COMMISSION IMPLEMENTING DECISION

of 20 December 2013

correcting Annex II to Implementing Decision 2012/707/EU establishing a common format for the submission of the information pursuant to Directive 2010/63/EU of the European Parliament and of the Council on the protection of animals used for scientific purposes

(notified under document C(2013) 9220)

(Text with EEA relevance)

(2014/11/EU)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes [1], and in particular Article 54(4) thereof,

Whereas:

(1) Verification revealed errors in Annex II to Commission Implementing Decision 2012/707/EU [2]. The flowchart included in that Annex erroneously indicated that input categories 'toxicity and other safety testing required by legislation' and 'legislative requirements' apply only to 'toxicity and other safety testing including pharmacology' and not to all other subcategories of 'regulatory use and routine production by type'. In order to clarify this issue the layout of the flowchart should be changed. To emphasise this further, the title of input category 'toxicity and other safety testing required by legislation' should be changed to 'testing by legislation'. Other minor changes to the layout of the flowchart should be introduced in order to improve clarity.

(2) Changes made to the flowchart should be mirrored in the second part of Annex II to Implementing Decision 2012/707/EU, containing the detailed instructions.

(3) Implementing Decision 2012/707/EU should therefore be corrected accordingly.

(4) The measures provided for in this Decision are in accordance with the opinion of the Committee established under Article 56(1) of Directive 2010/63/EU,

HAS ADOPTED THIS DECISION:

Article 1

Annex II to Implementing Decision 2012/707/EU shall be replaced by the Annex to this Decision.

Article 2

This Decision is addressed to the Member States.

Done at Brussels, 20 December 2013.

For the Commission

Janez POTOČNIK

Member of the Commission

[1] OJ L 276, 20.10.2010, p. 33.

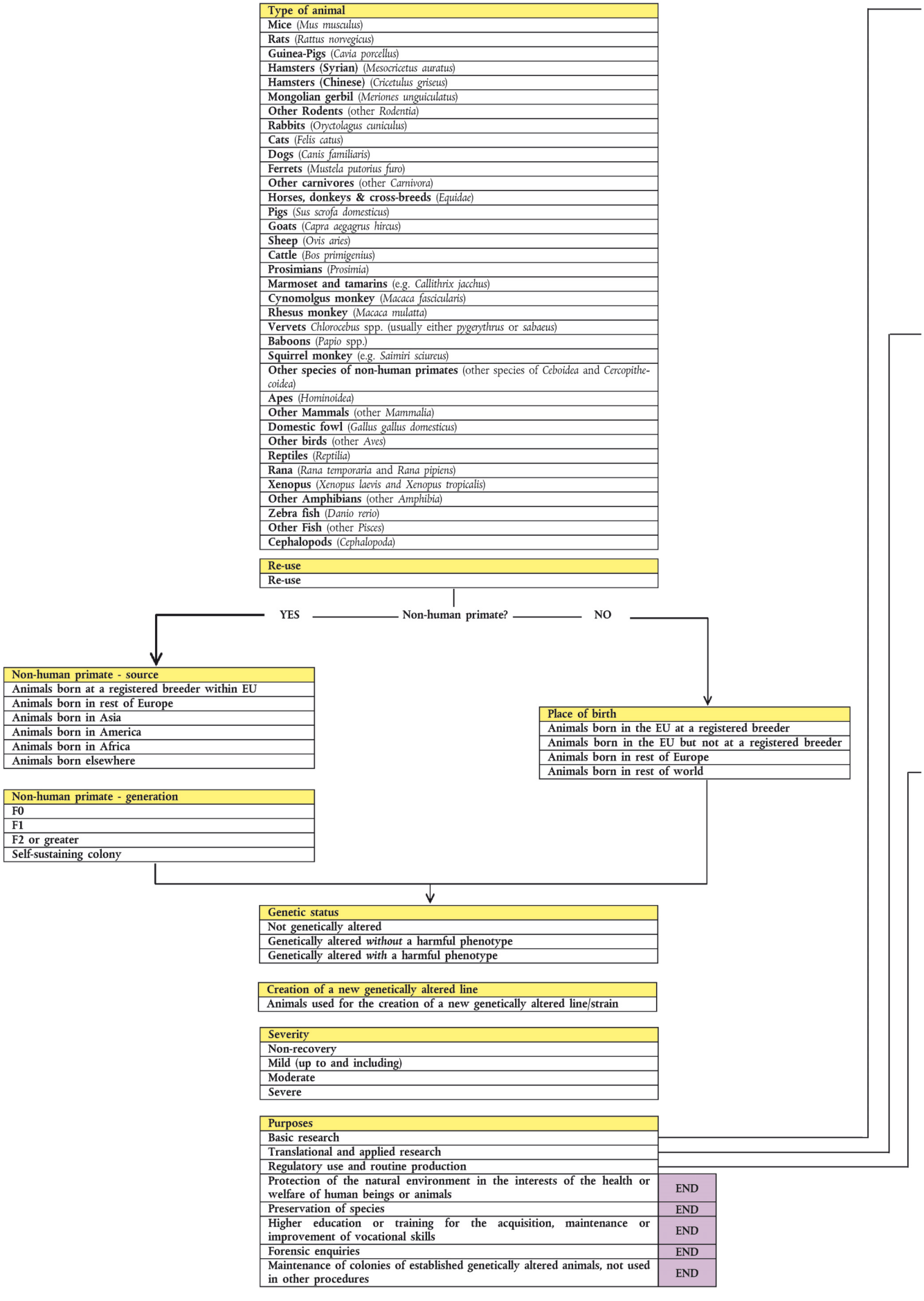
[2] Commission Implementing Decision 2012/707/EU of 14 November 2012 establishing a common format for the submission of the information pursuant to Directive 2010/63/EU of the European Parliament and of the Council on the protection of laboratory animals used for scientific purposes (OJ L 320, 17.11.2012, p. 33).

