ANNEX II

INFORMATION REQUIREMENTS FOR ACTIVE SUBSTANCES

1. This Annex sets out the information requirements for the preparation of the dossier referred to in point (a) of Article 6(1).

2. The data elements set down in this Annex comprise a Core Data Set (CDS) and an Additional Data Set (ADS). The data elements belonging to the CDS are considered as the basic data which should, in principle, be provided for all active substances. However, in some cases the physical or chemical properties of the substance may mean that it is impossible or unnecessary to provide specific data elements belonging to the CDS.

With regard to the ADS, the data elements to be provided for a specific active substance shall be determined by considering each of the ADS data elements indicated in this Annex taking into account, inter alia, the physical and chemical properties of the substance, existing data, information which is part of the CDS and the types of products in which the active substance will be used and the exposure patterns related to these uses.

Specific indications for the inclusion of some data elements are provided in column 1 of the Annex II table. The general considerations regarding adaptation of information requirements as set out in Annex IV shall also apply. In light of the importance of reducing testing on vertebrates, column 3 of the Annex II table gives specific indications for the adaptation of some of the data elements which might require the use of such tests on vertebrates. The information submitted shall, in any case, be sufficient to support a risk assessment demonstrating that the criteria referred to in Article 4(1) are met.

The applicant should consult the detailed technical guidance regarding the application of this Annex and the preparation of the dossier referred to in point (a) of Article 6(1), which is available on the website of the Agency.

The applicant has the obligation to initiate a pre-submission consultation. In addition to the obligation set down in Article 62(2), applicants may also consult with the competent authority that will evaluate the dossier with regard to the proposed information requirements and in particular the testing on vertebrates that the applicant proposes to carry out.

Additional information may need to be submitted if it is necessary to carry out the evaluation as indicated in Article 8(2).

3. A detailed and full description of the studies conducted or referred to and of the methods used shall be included. It is important to ensure that the data available is relevant and is of sufficient quality to fulfil the requirements. Evidence should also be provided to demonstrate that the active substance upon which the tests have been carried out is the same as the substance for which the application has been submitted.

4. The formats made available by the Agency must be used for submission of the dossiers. In addition, IUCLID must be used for those parts of the dossiers to which IUCLID applies. Formats and further guidance on data requirements and dossier preparation are available on the website of the Agency.

5. Tests submitted for the purpose of the approval of an active substance shall be conducted according to the methods described in Commission Regulation (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)[(1)]. However, if a

method is inappropriate or not described, other methods shall be used which are scientifically appropriate, whenever possible internationally recognised, and their appropriateness must be justified in the application. When test methods are applied to nanomaterials, an explanation shall be provided of their scientific appropriateness for nanomaterials, and where applicable, of the technical adaptations/adjustments that have been made in order to respond to the specific characteristics of these materials.

6. Tests performed should comply with the relevant requirements of protection of laboratory animals, set out in Directive 2010/63/EU of the European Parliament and the Council of 22 September 2010 on the protection of animals used for scientific purposes[(2)] and in the case of ecotoxicological and toxicological tests, good laboratory practice, set out in Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their application for tests on chemical substances[(3)] or other international standards recognised as being equivalent by the Commission or the Agency. Tests on physico-chemical properties and safety-relevant substance data should be performed at least according to international standards.

7. Where testing is done, a detailed description (specification) of the active substance used and its impurities must be provided. Testing should be performed with the active substance as manufactured or, in the case of some of the physical and chemical properties (see indications given in column I of the table), with a purified form of the active substance.

8. Where test data exist that have been generated before 1 September 2013 by methods other than those laid down in Regulation (EC) No 440/2008, the adequacy of such data for the purposes of this Regulation and the need to conduct new tests according to the Regulation (EC) No 440/2008 must be decided by the competent authority of the Member State concerned, on a case-by-case basis, taking into account, among other factors, the need to minimise testing on vertebrates.

9. New tests involving vertebrates shall be conducted as the last available option to comply with the data requirements set out in this Annex when all the other data sources have been exhausted. In-vivo testing with corrosive substances at concentration/dose levels causing corrosivity shall also be avoided.

TITLE 1

CHEMICAL SUBSTANCES

Core data set and additional data set for active substances

Information required to support the approval of an active substance is listed in the table below.

Conditions for not requiring a specific test that are set out in the appropriate test methods in the Regulation (EC) No 440/2008 and are not repeated in column 3, also apply.

Column 1Information required	**Column 2All data is CDS unless indicated as ADS**	**Column 3Specific rules for adaptation from standard information concerning some of the information requirements that may require recourse to testing of vertebrates**
1. APPLICANT		
1.1. Name and address		
1.2. Contact person		
1.3. Active substance manufacturer (name, address and location of manufacturing plant(s))		
2. IDENTITY OF THE ACTIVE SUBSTANCE		
For the active substance, the information given in this Section shall be sufficient to enable the active substance to be identified. If it is not technically possible or if it does not appear scientifically necessary to give information on one or more of the items below, the reasons shall be clearly stated		
2.1. Common name proposed or accepted by ISO and synonyms (usual name, trade name, abbreviation)		
2.2. Chemical name (IUPAC and CA nomenclature or		

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b The information provided should be for the purified active substance of stated specification.

c OJ L 20, 26.1.1980, p. 43.

d OJ L 372, 27.12.2006, p. 19.

