1 are not met
3	Any substance or mixture which, in the 1:1 mixture, by mass, of substance and cellulose tested, exhibits a mean pressure rise time less than or equal to the mean pressure rise time of a 1:1 mixture, by mass, of 65% aqueous nitric acid and cellulose; and the criteria for Category 1 and 2 are not met

7. **Oxidising solid.** A substance shall **not** meet the criteria for a Category 1, Category 2 or Category 3 oxidising solid, laid out in Table 7 below.

Table 7
Criteria for oxidising solids

Category	Criteria
1	Any substance or mixture which, in the 4:1 or 1:1 sample-to-cellulose ratio (by mass) tested, exhibits a mean burning time less than the mean burning time of a 3:2 mixture, by mass, of potassium bromate and cellulose.
2	Any substance or mixture which, in the 4:1 or 1:1 sample-to-cellulose ratio (by mass) tested, exhibits a mean burning time equal to or less than the mean burning time of a 2:3 mixture (by mass) of potassium bromate and cellulose and the criteria for Category 1 are not met.
3	Any substance or mixture which, in the 4:1 or 1:1 sample-to-cellulose ratio (by mass) tested, exhibits a mean burning time equal to or less than the mean burning time of a 3:7 mixture (by mass) of potassium bromate and cellulose and the criteria for Categories 1 and 2 are not met.

8. **Corrosive to metals.** A substance shall **not** meet the criteria for corrosive to metals, Category 1, laid out in Table 8 below.

Table 8
Criteria for substances corrosive to metals

Category	Criteria
1	Corrosion rate on steel or aluminium surfaces exceeding 6.25 mm per year at a test temperature of 55 °C.

9. **Self-reactive substance.** A substance shall **not** meet the criteria for a self-reactive substance, Types A to F, according to the criteria laid out in Table 9.

Table 9
Criteria for self-reactive substances

<p>(a) Any self-reactive substance which can detonate or deflagrate rapidly, as packaged, shall be defined as self-reactive substance TYPE A;</p> <p>(b) Any self-reactive substance possessing explosive properties and which, as packaged, neither detonates nor deflagrates rapidly, but is liable to undergo a thermal explosion in that package shall be defined as self-reactive substance TYPE B;</p> <p>(c) Any self-reactive substance possessing explosive properties when the substance or mixture as packaged cannot detonate or deflagrate rapidly or undergo a thermal explosion shall be defined as self-reactive substance TYPE C;</p> <p>(d) Any self-reactive substance which in laboratory testing:</p> <ul style="list-style-type: none">(i) detonates partially, does not deflagrate rapidly and shows no violent effect when heated under confinement; or(ii) does not detonate at all, deflagrates slowly and shows no violent effect when heated under confinement; or(iii) does not detonate or deflagrate at all and shows a medium effect when heated under confinement; <p>shall be defined as self-reactive substance TYPE D;</p> <p>(e) Any self-reactive substance which, in laboratory testing, neither detonates nor deflagrates at all and shows low or no effect when heated under confinement shall be defined as self-reactive substance TYPE E;</p> <p>(f) Any self-reactive substance which, in laboratory testing, neither detonates in the cavitated state nor deflagrates at all and shows only a low or no effect when heated under confinement as well as low or no explosive power shall be defined as self-reactive substance TYPE F;</p>

10. Pyrophoric liquid. A substance shall **not** meet the criteria for pyrophoric liquid, Category 1, laid out in Table 10 below.

Table 10
Criteria for pyrophoric liquids

Category	Criteria
1	The liquid ignites within 5 min when added to an inert carrier and exposed to air, or it ignites or chars a filter paper on contact with air within 5 min.

11. Pyrophoric solid, A substance shall **not** meet the criteria for pyrophoric solid, Category 1, laid out in Table 11 below.

Table 11
Criteria for pyrophoric solids

Category	Criteria
1	The solid ignites within 5 minutes of coming into contact with air.

