ANNEX

INTRODUCTION**Information to be submitted, its generation and its presentation**

1. The information submitted shall meet the following requirements.

1.1. The information shall be sufficient to evaluate the foreseeable risks, whether immediate or delayed, which the active substance may entail for humans, including vulnerable groups, animals and the environment and contain at least the information and results of the studies referred to in this Annex.

1.2. Any information on potentially harmful effects of the active substance, its metabolites and impurities on human and animal health or on groundwater shall be included.

1.3. Any information on potentially unacceptable effects of the active substance, its metabolites and impurities on the environment, on plants and plant products shall be included.

1.4. The information shall include all relevant data from the scientific peer reviewed open literature on the active substance, metabolites and breakdown or reaction products and plant protection products containing the active substance and dealing with side-effects on health, the environment and non-target species. A summary of this data shall be provided.

1.5. The information shall include a full and unbiased report of the studies conducted as well as a full description of them. Such information shall not be required, where one of the following conditions is fulfilled:

(a) it is not necessary owing to the nature of the product or its proposed uses, or it is not scientifically necessary;

(b) it is technically not possible to supply.

In such a case a justification shall be provided.

1.6. The simultaneous use of the active substance as a biocide or in veterinary medicine shall be reported.

If the applicant for the active substance in the plant protection product is identical to the one responsible for the notification of the active substance as a biocide or as a veterinary medicine, a summary of all relevant data submitted for approval of the biocide or the veterinary medicine, shall be submitted. This summary shall include toxicological reference values and MRL proposals, taking into account any possible cumulative exposure due to different uses of the same substance based on scientific methods accepted by the European competent authorities, together with a summary of the residues and toxicology data and information on the use of the product.

If the applicant for the active substance in the plant protection product is not identical to the one responsible for the notification of the active substance as a biocide or in veterinary medicine, a summary of all available data shall be submitted.

1.7. Where relevant, the information shall be generated using test methods, which are included in the list referred to in point 6. In the absence of suitable internationally or nationally validated test guidelines, test guidelines accepted by the European competent authority shall be used. Any deviations shall be described and justified.

1.8. The information shall include a full description of the test methods used.

1.9. The information shall include a list of endpoints for the active substance.

1.10. Where relevant, the information shall be generated in accordance with Directive 2010/63/EU of the European Parliament and of the Council[(1)].

1.11. The information on the active substance, taken together with the information concerning one or more plant protection products containing the active substance and together, if appropriate, with the information concerning safeners and synergists and other components of the plant protection product, shall be sufficient to:

(a) permit an assessment of the risks for humans, associated with handling and use of plant protection products containing the active substance;

(b) permit an assessment of the risks for human and animal health, arising from residues of the active substance and its metabolites, impurities, breakdown and reaction products remaining in water, air, food and feed;

(c) predict the distribution, fate and behaviour in the environment of the active substance and metabolites, breakdown and reaction products, where they are of toxicological or environmental significance, as well as the time courses involved;

(d) permit an assessment of the impact on non-target species (flora and fauna), including the impact on their behaviour, which are likely to be exposed to the active substance, its metabolites, breakdown and reaction products, where they are of toxicological or environmental significance. Impact can result from single, prolonged or repeated exposure and can be direct or indirect, reversible or irreversible;

(e) evaluate the impact on biodiversity and the ecosystem;

(f) identify non-target species and populations for which hazards arise because of potential exposure;

(g) permit an evaluation of short and long-term risks for non-target species, populations, communities and processes;

(h) classify the active substance as to hazard in accordance with Regulation (EC) No 1272/2008 of the European Parliament and of the Council[(2)];

(i) specify the pictograms, the signal words, and relevant hazard and precautionary statements for the protection of man, non-target species and the environment, which are to be used for labelling purposes;

(j) establish, where relevant, an acceptable daily intake (ADI) level for humans;

(k) establish acceptable operator exposure levels (AOEL);

(l) establish, where relevant, an acute reference dose, (ARfD) for humans;

(m) identify relevant first aid measures as well as appropriate diagnostic and therapeutic measures to be followed in the event of poisoning in humans;