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	other international chemical name(s))		
2.3.	Manufacturer's development code number(s)		
2.4.	CAS number plus EC, INDEX and CIPAC numbers		
2.5.	Molecular and structural formula (including SMILES notation, if available and appropriate)		
2.6.	Information on optical activity and full details of any isomeric composition (if applicable and appropriate)		
2.7.	Molar mass		
2.8.	Method of manufacture (syntheses pathway) of active substance including information on starting materials and solvents including suppliers, specifications and commercial availability		
2.9.	Specification of purity of the active substance as		

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	manufactured in g/kg, g/l or %w/w (v/v) as appropriate, providing inclusively the upper and lower limit		
2.10.	The identity of any impurities and additives including by-products of synthesis, optical isomers, degradation products (if the substance is unstable) un-reacted and end-groups etc. of polymers and un-reacted starting materials of UVC-substances		
2.11.	Analytical profile of at least five representative batches (g/kg active substance) including information on content of the impurities referred to in 2.10.		
2.12.	The origin of the natural active substance or the precursor(s) of the active substance, e.g. an extract of a flower		

3. PHYSICAL AND CHEMICAL

a	The information provided should be for the purified active substance of stated specification or for the active substance as manufactured, if different.
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PROPERTIES OF THE ACTIVE SUBSTANCE

3.1. Appearance[a]

3.1.1.	Aggregate state (at 20 °C and 101,3 kPa)		
3.1.2.	Physical state (i.e. viscous, crystalline, powder) (at 20 °C and 101,3 kPa)		
3.1.3.	Colour (at 20 °C and 101,3 kPa)		
3.1.4.	Odour (at 20 °C and 101,3 kPa)		
3.2.	Melting/freezing point[b]		
3.3.	Acidity, alkalinity		
3.4.	Boiling point[b]		
3.5.	Relative Density[b]		
3.6.	Absorption spectra data (UV/VIS, IR, NMR) and a mass spectrum, molar extinction coefficient at relevant wavelengths, where relevant[b]		

3.7. Vapour pressure[b]

3.7.1.	Henry's law constant must always be stated for		

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	solids and liquids if it can be calculated		
3.8.	Surface tension[b]		
3.9.	Water solubility[b]		
3.10.	Partition coefficient (n-octanol/ water) and its pH dependency[b]		
3.11.	Thermal stability, identity of breakdown products[b]		
3.12.	Reactivity towards container material		
3.13.	Dissociation constant	ADS	
3.14.	Granulometry		
3.15.	Viscosity	ADS	
3.16.	Solubility in organic solvents, including effect of temperature on solubility[b]	ADS	
3.17.	Stability in organic solvents used in biocidal products and identity of relevant breakdown products[a]	ADS	

4. PHYSICAL HAZARDS AND RESPECTIVE CHARACTERISTICS

a	The information provided should be for the purified active substance of stated specification or for the active substance as manufactured, if different.
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4.1.	Explosives		
4.2.	Flammable gases		
4.3.	Flammable aerosols		
4.4.	Oxidising gases		
4.5.	Gases under pressure		
4.6.	Flammable liquids		
4.7.	Flammable solids		
4.8.	Self-reactive substances and mixtures		
4.9.	Pyrophoric liquids		
4.10.	Pyrophoric solids		
4.11.	Self-heating substances and mixtures		
4.12.	Substances and mixtures which in contact with water emit flammable gases		
4.13.	Oxidising liquids		
4.14.	Oxidising solids		
4.15.	Organic peroxides		
4.16.	Corrosive to metals		

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4.17. Additional physical indicators for hazards		
4.17.1. Auto-ignition temperature (liquids and gases)		
4.17.2. Relative self ignition temperature for solids		
4.17.3. Dust explosion hazard		
5. METHODS OF DETECTION AND IDENTIFICATION		
5.1. Analytical methods including validation parameters for the determination of active substance as manufactured and where appropriate, for relevant residues, isomers and impurities of the active substance and additives (e.g. stabilisers) For impurities other than relevant impurities this only applies if they are present at ≥ 1 g/kg		
5.2. Analytical methods for monitoring purposes including recovery rates and the limits of quantification and detection for the active substance, and for residues thereof in/on the following where relevant		

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5.2.1.	Soil		
5.2.2.	Air		
5.2.3.	Water (surface, drinking etc.) and sediment		
5.2.4.	Animal and human body fluids and tissues		
5.3.	Analytical methods for monitoring purposes including recovery rates and the limit of quantification and detection for the active substance, and for residues thereof, in/on food of plant and animal origin or feeding stuffs and other products where relevant (not necessary if neither the active substance nor articles treated with it come into contact with food-producing animals, food of plant or animal origin or feeding stuffs)	ADS	
6. EFFECTIVENESS AGAINST TARGET ORGANISMS			
6.1.	Function, e.g. fungicide, rodenticide,		

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	insecticide, bactericide and mode of control e.g. attracting, killing, inhibiting		
6.2.	Representative organism(s) to be controlled and products, organisms or objects to be protected		
6.3.	Effects on representative target organism(s)		
6.4.	Likely concentration at which the active substance will be used in products and, where appropriate, in treated articles		
6.5.	Mode of action (including time delay)		
6.6.	Efficacy data to support these claims on biocidal products and, where label claims are made, on treated articles, including any available standard protocols, laboratory tests or field trials used including performance		

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	standards where appropriate		
6.7. Any known limitations on efficacy			
6.7.1.	Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies		
6.7.2.	Observations on undesirable or unintended side-effects, e.g. on beneficial and other non-target organisms		
7. INTENDED USES AND EXPOSURE			
7.1.	Field of use(s) envisaged for biocidal products and, where appropriate, treated articles		
7.2.	Product-type(s)		
7.3.	Detailed description of the intended use pattern(s) including in treated articles		
7.4.	Users e.g. industrial, trained professional, professional or general public (non-professional)		

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7.5.	Likely tonnage to be placed on the market per year and, where relevant, for the envisaged major use categories		
7.6. Exposure data in conformity with Annex VI to this Regulation			
7.6.1.	Information on human exposure associated with the intended uses and disposal of the active substance		
7.6.2.	Information on environmental exposure associated with the intended uses and disposal of the active substance		
7.6.3.	Information on exposure of food-producing animals and food and feeding stuffs associated with the intended uses of the active substance		
7.6.4.	Information on exposure from treated articles including leaching data (either laboratory studies or model data)		
8. TOXICOLOGICAL PROFILE FOR			