12. Self-heating substance. A substance shall **not** meet the criteria for a self-heating substance, Category 1 or Category 2, laid out in Table 12 below.

Table 2.11.1
Criteria for self-heating substances and mixtures

Category	Criteria
1	A positive result is obtained in a test using a 25 mm sample cube at 140°C
2	<p>(a) It does not meet the criteria for Category 1; and a positive result is obtained in a test using a 100 mm sample cube at 140°C; Exemptions from (a) for classification in Category 2</p> <p>(i) a negative result is obtained in a test using a 100 mm cube sample at 100°C <u>and</u> the unit volume of the substance is 450 litres or less;</p> <p>(ii) a negative result is obtained in a test using a 100 mm cube sample at 120°C <u>and</u> the unit volume of the substance is 3 m³ or less;</p> <p>(b) It does not meet the criteria for Category 1; and a positive result is obtained in a test using a 100 mm sample cube at 140°C; and it is not a substances exempted under (a), that gives a positive result in a test using a 100 mm cube sample at 100°C;</p>

13. Substance which in contact with water emits flammable gas. A substance shall **not** meet the criteria for a substance which in contact with water emits flammable gas, Category 1 Category 2 or Category 3, laid out in Table 13 below.

Table 13
Criteria for substances or mixtures which in contact with water emit flammable gases

Category	Criteria
1	Any substance or mixture which reacts vigorously with water at ambient temperatures and demonstrates generally a tendency for the gas produced to ignite spontaneously, or which reacts readily with water at ambient temperatures such that the rate of evolution of flammable gas is equal to or greater than 10 litres per kilogram of substance over any one minute.
2	Any substance or mixture which reacts readily with water at ambient temperatures such that the maximum rate of evolution of flammable gas is equal to or greater than 20 litres per kilogram of substance per hour, and which does not meet the criteria for Category 1.
3	Any substance or mixture which reacts slowly with water at ambient temperatures such that the maximum rate of evolution of flammable gas is equal to or greater than 1 litre per kilogram of substance per hour, and which does not meet the criteria for Categories 1 and 2.

14. **Organic peroxide.** A substance shall **not** meet the criteria for an organic peroxide of Types A to F, laid out in Table 14 below.

Table 14
Criteria for organic peroxides

<p>(a) Any organic peroxide which, as packaged, can detonate or deflagrate rapidly shall be defined as organic peroxide TYPE A;</p> <p>(b) Any organic peroxide possessing explosive properties and which, as packaged, neither detonates nor deflagrates rapidly, but is liable to undergo a thermal explosion in that package shall be defined as organic peroxide TYPE B;</p> <p>(c) Any organic peroxide possessing explosive properties when the substance or mixture as packaged cannot detonate or deflagrate rapidly or undergo a thermal explosion shall be defined as organic peroxide TYPE C;</p>

- (d) Any organic peroxide which in laboratory testing:
 - (i) Detonates partially, does not deflagrate rapidly and shows no violent effect when heated under confinement; or
 - (ii) Does not detonate at all, deflagrates slowly and shows no violent effect when heated under confinement; or
 - (iii) Does not detonate or deflagrate at all and shows a medium effect when heated under confinement;

shall be defined as **organic peroxide TYPE D**;

- (e) Any organic peroxide which, in laboratory testing, neither detonates nor deflagrates at all and shows low or no effect when heated under confinement shall be defined as **organic peroxide TYPE E**;
- (f) Any organic peroxide which, in laboratory testing, neither detonates in the cavitated state nor deflagrates at all and shows only a low or no effect when heated under confinement as well as low or no explosive power shall be defined as **organic peroxide TYPE F**;

APPENDIX IB

Criteria¹² for identification of mild skin and eye irritants, based on the results of in vivo testing