(n) establish the isomeric composition and the possible metabolic conversion of the isomers, when relevant;

(o) establish residues definitions appropriate for risk assessment;

(p) establish residues definitions appropriate for monitoring and enforcement purposes;

(q) permit a risk assessment of consumer exposure, including, where relevant, a cumulative risk assessment deriving from exposure to more than one active substance;

(r) permit an estimation of the exposure to operators, workers, residents and bystanders including, where relevant, the cumulative exposure to more than one active substance;

(s) establish maximum residue levels and concentration/dilution factors in accordance with Regulation (EC) No 396/2005 of the European Parliament and of the Council[(3)];

(t) permit an evaluation to be made as to the nature and extent of the risks for man, animals (species normally fed and kept by humans or food producing animals) and of the risks for other non-target vertebrate species;

(u) identify measures necessary to minimise contamination of the environment and impact on non-target species;

(v) decide whether or not the active substance has to be considered as persistent organic pollutant (POP), persistent, bio accumulative and toxic (PBT) or very persistent and very bio accumulative (vPvB) in accordance with the criteria laid down in Annex II to Regulation (EC) No 1107/2009;

(w) decide whether or not the active substance has to be considered as a candidate for substitution in accordance with the criteria laid down in Annex II to Regulation (EC) No 1107/2009;

(x) decide whether or not the active substance has to be considered as a low-risk active substance in accordance with the criteria laid down in Annex II to Regulation (EC) No 1107/2009;

(y) decide whether, or not, the active substance is to be approved;

(z) specify conditions or restrictions to be associated with any approval.

1.12. Where relevant, tests shall be designed and data analysed using appropriate statistical methods.

1.13. Exposure calculations shall refer to scientific methods accepted by the European Food Safety Authority, (the Authority), when available. Additional methods, when used, shall be justified.

1.14. For each section of the data requirements, a summary of all data, information and evaluation made shall be submitted. This shall include a detailed and critical assessment according to the provisions of Article 4 of Regulation (EC) No 1107/2009.

2. The requirements set out in this Regulation shall represent the minimum data to be submitted. Additional requirements at national level may be necessary in specific circumstances, that is to say specific scenarios, patterns of use other than those taken into account for approval. Careful attention shall be given to environmental, climatic and agronomic conditions when tests are set up and approved by the competent authorities.

3. **Good laboratory practice (GLP)**

3.1. Tests and analyses shall be conducted in accordance with the principles laid down in Directive 2004/10/EC of the European Parliament and of the Council[(4)] where testing is done to obtain data on the properties or safety with respect to human or animal health or the environment.

3.2. By way of derogation from point 3.1:

3.2.1. For active substances consisting of micro-organisms or viruses, tests and analyses done to obtain data on the properties and safety with respect to other aspects than human health, may be conducted by official or officially recognised testing facilities or organisations which satisfy at least the requirements under points 3.2 and 3.3 of the introduction of the Annex to Commission Regulation (EU) No 284/2013[(5)].

3.2.2. For tests and analyses made to obtain data for minor crops required under points 6.3 and 6.5.2 of Part A:

— the field phase may have been conducted by official or officially recognised testing facilities or organisations which satisfy at least the requirements as laid down in points 3.2 and 3.3 of the introduction of the Annex to Regulation (EU) No 284/2013;

— the analytical phase, if not done in accordance with the GLP requirements, shall be conducted by laboratories accredited for the relevant method in accordance with the European standard EN ISO/IEC 17025 'General requirements for the competence of testing and calibration laboratories'.

3.2.3. Studies conducted before the application of this Regulation, although not fully compliant with GLP requirements or with current test methods, may be integrated into the assessment, when accepted by the competent authorities as scientifically valid, thereby removing the need for repeating animal tests, especially for carcinogenicity and reprotoxicity studies. This derogation applies to studies on all vertebrate species.

4. **Test material**

4.1. A detailed description (specification) of the material used shall be provided. Where tests are done using the active substance, the material used shall comply with the specification that will be used in the manufacture of plant protection products to be authorised, except where radio-labelled material or the purified active substance is used.