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HUMAN AND ANIMAL INCLUDING METABOLISM		
8.1. Skin irritation or skin corrosion The assessment of this endpoint shall be carried out according to the sequential testing strategy for dermal irritation and corrosion set out in the Appendix to Test Guideline B.4. Acute Toxicity-Dermal Irritation/ Corrosion (Annex B.4. to Regulation (EC) No 440/2008)		
8.2. Eye irritation The assessment of this endpoint shall be carried out according to the sequential testing strategy for eye irritation and corrosion as set down in the Appendix to Test Guideline B.5.Acute Toxicity: Eye Irritation/ Corrosion (Annex B.5. to Regulation (EC) No 440/2008)		
8.3. Skin sensitisation The assessment of this endpoint shall comprise the following consecutive steps: 1. an assessment of the available human, animal and alternative data 2. in vivo testing The Murine Local Lymph Node Assay (LLNA) including, where appropriate, the reduced variant		Step 2 does not need to be conducted if: — the available information indicates that the substance should be classified for skin sensitisation or corrosivity, or — the substance is a strong acid (pH < 2,0) or base (pH > 11,5)

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	of the assay, is the first-choice method for in vivo testing. If another skin sensitisation test is used justification shall be provided		
8.4.	Respiratory sensitisation	ADS	
8.5. Mutagenicity			
The assessment of this endpoint shall comprise the following consecutive steps: — an assessment of the available in vivo genotoxicity data — an in vitro test for gene mutations in bacteria, an in vitro cytogenicity test in mammalian cells and an in vitro gene mutation test in mammalian cells are required — appropriate in vivo genotoxicity studies shall be considered in case of a positive result in any of the in vitro genotoxicity studies			
8.5.1.	In vitro gene mutation study in bacteria		
8.5.2.	In vitro cytogenicity study in mammalian cells		

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8.5.3. In vitro gene mutation study in mammalian cells		
8.6. In vivo genotoxicity study The assessment of this endpoint shall comprise the following consecutive steps: — If there is a positive result in any of the in vitro genotoxicity studies and there are no results available from an in vivo study already, an appropriate in vivo somatic cell genotoxicity study shall be proposed/ conducted by the applicant — If either of the in vitro gene mutation tests is positive, an in vivo test to investigate unscheduled DNA synthesis shall be conducted — A second in vivo somatic cell test may be necessary, depending on the results, quality and relevance of all the available data — If there is a positive result from an in vivo somatic cell study available, the potential for germ cell mutagenicity should	ADS	The study/ies do(es) not generally need to be conducted if: — the results are negative for the three in vitro tests and if no metabolites of concern are formed in mammals or — valid in vivo micronucleus data is generated within a repeat dose study and the in vivo micronucleus test is the appropriate test to be conducted to address this information requirement — the substance is known to be carcinogenic category 1A or 1B or mutagenic category 1A, 1B or 2.

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be considered on the basis of all available data, including toxicokinetic evidence to demonstrate that the substance reached the tested organ. If no clear conclusions about germ cell mutagenicity can be made, additional investigations shall be considered		
8.7. Acute toxicity In addition to the oral route of administration (8.7.1), for substances other than gases, the information mentioned under 8.7.2 to 8.7.3 shall be provided for at least one other route of administration — The choice for the second route will depend on the nature of the substance and the likely route of human exposure — Gases and volatile liquids should be administered by the inhalation route — If the only route of exposure is the oral route, then information for only that route need be provided. If either the dermal or inhalation route is the only route of exposure to		The study/ies do(es) not generally need to be conducted if: — the substance is classified as corrosive to the skin

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humans then an oral test may be considered. Before a new dermal acute toxicity study is carried out, an in vitro dermal penetration study (OECD 428) should be conducted to assess the likely magnitude and rate of dermal bioavailability — There may be exceptional circumstances where all routes of administration are deemed necessary		
8.7.1. By oral route The Acute Toxic Class Method is the preferred method for the determination of this endpoint		The study need not be conducted if: — the substance is a gas or a highly volatile substance
8.7.2. By inhalation Testing by the inhalation route is appropriate if exposure of humans via inhalation is likely taking into account: — the vapour pressure of the substance (a volatile substance has vapour pressure > 1×10^{-2} Pa at 20 °C) and/or — the active substance is a powder containing a significant proportion (e.g. 1 % on a weight		

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basis) of particles with particle size MMAD < 50 micrometers or — the active substance is included in products that are powders or are applied in a manner that generates exposure to aerosols, particles or droplets of an inhalable size (MMAD < 50 micrometers) — the Acute Toxic Class Method is the preferred method for the determination of this endpoint		
8.7.3. By dermal route Testing by the dermal route is necessary only if: — inhalation of the substance is unlikely, or — skin contact in production and/or use is likely, and either — the physicochemical and toxicological properties suggest potential for a significant rate of absorption through the skin, or — the results of an in vitro dermal penetration study (OECD 428) demonstrate high		

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dermal absorption and bioavailability		
8.8. Toxicokinetics and metabolism studies in mammals		
The toxicokinetics and metabolism studies should provide basic data about the rate and extent of absorption, the tissue distribution and the relevant metabolic pathway including the degree of metabolism, the routes and rate of excretion and the relevant metabolites		
8.8.1. Further toxicokinetic and metabolism studies in mammals Additional studies might be required based on the outcome of the toxicokinetic and metabolism study conducted in rat. These further studies shall be required if: — there is evidence that metabolism in the rat is not relevant for human exposure — route-to-route extrapolation from oral to dermal/ inhalation exposure is not feasible Where it is considered appropriate to obtain information on dermal absorption, the assessment of this endpoint shall proceed using a tiered approach	ADS	