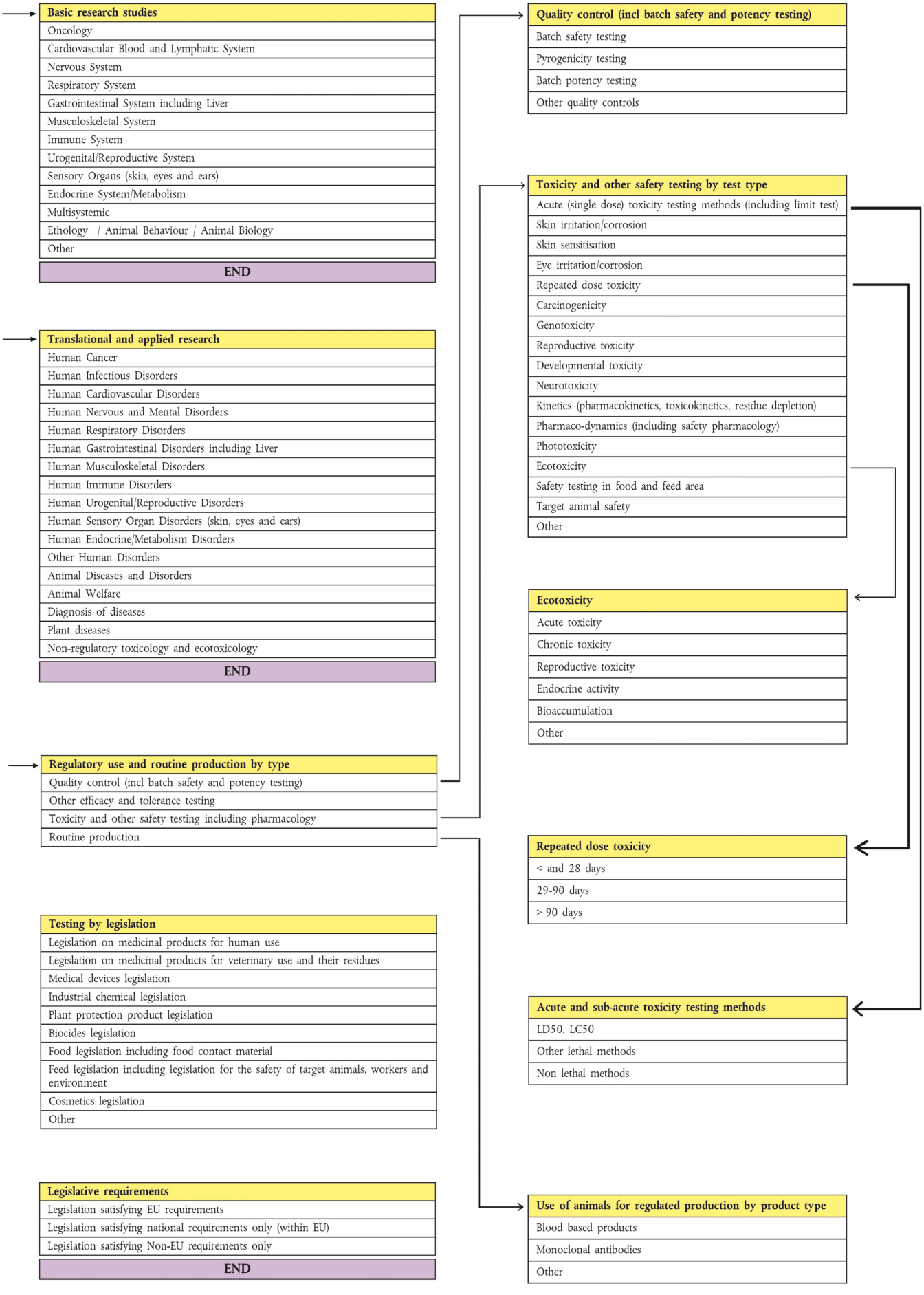
ANNEX

'ANNEX II

PART A

FLOWCHART OF STATISTICAL DATA INPUT CATEGORIES UNDER ARTICLE 54(2)


Type of animal
Mice (Mus musculus)
Rats (Rattus norvegicus)
Guinea-Pigs (Cavia porcellus)
Hamsters (Syrian) (Mesocricetus auratus)
Hamsters (Chinese) (Cricetulus griseus)
Mongolian gerbil (Meriones unguiculatus)
Other Rodents (other Rodentia)
Rabbits (Oryctolagus cuniculus)
Cats (Felis catus)
Dogs (Canis familiaris)
Ferrets (Mustela putorius furo)
Other carnivores (other Carnivora)
Horses, donkeys & cross-breeds (Equidae)
Pigs (Sus scrofa domesticus)
Goats (Capra aegagrus hircus)
Sheep (Ovis aries)
Cattle (Bos primigenius)
Prosimians (Prosimia)
Marmoset and tamarins (e.g. Callithrix jacchus)
Cynomolgus monkey (Macaca fascicularis)
Rhesus monkey (Macaca mulatta)
Vervets Chlorocebus spp. (usually either pygerythrus or sabaeus)
Baboons (Papio spp.)
Squirrel monkey (e.g. Saimiri sciureus)
Other species of non-human primates (other species of Ceboidea and Cercopithecoidea)
Apes (Hominoidea)
Other Mammals (other Mammalia)
Domestic fowl (Gallus gallus domesticus)
Other birds (other Aves)
Reptiles (Reptilia)
Rana (Rana temporaria and Rana pipiens)
Xenopus (Xenopus laevis and Xenopus tropicalis)
Other Amphibians (other Amphibia)
Zebra fish (Danio rerio)
Other Fish (other Pisces)
Cephalopods (Cephalopoda)
Re-use
Re-use
YES
Non-human primate?
NO
Non-human primate - source
Animals born at a registered breeder within EU
Animals born in rest of Europe
Animals born in Asia
Animals born in America
Animals born in Africa
Animals born elsewhere
Place of birth
Animals born in the EU at a registered breeder
Animals born in the EU but not at a registered breeder
Animals born in rest of Europe
Animals born in rest of world
Non-human primate - generation
F0
F1
F2 or greater
Self-sustaining colony
Genetic status
Not genetically altered
Genetically altered without a harmful phenotype
Genetically altered with a harmful phenotype
Creation of a new genetically altered line
Animals used for the creation of a new genetically altered line/strain
Severity
Non-recovery
Mild (up to and including)
Moderate
Severe
Purposes
Basic research
Translational and applied research
Regulatory use and routine production
Protection of the natural environment in the interests of the health or welfare of human beings or animals
END
Preservation of species
END
Higher education or training for the acquisition, maintenance or improvement of vocational skills
END
Forensic enquiries
END
Maintenance of colonies of established genetically altered animals, not used in other procedures
END