- Mild skin irritant:** A mean value of ≥ 1.5 - < 2.3 has been obtained for erythema/eschar or for oedema from gradings in at least 2 of 3 tested animals from grades at 24, 48 and 72 hours or, if reactions are delayed, from grades on 3 consecutive days after the onset of skin reactions, and the substance has not been classified as a skin irritant based on the criteria laid down in Annex VI of Directive 67/548/EEC.
- Mild eye irritant:** the substance meets the criteria laid down in Annex VI of Directive 67/548/EEC for classification as an eye irritant, namely produces at least in 2 of 3 tested animals a positive response of:
- corneal opacity ≥ 1 and/or
 - iritis ≥ 1 , and/or
 - conjunctival redness ≥ 2 , and/or
 - conjunctival oedema (chemosis) ≥ 2
- calculated as the mean scores following grading at 24, 48 and 72 hours after installation of the test material,
- BUT**
- which fully reverses within an observation period of 7 days

¹² These criteria reflect the criteria established for mild skin irritants (category 3) Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (http://www.unece.org/trans/danger/publi/ghs/ghs_rev00/00files_e.html)

APPENDIX 2

Format of Dossier

The dossier shall be completed by the applicant seeking the addition of a substance to Annex IV, or by applicants advocating for a deletion of a substance from the existing Annex IV.

Table 1 shall contain a clear identification of the substance in accordance with the substance identifiers described in Annex VI, section 2.

Table 2 shall contain the applicant's conclusions (descriptive and numerical) on minimum risk based on the intrinsic properties of the substance, which shall be summarised for the main end-points.

Table 3 shall contain a clear identification of substances for which data have been used in accordance with the rules for grouping or read-across approach (set out in Annex XI, section 1.5).

Table 4 shall contain an overview of the information submitted by the applicant, including a confirmation that the information requirements in section 3 of the criteria document have been met, confirmation of compliance with the endpoint-specific criteria, values for each endpoint, and indications of adaptations according to column 2 of Annexes VII-X and Annex XI section 1 and 2, if appropriate.

More detailed information shall be provided in Annexes A-C of the submission (see below).

The dossier shall include robust study summaries in Annex A of the submission.

A description and justification shall be included in Annex B of the submission, if the specific rules for adaptation of the standard information requirements (column 2 in Annexes VII-X) have been applied.

A description and justification shall be included in Annex C of the submission, if the general rules for adaptation of the standard testing regime set out in Annexes VII-X have been applied (in accordance with Annex XI, sections 1 and 2).

Table 1 Substance identification (according to Annex VI, section 2)

2.1. Name or other identifier of each substance	
2.1.1. Name(s) in the IUPAC nomenclature or other international chemical name(s)	
2.1.2. Other names (usual name, trade name,	

<p>abbreviation)</p> <p>2.1.3. EINECS or ELINCS number (if available and appropriate)</p> <p>2.1.4. CAS name and CAS number (if available)</p> <p>2.1.5. Other identity code (if available)</p>	
<p>2.2. Information related to molecular and structural formula of each substance</p>	
<p>2.2.1. Molecular and structural formula (including SMILES notation, if available)</p> <p>2.2.2 Information on optical activity (if applicable and appropriate)</p> <p>2.2.3. Molecular weight or molecular weight range</p>	
<p>2.3. Composition of each substance</p>	
<p>2.3.1. Degree of purity (%)</p> <p>2.3.2. Nature of impurities, including isomers and by-products</p> <p>2.3.3. Percentage of (significant) main impurities</p> <p>2.3.4. Nature and order of magnitude (.....ppm,%) of any additives (e.g. stabilising agents or inhibitors)</p> <p>2.3.5. Spectral data (ultra-violet, infra-red, nuclear magnetic resonance or mass spectrum)</p> <p>2.3.6. High-pressure liquid chromatogram, gas chromatogram</p> <p>2.3.7. Description of the analytical methods or the appropriate bibliographical references for the identification of the substance and, where appropriate, for the identification of impurities and additives. This information shall be sufficient to allow the methods to be reproduced.</p>	

Conclusion on minimum risk:

The table shall be completed by the applicant. For each of the endpoints listed below, conclusions on minimum risk based on the intrinsic properties of the substance shall be provided (descriptive text relating the appropriate data to the criterion for the endpoints). The results of relevant robust study summaries attached at Annex A shall also be summarised.