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for assessment of dermal absorption		
8.9. Repeated dose toxicity In general, only one route of administration is necessary and the oral route is the preferred route. However, in some cases it may be necessary to evaluate more than one route of exposure. For the evaluation of the safety of consumers in relation to active substances that may end up in food or feed, it is necessary to conduct toxicity studies by the oral route Testing by the dermal route shall be considered if: — skin contact in production and/or use is likely, and — inhalation of the substance is unlikely, and — one of the following conditions is met: (i) toxicity is observed in an acute dermal toxicity test at lower doses than in the oral toxicity test, or (ii) information or test data indicate dermal		The repeated dose toxicity study (28 or 90 days) does not need to be conducted if: — a substance undergoes immediate disintegration and there are sufficient data on the cleavage products for systemic and local effects and no synergistic effects are expected, or — relevant human exposure can be excluded in accordance with Section 3 of Annex IV In order to reduce testing carried out on vertebrates and in particular the need for free-standing single-endpoint studies, the design of the repeated dose toxicity studies shall take account of the possibility to explore several endpoints within the framework of one study

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absorption is comparable or higher than oral absorption, or (iii) dermal toxicity is recognised for structurally related substances and for example is observed at lower doses than in the oral toxicity test or dermal absorption is comparable or higher than oral absorption Testing by the inhalation route shall be considered if: — exposure of humans via inhalation is likely taking into account the vapour pressure of the substance (volatile substances and gases have vapour pressure > 1×10^{-2} Pa at 20 °C), and/or — there is the possibility of exposure to aerosols, particles		

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	or droplets of an inhalable size (MMAD < 50 micrometers)		
8.9.1.	Short-term repeated dose toxicity study (28 days), preferred species is rat		The short-term toxicity study (28 days) does not need to be conducted if: (i) a reliable sub-chronic (90 day) study is available, provided that the most appropriate species, dosage, solvent and route of administration were used, (ii) the frequency and duration of human exposure indicates that a longer term study is appropriate and one of the following conditions is met: — other available data indicate that the substance may have a dangerous property that cannot be detected in a short-term toxicity study, or — appropriately designed toxicokinetic studies

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			reveal accumulation of the substance or its metabolites in certain tissues or organs which would possibly remain undetected in a short term toxicity study but which are liable to result in adverse effects after prolonged exposure
8.9.2.	Sub-chronic repeated dose toxicity study (90 days), preferred species is rat		The sub-chronic toxicity study (90 days) does not need to be conducted if: — a reliable short-term toxicity study (28 days) is available showing severe toxicity effects according to the criteria for classifying the substance as H372 and H373 (Regulation (EC) No 1272/2008), for which the observed NOAEL-28 days, with the application of an appropriate

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			uncertainty factor allows the extrapolation towards the NOAEL-90 days for the same route of exposure, and — a reliable chronic toxicity study is available, provided that an appropriate species and route of administration were used, or — the substance is unreactive, insoluble, not bioaccumulative and not inhalable and there is no evidence of absorption and no evidence of toxicity in a 28-day 'limit test', particularly if such a pattern is coupled with limited human exposure
8.9.3.	Long-term repeated dose toxicity (≥ 12 months)		The long-term toxicity study (≥ 12 months) does not need to be conducted if: — Long-term exposure can be excluded and no effects have been seen at the limit dose in the 90-day study or — a combined long-term repeated dose/ carcinogenicity study (8.11.1) is undertaken

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e	OJ L 348, 24.12.2008, p. 84.

8.9.4. Further repeat dose studies Further repeat dose studies including testing on a second species (non-rodent), studies of longer duration or through a different route of administration shall be undertaken in case of: — no other information on toxicity for a second non-rodent species is provided for, or — failure to identify a no observed adverse effect level (NOAEL) in the 28- or the 90-day study, unless the reason is that no effects have been observed at the limit dose, or — substances bearing positive structural alerts for effects for which the rat or mouse is an inappropriate or insensitive model, or — toxicity of particular concern (e.g. serious/severe effects), or — indications of an effect for which the available data is inadequate for toxicological and/or risk characterisation. In such cases it may also be more appropriate to	ADS	

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c	OJ L 20, 26.1.1980, p. 43.
d	OJ L 372, 27.12.2006, p. 19.
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	perform specific toxicological studies that are designed to investigate these effects (e.g. immunotoxicity, neurotoxicity, hormonal activity), or — concern regarding local effects for which a risk characterisation cannot be performed by route-to route extrapolation, or — particular concern regarding exposure (e.g. use in biocidal products leading to exposure levels which are close to the toxicologically relevant dose levels), or — effects shown in substances with a clear relationship in molecular structure with the substance being studied were not detected in the 28- or the 90-day study, or — the route of administration used in the initial repeated dose study was inappropriate in relation to the expected route of human exposure and route-to-route		

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extrapolation cannot be made.		
8.10. Reproductive toxicity For evaluation of consumer safety of active substances that may end up in food or feed, it is necessary to conduct toxicity studies by the oral route		The studies need not be conducted if: — the substance is known to be a genotoxic carcinogen and appropriate risk management measures are implemented including measures related to reproductive toxicity, or — the substance is known to be a germ cell mutagen and appropriate risk management measures are implemented including measures related to reproductive toxicity, or — the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available provided that the dataset is sufficiently comprehensive and informative), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood

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		concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and the pattern of use indicates there is no or no significant human exposure — If a substance is known to have an adverse effect on fertility, meeting the criteria for classification as Reproductive toxicity Cat 1A or 1B: May damage fertility (H360F), and the available data are adequate to support a robust risk assessment, then no further testing for fertility will be necessary. However, testing for developmental toxicity must be considered — If a substance is known to cause developmental toxicity, meeting the criteria for classification as Reproductive toxicity Cat 1A or 1B: May damage the unborn child (H360D), and