Basic research studies
Oncology
Cardiovascular Blood and Lymphatic System
Nervous System
Respiratory System
Gastrointestinal System including Liver
Musculoskeletal System
Immune System
Urogenital/Reproductive System
Sensory Organs (skin, eyes and ears)
Endocrine System/Metabolism
Multisystemic
Ethology / Animal Behaviour / Animal Biology
Other
END
Translational and applied research
Human Cancer
Human Infectious Disorders
Human Cardiovascular Disorders
Human Nervous and Mental Disorders
Human Respiratory Disorders
Human Gastrointestinal Disorders including Liver
Human Musculoskeletal Disorders
Human Immune Disorders
Human Urogenital/Reproductive Disorders
Human Sensory Organ Disorders (skin, eyes and ears)
Human Endocrine/Metabolism Disorders
Other Human Disorders
Animal Diseases and Disorders
Animal Welfare
Diagnosis of diseases
Plant diseases
Non-regulatory toxicology and ecotoxicology
END
Regulatory use and routine production by type
Quality control (incl batch safety and potency testing)
Other efficacy and tolerance testing
Toxicity and other safety testing including pharmacology
Routine production
Testing by legislation
Legislation on medicinal products for human use
Legislation on medicinal products for veterinary use and their residues
Medical devices legislation
Industrial chemical legislation
Plant protection product legislation
Biocides legislation
Food legislation including food contact material
Feed legislation including legislation for the safety of target animals, workers and environment
Cosmetics legislation
Other
Legislative requirements
Legislation satisfying EU requirements
Legislation satisfying national requirements only (within EU)
Legislation satisfying Non-EU requirements only
END
Quality control (incl batch safety and potency testing)
Batch safety testing
Pyrogenicity testing
Batch potency testing
Other quality controls
Toxicity and other safety testing by test type
Acute (single dose) toxicity testing methods (including limit test)
Skin irritation/corrosion
Skin sensitisation
Eye irritation/corrosion
Repeated dose toxicity
Carcinogenicity
Genotoxicity
Reproductive toxicity
Developmental toxicity
Neurotoxicity
Kinetics (pharmacokinetics, toxicokinetics, residue depletion)
Pharmaco-dynamics (including safety pharmacology)
Phototoxicity
Ecotoxicity
Safety testing in food and feed area
Target animal safety
Other
Ecotoxicity
Acute toxicity
Chronic toxicity
Reproductive toxicity
Endocrine activity
Bioaccumulation
Other
Repeated dose toxicity
< and 28 days
29-90 days
> 90 days
Acute and sub-acute toxicity testing methods
LD50, LC50
Other lethal methods
Non lethal methods
Use of animals for regulated production by product type
Blood based products
Monoclonal antibodies
Other