4.2. Where studies are conducted using an active substance produced in the laboratory or in a pilot plant production system, the studies shall be repeated using the active substance as manufactured, unless the applicant shows that the test material used is essentially the same, for the purposes of toxicological, ecotoxicological, environmental and residue testing and assessment. In cases of uncertainty, bridging studies shall be submitted to serve as a basis for a decision as to the possible need for repetition of the studies.

4.3. Where studies are conducted using an active substance of different purity or which contains different impurities or different levels of impurities to the technical specification or where the active substance is a mixture of components, the significance of the differences shall be addressed either by data or scientific case. In cases of uncertainty, appropriate studies using the active substance as manufactured for commercial production shall be submitted to serve as a basis for a decision.

4.4. In the case of studies in which dosing extends over a period (for example repeated dose studies), dosing shall be done using a single batch of active substance if stability permits. Whenever a study implies the use of different doses, the relationship between dose and adverse effect shall be reported.

4.5. When tests shall be conducted using purified active substance (≥ 980 g/kg) of stated specification, the purity of such test material shall be as high as can be achieved using the best available technology and shall be reported. A justification shall be provided in

cases where the degree of purity achieved is less than 980 g/kg. Such justification shall demonstrate that all technically feasible and reasonable possibilities for the production of the purified active substance have been exhausted.

4.6. Where radio-labelled test material is used, radio-labels shall be positioned at sites (one or more as necessary), to facilitate elucidation of metabolic and transformation pathways and to facilitate investigation of the distribution of the active substance and of its metabolites, reaction and breakdown products.

5. **Tests on vertebrate animals**

5.1. Tests on vertebrate animals shall be undertaken only where no other validated methods are available. Alternative methods to be considered shall include *in vitro* methods and *in silico* methods. Reduction and refinement methods for *in vivo* testing shall also be encouraged to keep the number of animals used in testing to a minimum.

5.2. The principles of replacement, reduction and refinement of the use of animals shall be taken into account in the design of the test methods, in particular when appropriate validated methods become available to replace, reduce or refine animal testing.

5.3. Tests involving the deliberate administration of the active substance or the plant protection product to humans and non-human primates shall not be performed for the purpose of this Regulation.

5.4. For ethical reasons, study designs shall be carefully considered, taking into account the scope for reduction, refinement and replacement of animal tests. For example, by including one or more additional dose groups or time points for blood sampling in one study, it may be possible to avoid the need for another study.

6. For purposes of information and of harmonisation the list of test methods and guidance documents relevant to the implementation of this Regulation shall be published in the *Official Journal of the European Union*. This list shall be regularly updated.

(**1**) OL L 276, 20.10.2010, p. 33.

(**2**) OJ L 353, 31.12.2008, p. 1.

(**3**) OJ L 70, 16.3.2005, p. 1.

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

(**5**) See page 85 of his Official Journal.

Changes to legislation:
There are outstanding changes not yet made to Commission Regulation (EU) No 283/2013. Any changes that have already been made to the legislation appear in the content and are referenced with annotations.
View outstanding changes

Changes and effects yet to be applied to the whole legislation item and associated provisions

- Signature words omitted by S.I. 2019/556 reg. 21(4)
- Annex Pt. A s. 8 word omitted by S.I. 2019/556 reg. 21(5)(b)(xiv)
- Annex Pt. A s. 1 point 1.4 word substituted in earlier amending provision S.I. 2019/720, Sch. 2 para. 176(2)(a)(i) by S.I. 2020/1567 Sch. 2 para. 61
- Annex Pt. A s. 1 point 1.4.1 word substituted in earlier amending provision S.I. 2019/720, Sch. 2 para. 176(2)(b) by S.I. 2020/1567 Sch. 2 para. 61
- Annex Pt. B s. 9 words omitted by S.I. 2019/556 reg. 21(5)(c)(vi)
- Art. 1(1) Art. 1 renumbered as Art. 1(1) by S.I. 2019/556 reg. 21(2)(a)
- Art. 1(2) inserted by S.I. 2019/556 reg. 21(2)(b)