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		the available data are adequate to support a robust risk assessment, then no further testing for developmental toxicity will be necessary. However, testing for effects on fertility must be considered
8.10.1. Pre-natal developmental toxicity study, preferred species is rabbit; oral route of administration is the preferred route. The study shall be initially performed on one species		
8.10.2. Two-generation reproductive toxicity study, rat, oral route of administration is the preferred route. If another reproductive toxicity test is used justification shall be provided. The extended one-generation reproductive toxicity study adopted at OECD level shall be considered as an alternative approach to the multi-generation study		
8.10.3. Further pre-natal developmental toxicity study. A decision on the need to perform additional studies	ADS	

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on a second species or mechanistic studies should be based on the outcome of the first test (8.10.1) and all other relevant available data (in particular rodent reprotox studies). Preferred species is rat, oral route of administration		
8.11. Carcinogenicity See 8.11.1 for new study requirements		A carcinogenicity study does not need to be conducted if: — the substance is classified as mutagen category 1A or 1B. The default presumption would be that a genotoxic mechanism for carcinogenicity is likely. In these cases, a carcinogenicity test will normally not be required
8.11.1. Combined carcinogenicity study and long-term repeated dose toxicity Rat, oral route of administration is the preferred route. If an alternative route is proposed a justification must be provided. For evaluation of consumer safety of active substances that may end up in food or feed, it is necessary to		

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conduct toxicity studies by the oral route		
8.11.2. Carcinogenicity testing in a second species — A second carcinogenicity study should normally be conducted using the mouse as test species — For evaluation of consumer safety of active substances that may end up in food or feed, it is necessary to conduct toxicity studies by the oral route		
8.12. Relevant health data, observations and treatments		
Justification should be provided if data is not available		
8.12.1. Medical surveillance data on manufacturing plant personnel		
8.12.2. Direct observation, e.g. clinical cases, poisoning incidents		
8.12.3. Health records, both from industry and any other available sources		

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8.12.4. Epidemiological studies on the general population		
8.12.5. Diagnosis of poisoning including specific signs of poisoning and clinical tests		
8.12.6. Sensitisation/ allergenicity observations		
8.12.7. Specific treatment in case of an accident or poisoning: first aid measures, antidotes and medical treatment, if known		
8.12.8. Prognosis following poisoning		
8.13. Additional studies Additional data which may be required depending on the characteristics and intended use of the active substance Other available data: Available data from emerging methods and models, including toxicity pathway-based risk assessment, in vitro and 'omic' (genomic, proteomic, metabolomic, etc.) studies, systems biology, computational toxicology, bioinformatics, and high-throughput screening shall be submitted in parallel	ADS	

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8.13.1. Phototoxicity	ADS	
8.13.2. Neurotoxicity including developmental neurotoxicity — The preferred test species is the rat unless another test species is justified to be more appropriate — For delayed neurotoxicity tests the preferred species will be the adult hen — If anticholinesterase activity is detected a test for response to reactivating agents should be considered If the active substance is an organophosphorus compound or if there is any evidence e.g. knowledge of the mechanism of action or from repeat dose studies that the active substance may have neurotoxic or developmental neurotoxic properties then additional information or specific studies will be required. For evaluation of consumer safety of active substances that may end up in food or feed, it is necessary to conduct toxicity studies by the oral route	ADS	
8.13.3. Endocrine disruption	ADS	

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If there is any evidence from in vitro, repeat dose or reproduction toxicity studies, that the active substance may have endocrine disrupting properties then additional information or specific studies shall be required to: — elucidate the mode/ mechanism of action — provide sufficient evidence for relevant adverse effects For evaluation of consumer safety of active substances that may end up in food or feed, it is necessary to conduct toxicity studies by the oral route		
8.13.4. Immunotoxicity including developmental immunotoxicity If there is any evidence, from skin sensitisation, repeat dose or reproduction toxicity studies, that the active substance may have immunotoxic properties then additional information or specific studies shall be required to: — elucidate the mode/ mechanism of action — provide sufficient evidence for relevant adverse effects in humans For evaluation of consumer safety of active substances that may end up in food	ADS	

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or feed, it is necessary to conduct toxicity studies by the oral route		
8.13.5. Mechanistic data — any studies necessary to clarify effects reported in toxicity studies	ADS	
8.14. Studies related to the exposure of humans to the active substance	ADS	
8.15. Toxic effects on livestock and pets	ADS	
8.16. Food and feeding stuffs studies including for food-producing animals and their products (milk, eggs and honey) Additional information related to the exposure of humans to the active substance contained in biocidal products	ADS	
8.16.1. Proposed acceptable residue levels i.e. maximum residue limits (MRL) and the justification of their acceptability	ADS	
8.16.2. Behaviour of the residue of the active substance on the treated or contaminated food or feeding	ADS	

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stuffs including the kinetics of disappearance Residue definitions should be provided where relevant. It is also important to compare residues found in toxicity studies with residues formed in food-producing animals and their products, as well as food and feed		
8.16.3. Overall material balance for the active substance Sufficient residue data from supervised trials on food-producing animals and their products, as well as food and feed, to demonstrate that residues likely to arise from the proposed use would not be of concern for human or animal health	ADS	
8.16.4. Estimation of potential or actual exposure of humans to the active substance and residues through diet and other means	ADS	
8.16.5. If residues of the active substance occur in or on feeding stuffs for a significant period of time or are found in food of animal origin after treatment on or around food-producing	ADS	

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animals (e.g. direct treatment on animals or indirect treatment of animal houses or surroundings) then feeding and metabolism studies in livestock shall be required to permit evaluation of residues in food of animal origin		
8.16.6. Effects of industrial processing and/ or domestic preparation on the nature and magnitude of residues of the active substance	ADS	
8.16.7. Any other available information that is relevant It may be appropriate to include information on migration into food, especially in the case of treatment of food contact materials	ADS	
8.16.8. Summary and evaluation of data submitted under 8.16.1 to 8.16.8 It is important to establish whether the metabolites found in food (from animals or plants) are the same as those tested in toxicity studies. Otherwise values for risk assessment (e.g. ADI)	ADS	