PART B

DETAILED INSTRUCTIONS FOR THE PROVISION OF STATISTICAL DATA ON THE USE OF ANIMALS FOR SCIENTIFIC PURPOSES UNDER ARTICLE 54(2)

REPORTING FORMAT FOR THE SUBMISSION OF THE INFORMATION REFERRED TO IN ARTICLE 54(2) OF DIRECTIVE 2010/63/EU

1. The data should be entered on each use of an animal.

2. When entering data for an animal, only one option *within* a category can be selected.

3. Animals killed for organs and tissues, as well as sentinels, are excluded from the provision of statistical data, unless the killing is performed under a project authorisation using a method not included in Annex IV or where the animal has gone through a previous intervention, prior to being killed, and which has been above the threshold of minimum pain, suffering, distress and lasting harm.

4. Surplus animals that are killed are not included in the statistical data apart from genetically altered animals with intended and exhibited harmful phenotype.

5. Larval forms of animals are to be counted once they become capable of independent feeding.

6. Foetal and embryonic forms of mammalian species are not counted; only animals that are born, including by Caesarean section, and live, are to be counted.

7. Whenever the "severe" classification is exceeded, whether pre-authorised or not, these animals and their use are to be reported normally like any other use, and under the "severe" category. Commentary should be added in the "Member State" narrative section covering the species, numbers, whether prior exemption was authorised, the details of the use and the reasons why "severe" classification was exceeded.

8. The data are to be reported for the year that the procedure ends. In case of studies running across 2 calendar years, all of the animals may be accounted for together in the year in which the last procedure ends *if this exemption to annual reporting is authorised by the competent authority*. For projects running longer than 2 calendar years, animals are reported on the year they are killed or die.

9. The use of "other" category requires a compulsory entry in the narratives to provide further details.

A. GENETICALLY ALTERED ANIMALS

1. For the purposes of statistical reporting, "genetically altered animals" include genetically modified (transgenic, knock-out and other forms of genetic alteration) and naturally occurring or induced mutant animals.

2. Genetically altered animals are reported either:

(a) when used for the creation of a new line;

(b) when used for the maintenance of an established line with an intended *and* exhibited harmful phenotype; or

(c) when used in other (scientific) procedures (i.e. not for creation or for the maintenance of a line).

3. All animals *carrying the genetic alteration* should be reported during the creation of a new line. In addition, those used for superovulation, vasectomy, embryo implantation should equally be reported (these may or may not be genetically altered themselves). Genetically normal animals (wild type offspring) produced as a result of creation of a new genetically altered line should not be reported.

4. In the category "Purposes", the animals used for the *creation* of a new genetically altered line should be reported under "basic research" or "translational and applied research" in the *respective category the line is being created for*.

5. **A new strain or line of genetically altered animals is considered to be "established"** when transmission of the genetic alteration is stable, which will be a minimum of two generations, and a welfare assessment has been completed.

6. The welfare assessment will determine if the newly created line is expected to have an *intended harmful phenotype* and, if this is the case, the animals from this point onwards shall be reported under category "Maintenance of colonies of established genetically altered animals, not used in other procedures" — or, if appropriate, in the other procedures they are being used for. If the welfare assessment concludes that the line is *not* expected to have a harmful phenotype, its *breeding* falls outside the scope of a procedure and no longer needs to be reported.

7. "**Maintenance of colonies of established genetically altered animals, not used in other procedures**" contains the animals required for the *maintenance* of colonies of genetically altered animals of established lines *with an intended harmful phenotype* and *which have exhibited* pain, suffering, distress or lasting harm as a consequence of the harmful genotype. The intended purpose for which the line is being maintained for is not recorded.

8. **All genetically altered animals which are used in other procedures** (not for the creation or maintenance of a genetically altered line) should be reported under their respective purposes (the same way as any non-genetically altered animal). These animals may or may not exhibit a harmful phenotype.