Table 2 Conclusion on minimum risk

Ref. No.	Properties	Summary
	Physicochemical properties	
	Explosive properties	
	Flammability	
	Oxidising properties	
	Corrosive to metals	
	Self-reactive substance	
	Pyrophoric properties;	
	Self-heating substance	
	Substance which in contact with water emits flammable gas	
	Organic peroxides	
	Toxicological information	

8.1	Skin irritation	
8.2	Eye irritation	
8.3	Skin sensitisation	
8.4	Mutagenicity	
8.5	Acute toxicity	
8.6	Repeated dose toxicity	
8.7	Reproductive toxicity	
8.8	Carcinogenicity	
8.9	Toxicokinetics	
Ecotoxicological information		
9.1	Aquatic toxicity	
9.2	Degradation	
9.3	Fate and behaviour in the environment	

Please also complete the following:

	YES	NO
Is the substance, due to its intrinsic properties, fulfilling the criteria for PBT and/or vPvB, or is it listed in the PBT working group list?		
Is the substance identified or suspected to have		

endocrine disrupting properties?		
Is the substance listed in Annex II or Annex III of the Cosmetic Directive 76/768/EEC?		
Is the substance listed in Annex I of EC 2037/2000?		

Table of information:

This table shall be completed by the applicant.

Table 4 Overview of information in the submission

Annex	Ref	End Points	Information as required in section 3 of the criteria document have been submitted	Compliance with criteria confirmed	Value of endpoints	Adaptation according to column 2 of Annexes VII-X applied	Adaptation according to Annex XI sections 1 and 2 applied
			Yes/No or NA according to column 2 Annex VII-X or Annex XI	Yes/No/NA* * not appropriate	Unit has to be given for each individual endpoint	Yes/No Justification is to be annexed as separate documentation	Yes/No Justification is to be annexed as separate documentation
		Physicochemical properties					
VII	7.1	State of the substance					
VII	7.3	Boiling point					
VII	7.5	Vapour pressure					
VII	7.7	Water solubility					
VII	7.8	Partition coefficient n-octanol/water					
VII	7.9	Flash point					
VII	7.10	Flammability					
VII	7.11	Explosive properties					

Annex	Ref	End Points	Information as required in section 3 of the criteria document have been submitted	Compliance with criteria confirmed	Value of endpoints	Adaptation according to column 2 of Annexes VII-X applied	Adaptation according to Annex XI sections 1 and 2 applied
VII	7.12	Self-ignition temperature					
VII	7.13	Oxidising properties					
VII	7.14	Granulometry					
IX	7.17	Viscosity					
		Toxicological information					
VII	8.1	Skin irritation					
VIII	8.1.1	In vivo skin irritation					
VII	8.2	Eye irritation					
VIII	8.2.1	In vivo eye irritation					
VII	8.3	Skin sensitisation					
VII	8.4	Mutagenicity					
VII	8.4.1	In vitro gene mutation in bacteria					
VIII	8.4.2	In vitro cytogenicity study in mammalian cells or in vitro micronucleus study					
VIII	8.4.3	In vitro gene mutation study in mammalian cells					
VII	8.5	Acute toxicity					
VII	8.5.1	By oral route					
VIII	8.5.2	By inhalation					
VIII	8.5.3	By dermal route					
VIII	8.6	Repeated dose toxicity					
VIII	8.6.1	Short-term repeated dose toxicity study (28 days)					
IX	8.6.2	Sub-chronic toxicity study (90					