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are not valid for the residues found		
8.17. If the active substance is to be used in products for action against plants including algae then tests shall be required to assess toxic effects of metabolites from treated plants, if any, where different from those identified in animals	ADS	
8.18. Summary of mammalian toxicology Provide overall evaluation and conclusion with regard to all toxicological data and any other information concerning the active substances including NOAEL		
9. ECOTOXICOLOGICAL STUDIES		
9.1. Toxicity to Aquatic Organisms		
9.1.1. Short-term toxicity testing on fish When short-term fish toxicity data is required the threshold approach (tiered strategy) should be applied		The study does not need to be conducted if: — a valid long-term aquatic toxicity study on fish is available
9.1.2. Short-term toxicity testing on aquatic invertebrates		
9.1.2.1. Daphnia magna		

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9.1.2.2. Other species	ADS	
9.1.3. Growth inhibition study on algae		
9.1.3.1. Effects on growth rate of green algae		
9.1.3.2. Effects on growth rate of cyanobacteria or diatoms		
9.1.4. Bioconcentration 9.1.4.1. Estimation methods 9.1.4.2. Experimental determination		The experimental determination may not need to be carried out if: — it can be demonstrated on the basis of physico-chemical properties (e.g. log Kow < 3) or other evidence that the substance has a low potential for bioconcentration
9.1.5. Inhibition of microbial activity The study may be replaced by a nitrification inhibition test if available data show that the substance is likely to be an inhibitor of microbial growth or function, in particular nitrifying bacteria		
9.1.6. Further Toxicity Studies on Aquatic Organisms If the results of the ecotoxicological studies, studies on fate and behaviour and/or the intended use(s) of the active substance indicate a risk for the aquatic	ADS	

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environment, or if long-term exposure is expected, then one or more of the tests described in this Section shall be conducted		
9.1.6.1. Long term toxicity testing on Fish (a) Fish Early Life Stage (FELS) Test (b) Fish short term toxicity test on embryo and sack fry stages (c) Fish juvenile growth test (d) Fish full life cycle test	ADS	
9.1.6.2. Long term toxicity testing on invertebrates (a) Daphnia growth and reproduction study (b) Other species reproduction and growth (e.g. Mysid) (c) Other species development and emergence (e.g. Chironomus)	ADS	
9.1.7. Bioaccumulation in an appropriate aquatic species	ADS	
9.1.8. Effects on any other specific, non-target organisms (flora and fauna) believed to be at risk	ADS	

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9.1.9.	Studies on sediment- dwelling organisms	ADS	
9.1.10.	Effects on aquatic macrophytes	ADS	
9.2.	Terrestrial toxicity, initial tests	ADS	
9.2.1.	Effects on soil micro-organisms		
9.2.2.	Effects on earthworms or other soil- dwelling non-target invertebrates		
9.2.3.	Acute toxicity to plants		
9.3.	Terrestrial tests, long term	ADS	
9.3.1.	Reproduction study with earthworms or other soil-dwelling non-target invertebrates		
9.4.	Effects on birds	ADS	For endpoint 9.4.3 the study does not need to be conducted if: — the dietary toxicity study shows that the LC_{50} is above 2 000 mg/kg
9.4.1.	Acute oral toxicity		
9.4.2.	Short-term toxicity — eight-day dietary study in at least one species (other than chickens, ducks and geese)		

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9.4.3.	Effects on reproduction		
9.5.	Effects on arthropods	ADS	
9.5.1.	Effects on honeybees		
9.5.2.	Other non-target terrestrial arthropods, e.g. predators		
9.6.	Bioconcentration, terrestrial	ADS	
9.7.	Bioaccumulation, terrestrial	ADS	
9.8.	Effects on other non-target, non-aquatic organisms	ADS	
9.9.	Effects on mammals	ADS	Data are derived from the mammalian toxicological assessment. The most sensitive relevant mammalian long-term toxicological endpoint (NOAEL) expressed as mg test compound/kg bw/ day shall be reported
9.9.1.	Acute oral toxicity		
9.9.2.	Short term toxicity		
9.9.3.	Long term toxicity		
9.9.4.	Effects on reproduction		
9.10.	Identification of endocrine activity	ADS	
10. ENVIRONMENTAL FATE AND BEHAVIOUR			
10.1. Fate and behaviour in water and sediment			

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10.1.1. Degradation, initial studies		
If the assessment performed indicates the need to investigate further the degradation of the substance and its degradation products or the active substance has an overall low or absent abiotic degradation, then the tests described in 10.1.3 and 10.3.2 and where appropriate — in 10.4 shall be required. The choice of the appropriate test(s) depends on the results of the initial assessment performed		
10.1.1.1. Abiotic		
(a) Hydrolysis as a function of pH and identification of breakdown products — The identification of breakdown products is required when the breakdown products at any sampling time are present at ≥ 10 %		
(b) Phototransformation in water, including identification of transformation products		
10.1.1.2. Biotic		
(a) Ready biodegradability		

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(b)	Inherent biodegradability (where appropriate)		
10.1.2.	Adsorption/ desorption		
10.1.3. Rate and route of degradation including identification of metabolites and degradation products			
10.1.3.1.	Biological sewage treatment		
(a)	Aerobic biodegradation	ADS	
(b)	Anaerobic biodegradation	ADS	
(c)	STP simulation test	ADS	
10.1.3.2.	Biodegradation in freshwater		
(a)	Aerobic aquatic degradation study	ADS	
(b)	Water/sediment degradation test	ADS	
10.1.3.3.	Biodegradation in sea water	ADS	
10.1.3.4.	Biodegradation during manure storage	ADS	
10.1.4.	Adsorption and desorption in water/ aquatic sediment	ADS	