9. Genetically altered animals, expressing a harmful phenotype, and killed for their organs and tissue, should be reported under the respective primary purposes for which the organs/tissue were used.

B. DATA CATEGORIES

The sections below follow the order of the categories and related headings in the flow chart.

1. **Type of animal**

(i) All cephalopod species are to be reported under heading cephalopod from the stage at which the animal becomes capable of independent feeding, i.e. immediately post-hatching for octopus and squid; and around 7 days after hatching for cuttlefish.

(ii) Fish should be counted from the stage of being capable of independent feeding onward. Zebrafish kept in optimal breeding conditions (approximately + 28 °C) should be counted 5 days post fertilisation.

(iii) Due to the small size of some fish and cephalopod species, the count may be done on the basis of estimation.

2. **Reuse**

(i) Each use of the animal should be reported at the end of each procedure.

(ii) The statistics will present the **number of naïve animals only in connection with their species and place of birth**. For reused animals, their "place of birth" is therefore not recorded.

(iii) Any **subsequent categories** will show the **number of uses of animals in procedures**. Thus these numbers cannot be cross referenced with the total numbers of naïve animals.

(iv) The number of animals that are reused cannot be deduced from the data due to the fact that some animals may be reused more than once.

(v) The actual suffering of the animal in the procedure should be reported. In some cases this could be influenced by a previous use. However, the severity will not always increase in a subsequent use and in some cases even decrease as a result (habituation). Therefore there should be no attempt to automatically add up the severities from its previous uses. This should always be judged on a case-by-case basis.

Reuse versus continued use

A procedure means a use of one animal for a single scientific/experimental/educational/training purpose. A single use extends from the time when the first technique is applied to the animal until the completion of data collection, observations or achievement of educational objective. This is usually a single experiment, test or training of a technique.

A single procedure may contain a number of steps (techniques) all necessarily related to achieve a single outcome and which require the use of the same animal.

The end user will report **the entire procedure** including any preparation (regardless of the location this has taken place) and take into account the severity associated with the preparation.

Examples of preparation include surgical procedures (such as cannulation, implantation of telemetry, ovariectomy, castration, hypophysectomy, etc.) and non-surgical (such as feeding modified diets, induction of diabetes, etc.). The same applies to the breeding of genetically altered animals, i.e. when the animal is used in its intended procedure, the end user will report the entire procedure taking into account the severity associated with the phenotype. See section on genetically altered animals for more details.

Should, for exceptional reasons, a prepared animal not be used for a scientific purpose, the establishment having prepared the animal should report the details of the preparation as an independent procedure in the statistics as per the intended purpose, provided the preparation of the animal has been above the threshold of minimum pain, suffering, distress and lasting harm.

3. **Place of birth**

Animals born in the EU at a registered breeder
Animals born in the EU but not at a registered breeder
Animals born in rest of Europe
Animals born in rest of world

(i) Origin is based on the place of birth, i.e. "born in" and not according to where the animal is supplied from.

(ii) Animals born in the EU at a registered breeder covers animals born at breeders as authorised and registered under Article 20 of Directive 2010/63/EU.

(iii) Animals born in the EU but not at a registered breeder includes animals born outside a registered breeder such as wild animals, farm animals (unless the breeder is authorised and registered), as well as any exemptions granted under Article 10(3) of Directive 2010/63/EU.

(iv) Animals born in rest of Europe and Animals born in rest of world groups together all animals regardless of whether they have been bred in registered breeding establishments, other establishments and includes animals that have been captured in the wild.

4. **Non-human primate — source**

Animals born at a registered breeder within EU
Animals born in rest of Europe
Animals born in Asia
Animals born in America
Animals born in Africa
Animals born elsewhere

For the purposes of this reporting:

(i) Animals born in rest of Europe is to include animals born in Turkey, Russia and Israel.

(ii) Animals born in Asia is to include animals born in China.

(iii) Animals born in America is to include animals born in the North, Central and South America.