Annex	Ref	End Points	Information as required in section 3 of the criteria document have been submitted	Compliance with criteria confirmed	Value of endpoints	Adaptation according to column 2 of Annexes VII-X applied	Adaptation according to Annex XI sections 1 and 2 applied
		day)					
VIII	8.7	Reproductive toxicity					
VIII	8.7.1	Screening for reproductive/developmental toxicity					
IX	8.7.2	Pre-natal development toxicity study					
IX	8.7.3	Two-generation reproductive toxicity study					
X	8.7.2	Developmental toxicity study (if available)					
X	8.7.3	Two-generation reproductive toxicity study (if available)					
X	8.9.1	Carcinogenicity study (if available)					
VIII	8.8	Toxicokinetics					
VIII	8.8.1	Assessment of the toxicokinetic behaviour of the substance to the extent that can be derived from relevant available information					
		Ecotoxicological information					
VII	9.1	Aquatic toxicity					
VII	9.1.1	Short term toxicity testing on invertebrates (<i>Daphnia</i>)					

Annex	Ref	End Points	Information as required in section 3 of the criteria document have been submitted	Compliance with criteria confirmed	Value of endpoints	Adaptation according to column 2 of Annexes VII-X applied	Adaptation according to Annex XI sections 1 and 2 applied
VII	9.1.2	Growth inhibition study aquatic plants (algae)					
VIII	9.1.3	Short term toxicity testing on fish					
VIII	9.1.4	Activated sludge respiration inhibition test					
IX	9.1.5	Long term toxicity testing on invertebrates (<i>Daphnia</i>)					
IX	9.1.6	Long term toxicity testing on fish					
IX	9.1.6.1	Fish early-life stage (FELS) toxicity test					
IX	9.1.6.2	Fish short-term toxicity test on embryo and sac-fry stages					
IX	9.1.6.3	Fish, juvenile growth test					
VII	9.2	Degradation					
VII	9.2.1	Biotic					
VII	9.2.1.1	Ready biodegradability					
IX	9.2.1.2	Simulation testing on ultimate degradation in surface water					
IX	9.2.1.3	Soil simulation testing					
IX	9.2.1.4	Sediment simulation testing					
VIII	9.2.2	Abiotic					
VIII	9.2.2.1	Hydrolysis as a function of pH					
IX	9.2.3	Identification of degradation products					
VIII	9.3	Fate and behaviour in the					

Annex	Ref	End Points	Information as required in section 3 of the criteria document have been submitted	Compliance with criteria confirmed	Value of endpoints	Adaptation according to column 2 of Annexes VII-X applied	Adaptation according to Annex XI sections 1 and 2 applied
		environment					
VIII	9.3.1	Adsorption/desorption screening					
IX	9.3.2	Bioaccumulation in aquatic species, preferable fish					
IX	9.3.3	Further information on adsorption/desorption					
X	9.3.4	Further information on the environmental fate and behaviour of the substance and/or the degradation products (if available)					
IX	9.4	Effects on terrestrial organisms					
IX	9.4.1	Short-term toxicity in invertebrates					
IX	9.4.2	Effects on soil micro-organisms					
IX	9.4.3	Short-term toxicity to plants					
X	9.4.4	Long-term toxicity testing on invertebrates (if available)					
X	9.4.6	Long-term toxicity testing on plants (if available)					
X	9.5.1	Long-term toxicity to sediment organisms (if available)					
X	9.6.1	Long-term or reproductive toxicity to birds (if available)					

Annex A Robust study summaries

Robust study summaries shall be included in Annex A and shall be clearly marked with the substance name and the reference number of the relevant section in Annexes VII-X.

Annex B Adaptation according to column 2 of Annex VII-X

A description and justification shall be included in Annex B, if the specific rules for adaptation of the standard information requirements (column 2 in Annexes VII-X) have been applied. The description shall clearly indicate the substance name and the reference number(s) for the information requirements in Annexes VII-X, where adaptations have been applied.

Annex C Adaptation according to Annex XI Section 1 or 2

A description and justification shall be included in Annex C, if the general rules for adaptation of the standard testing regime set out in Annexes VII-X have been applied (in accordance with Annex XI, sections 1 and 2). The description shall clearly indicate the substance name and the reference number(s) for the information requirements in Annexes VII-X, where adaptations have been applied.