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	systems and, where relevant, adsorption and desorption of metabolites and degradation products		
10.1.5.	Field study on accumulation in sediment	ADS	
10.1.6.	Inorganic substances: information on fate and behaviour in water	ADS	
10.2.	Fate and behaviour in soil	ADS	
10.2.1.	Laboratory study on rate and route of degradation including identification of the processes involved and identification of any metabolites and degradation products in one soil type (unless pH dependent route) under appropriate conditions Laboratory studies on rate of degradation in three additional soil types	ADS	
10.2.2.	Field studies, two soil types	ADS	
10.2.3.	Soil accumulation studies	ADS	

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10.2.4. Adsorption and desorption in at least three soil types and, where relevant, adsorption and desorption of metabolites and degradation products	ADS	
10.2.5. Further studies on sorption		
10.2.6. Mobility in at least three soil types and where relevant mobility of metabolites and degradation products	ADS	
10.2.6.1. Column leaching studies		
10.2.6.2. Lysimeter studies		
10.2.6.3. Field leaching studies		
10.2.7. Extent and nature of bound residues The determination and characteristics of bound residues is recommended to be combined with a soil simulation study	ADS	
10.2.8. Other soil degradation studies	ADS	
10.2.9. Inorganic substances: information on fate		

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and behaviour in soil		
10.3. Fate and behaviour in air		
10.3.1. Phototransformation in air (estimation method) Identification of transformation products		
10.3.2. Fate and behaviour in air, further studies	ADS	
10.4. Additional studies on fate and behaviour in the environment	ADS	
10.5. Definition of the residue	ADS	
10.5.1. Definition of the residue for risk assessment		
10.5.2. Definition of the residue for monitoring		
10.6. Monitoring data	ADS	
10.6.1. Identification of all degradation products (> 10 %) must be included in the studies on degradation in soil, water and sediments		
11. MEASURES NECESSARY TO PROTECT HUMANS,		

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ANIMALS AND THE ENVIRONMENT

11.1.	Recommended methods and precautions concerning handling, use, storage, transport or fire		
11.2.	In case of fire, nature of reaction products, combustion gases etc.		
11.3.	Emergency measures in case of accident		
11.4.	Possibility of destruction or decontamination following release in or on the following:		
(a)	air		
(b)	water, including drinking water		
(c)	soil		
11.5.	Procedures for waste management of the active substance for industry or professional users		
11.6.	Possibility of reuse or recycling		
11.7.	Possibility of neutralisation of effects		

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11.8.	Conditions for controlled discharge including leachate qualities on disposal		
11.9.	Conditions for controlled incineration		
11.10.	Identification of any substances falling within the scope of List I or List II of the Annex to Council Directive 80/68/EEC of 17 December 1979 on the protection of groundwater against pollution caused by certain dangerous substances[c], of Annexes I and II to Directive 2006/118/EC of the European Parliament and of the Council of 12 December 2006 on the protection of groundwater against pollution and deterioration[d], of Annex I to Directive 2008/105/EC of the European Parliament and of the Council of 16 December 2008 on environmental quality standards in the field of water policy[e], of Part B of Annex I to Directive 98/83/EC		

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	or Annexes VIII and X to Directive 2000/60/EC		
12. CLASSIFICATION, LABELLING AND PACKAGING			
12.1.	State any existing classification and labelling		
12.2. The hazard classification of the substance resulting from the application of Regulation (EC) No 1272/2008			
In addition, for each entry, the reasons why no classification is given for an endpoint should be provided			
12.2.1.	Hazard classification		
12.2.2.	Hazard pictogram		
12.2.3.	Signal word		
12.2.4.	Hazard statements		
12.2.5.	Precautionary statements including prevention, response, storage and disposal		
12.3.	Specific concentration limits, where applicable, resulting from the application		

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of Regulation (EC) No 1272/2008		
13. SUMMARY AND EVALUATION The key information identified from the endpoints in each subsection (2-12) is summarised, evaluated and a draft risk assessment is performed		

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TITLE 2

MICRO-ORGANISMS

Core data set and additional data set for active substances

Information required to support the approval of an active substance is listed in the table below.

Conditions for not requiring a specific test that are set out in the appropriate test methods in Regulation (EC) No 440/2008 that are not repeated in column 3, also apply.

Column 1Information required	**Column 2All data is CDS unless indicated as ADS**	**Column 3Specific rules for adaptation from standard information concerning some of the information requirements that may require recourse to testing of vertebrates**
1. APPLICANT		
1.1. Name and address		
1.2. Contact person		
1.3. Manufacturer (name, address and location of manufacturing plant)		
2. IDENTITY OF THE MICRO-ORGANISM		

2.1.	Common name of the micro-organism (including alternative and superseded names)		
2.2.	Taxonomic name and strain		
2.3.	Collection and culture reference number where the culture is deposited		
2.4.	Methods, procedures and criteria used to establish the presence and identity of the micro-organism		
2.5.	Specification of the technical grade active ingredient		
2.6.	Method of production and quality control		
2.7.	Content of the micro-organism		
2.8.	Identity and content of impurities, additives, contaminating micro-organisms		
2.9.	Analytical profile of batches		
3. BIOLOGICAL PROPERTIES OF THE MICRO-ORGANISM			
3.1. General information on the micro-organism			
3.1.1.	Historical background		