(iv) Animals born in Africa is to include animals born in Mauritius.

(v) Animals born elsewhere is to include animals born in Australasia.

The origins of animals recorded under Animals born elsewhere are to be detailed to the competent authority with the data submission.

5. **Non-human primate — generation**

F0
F1
F2 or greater
Self-sustaining colony

(i) As long as the colony is not self-sustained, animals born in that colony should be reported under F0, F1, F2 or greater according to their generation derived from the maternal line.

(ii) Once the whole colony is self-sustained, all animals born in that colony should be reported under Self-sustaining colony regardless of their generation derived from the maternal line.

6. **Genetic status**

Not genetically altered
Genetically altered without a harmful phenotype
Genetically altered with a harmful phenotype

(i) Not genetically altered covers all animals that have not been genetically altered, including genetically normal parent animals used for the creation of a new genetically altered animal line/strain.

(ii) Genetically altered without a harmful phenotype includes animals used for the **creation of a new line**, carrying the genetic alteration but exhibiting no harmful phenotype and genetically altered animals **used** in other procedures (not for creation or maintenance) but exhibiting no harmful phenotype.

(iii) Genetically altered with a harmful phenotype includes:

(a) animals used for the **creation of a new line** and exhibiting a harmful phenotype;

(b) those used for **maintaining an established line** with an intended harmful phenotype and exhibiting a harmful phenotype; and

(c) genetically altered animals **used** in other procedures (not for creation or maintenance) and exhibiting a harmful phenotype.

7. **Creation of a new genetically altered line**

Animals used for the creation of a new genetically altered line/strain

Animals used for the creation of a new genetically altered line/strain identifies animals which are *used for the creation* of a new genetically altered line/strain, separating from other animals used for the purposes of "basic research" or "translational and applied research".

8. **Severity**

(i) **Non-recovery** — Animals which have undergone a procedure that has been performed entirely under general anaesthesia from which the animal has not recovered consciousness shall be reported as non-recovery.

(ii) **Mild (up to and including)** — Animals which have undergone a procedure as a result of which the animals have experienced up to, and including, short-term mild pain, suffering or distress, as well as when there has been no significant impairment of the well-being or general condition of the animals shall be reported as Mild. NB: This should also include any animals used in an authorised project, but which have ultimately not been observed to have experienced a level of pain, suffering, distress or lasting harm equivalent to that caused by the introduction of a needle in accordance with good veterinary practice, with the exception of animals required for the *maintenance* of colonies of genetically altered animals of established lines *with an intended harmful phenotype* and *which have not exhibited* pain, suffering, distress or lasting harm as a consequence of the harmful genotype.

(iii) **Moderate** — Animals which have undergone a procedure as a result of which the animals have experienced short-term moderate pain, suffering or distress, or long-lasting mild pain, suffering or distress as well as procedures that have caused moderate impairment of the well-being or general condition of the animals shall be reported as Moderate.

(iv) **Severe** — Animals which have undergone a procedure as a result of which the animals have experienced severe pain, suffering or distress, or long-lasting moderate pain, suffering or distress as well as procedures, that have caused severe impairment of the well-being or general condition of the animals shall be reported as Severe.

(v) If the "severe" classification is exceeded, whether pre-authorised or not, these animals and their use are to be reported under Severe. Commentary should be added in the "Member State" narrative section covering the species, numbers, whether prior exemption was authorised, the details of the use and the reasons why "severe" classification was exceeded.

9. **Purposes**

Basic research
Translational and applied research
Regulatory use and routine production
Protection of the natural environment in the interests of the health or welfare of human beings or animals
Preservation of species
Higher education or training for the acquisition, maintenance or improvement of vocational skills
Forensic enquiries
Maintenance of colonies of established genetically altered animals, not used in other procedures

(i) Basic research

Basic research includes studies of a fundamental nature including physiology. Studies that are designed to add knowledge about normal and abnormal structure, functioning and behaviour of living organisms and environment, this includes fundamental studies in toxicology. Investigation and analysis focused on a better or fuller understanding of a subject, phenomenon, or a basic law of nature instead of on a specific practical application of the results.