3.1.2.	Historical uses		
3.1.3.	Origin, natural occurrence and geographical distribution		
3.2.	Development stages/life cycle of the micro-organism		
3.3.	Relationships to known plant or animal or human pathogens		
3.4.	Genetic stability and factors affecting it		
3.5.	Information on the production of metabolites (especially toxins)		
3.6.	Production and resistance to antibiotics and other anti-microbial agents		
3.7.	Robustness to environmental factors		
3.8.	Further information on the micro-organism		
4. METHODS OF DETECTION AND IDENTIFICATION			
4.1.	Analytical methods for the analysis of the micro-organism as manufactured		
4.2.	Methods used for monitoring purposes to		

	determine and quantify residues (viable or non-viable)		
5. EFFECTIVENESS AGAINST TARGET ORGANISM			
5.1.	Function and mode of control e.g. attracting, killing, inhibiting		
5.2.	Infectiveness, dispersal and colonisation ability		
5.3.	Representative organism(s) controlled and products, organisms or objects to be protected		
5.4.	Effects on representative target organism(s) Effects on materials, substances and products		
5.5.	Likely concentration at which the micro-organism will be used		
5.6.	Mode of action (including time delay)		
5.7.	Efficacy data		
5.8. Any known limitations on efficacy			
5.8.1.	Information on the occurrence or possible occurrence of the development of resistance of the target organism(s) and appropriate		

	management strategies		
5.8.2.	Observations on undesirable or unintended side effects		
5.8.3.	Host specificity, range and effects on species other than the target organism		
5.9.	Methods to prevent loss of virulence of seed stock of the micro-organism		
6. INTENDED USES AND EXPOSURE			
6.1.	Field of use(s) envisaged		
6.2.	Product-type(s)		
6.3.	Detailed description of the use pattern(s)		
6.4.	Category of users for which the micro-organism should be approved		
6.5. Exposure data applying, as appropriate, the methodologies described in Section 5 of Annex I to Regulation (EC) No 1907/2006			
6.5.1.	Information on human exposure associated with the intended uses and disposal of the active substance		
6.5.2.	Information on environmental exposure associated with the intended		

	uses and disposal of the active substance		
6.5.3.	Information on exposure of food-producing animals and food and feeding stuffs associated with the intended uses of the active substance		
7.	EFFECT ON HUMAN AND ANIMAL HEALTH		Information requirements in this Section may be adapted as appropriate in accordance with the specifications of Title 1 of this Annex.
7.1. Basic information			
7.1.1.	Medical data		
7.1.2.	Medical surveillance on manufacturing plant personnel		
7.1.3.	Sensitisation/ allergenicity observations		
7.1.4.	Direct observation, e.g. clinical cases Any pathogenicity and infectiveness to humans and other mammals under conditions of immunosuppression		
7.2. Basic studies			
7.2.1.	Sensitisation		
7.2.2. Acute toxicity, pathogenicity, and infectiveness			
7.2.2.1.	Acute oral toxicity, pathogenicity and infectiveness		
7.2.2.2.	Acute inhalatory toxicity,	ADS	

	pathogenicity and infectiveness		
7.2.2.3.	Intraperitoneal/ subcutaneous single dose	ADS	
7.2.3.	In vitro genotoxicity testing		
7.2.4.	Cell culture study		
7.2.5.	Information on short-term toxicity and pathogenicity	ADS	
7.2.5.1.	Health effects after repeated inhalatory exposure	ADS	
7.2.6.	Proposed treatment: first aid measures, medical treatment		
7.3.	Specific toxicity, pathogenicity and infectiveness studies	ADS	
7.4.	Genotoxicity — in vivo studies in somatic cells	ADS	
7.5.	Genotoxicity — in vivo studies in germ cells	ADS	
7.6.	Summary of mammalian toxicity, pathogenicity and infectiveness and overall evaluation		
7.7.	Residues in or on treated articles, food and feedingstuffs	ADS	
7.7.1.	Persistence and likelihood of	ADS	

	multiplication in or on treated articles, feedingstuffs or foodstuffs		
7.7.2.	Further information required	ADS	
7.7.2.1.	Non-viable residues	ADS	
7.7.2.2.	Viable residues	ADS	
7.8.	Summary and evaluation of residues in or on treated articles, food and feedingstuffs	ADS	
8.	EFFECTS ON NON-TARGET ORGANISMS		Information requirements in this Section may be adapted as appropriate in accordance with the specifications of Title 1 of this Annex.
8.1. Effects on aquatic organisms			
8.1.1.	Effects on fish		
8.1.2.	Effects on freshwater invertebrates		
8.1.3.	Effects on algae growth		
8.1.4.	Effects on plants other than algae	ADS	
8.2.	Effects on earthworms		
8.3.	Effects on soil micro-organisms		
8.4.	Effects on birds		
8.5.	Effects on bees		

8.6.	Effects on arthropods other than bees		
8.7.	Further studies	ADS	
8.7.1.	Terrestrial plants	ADS	
8.7.2.	Mammals	ADS	
8.7.3.	Other relevant species and processes	ADS	
8.8.	Summary and evaluation of effects on non-target organisms		
9. ENVIRONMENTAL FATE AND BEHAVIOUR			
9.1. Persistence and multiplication			
9.1.1.	Soil		
9.1.2.	Water		
9.1.3.	Air		
9.1.4.	Mobility		
9.1.5.	Summary and evaluation of fate and behaviour in the environment		
10. MEASURES NECESSARY TO PROTECT HUMANS, ANIMALS AND THE ENVIRONMENT			
10.1.	Recommended methods and precautions concerning handling, storage, transport or fire		

10.2.	Emergency measures in case of an accident		
10.3.	Procedures for destruction or decontamination		
10.4.	Procedures for waste management		
10.5.	Monitoring plan to be used for the active micro-organism including handling, storage, transport and use		
11. CLASSIFICATION, LABELLING AND PACKAGING OF THE MICRO-ORGANISM			
11.1.	Relevant risk group specified in Article 2 of Directive 2000/54/EC		
12.	SUMMARY AND EVALUATION The key information identified from the endpoints in each subsection (2-12) is summarised, evaluated and a draft risk assessment is performed		

(**1**) OJ L 142, 31.5.2008, p. 1.

(**2**) OJ L 276, 20.10.2010, p. 33.

(**3**) OJ L 50, 20.2.2004, p. 44.

Status:
Point in time view as at 31/01/2020.

Changes to legislation:
There are outstanding changes not yet made to Regulation (EU) No 528/2012 of the European Parliament and of the Council. Any changes that have already been made to the legislation appear in the content and are referenced with annotations.