The animals used for the creation of a new genetically altered animal line (including crossing of two lines) *intended to be used for the* ***purposes of basic research*** (e.g. developmental biology, immunology) should be recorded *according to the purpose* they are being created for. In addition they should be reported in "Creation of a new genetic line — Animals used for the creation of a new genetically altered line/strain".

All animals carrying the genetic alteration should be reported during the creation of a new line. Also animals used in creation, such as for superovulation, vasectomy and embryo implantation, are reported here. The reporting should exclude non-genetically altered (wild type) offspring.

A new strain or line of genetically altered animals is considered to be "established" when transmission of the genetic alteration is stable, which will be a *minimum* of two generations, and a welfare assessment has been completed.

(ii) Translational and applied research

Translational and applied research includes animals used for purposes as described in Article 5(b) and (c) excluding any regulatory use of animals.

This also includes discovery toxicology and investigations to prepare for the regulatory submission and method development. This does not include studies required for regulatory submissions.

The animals used for the *creation* of a new genetically altered animal line (including crossing of two lines) *intended to be used for the* ***purposes of translational or applied research*** (e.g. cancer research, vaccine development) should be recorded *according to the purpose* they are being created for. In addition, they should be reported in "Creation of a new genetic line — Animals used for the creation of a new genetically altered line/strain".

All animals carrying the genetic alteration should be reported during the creation of a new line. Also animals used in creation, such as for superovulation, vasectomy and embryo implantation, are reported here. The reporting should exclude non-genetically altered (wild type) offspring.

A new strain or line of genetically altered animals is considered to be "established" when transmission of the genetic alteration is stable, which will be a *minimum* of two generations, and a welfare assessment has been completed.

(iii) Regulatory use and routine production by type

Use of animals in procedures carried out with a view to satisfying legal requirements for producing, placing and maintaining products/substances on the market, including safety and risk assessment for food and feed. This includes tests carried out on products/substances for which no regulatory submission is ultimately made if those tests would have been included in a regulatory submission had a regulatory submission occurred (i.e. tests performed on those products/substances that fail to reach the end of the development process).

This also includes animals used in the manufacturing process of products if that manufacturing process requires regulatory approval (e.g. animals used in the manufacturing serum-based medicinal products should be included within this category).

The efficacy testing during the development of new medicinal products is excluded and should be reported under category "Translational and applied research".

(iv) Protection of the natural environment in the interests of the health or welfare of human beings or animals

This includes studies aimed at investigating and understanding phenomena such as environmental pollution, loss of biodiversity, and epidemiology studies in wild animals.

This excludes any regulatory use of animals for ecotoxicology purposes.

(v) Higher education or training for the acquisition, maintenance or improvement of vocational skills

This includes training to acquire and maintain practical competence in techniques as required under Article 23(2).

(vi) Maintenance of colonies of established genetically altered animals, not used in other procedures

This contains the number of animals required for the *maintenance* of colonies of genetically altered animals of established lines *with an intended harmful phenotype* and which have exhibited pain, suffering, distress or lasting harm as a consequence of the harmful genotype. The intended purpose for which the line is being bred for is not recorded.

This excludes all animals needed for the *creation* of a new genetically altered line and those used *in other procedures* (other than creation/breeding).

10. **Basic research studies**

Oncology
Cardiovascular Blood and Lymphatic System
Nervous System
Respiratory System
Gastrointestinal System including Liver
Musculoskeletal System
Immune System
Urogenital/Reproductive System
Sensory Organs (skin, eyes and ears)
Endocrine System/Metabolism
Multisystemic
Ethology/Animal Behaviour/Animal Biology
Other

(i) Oncology

Any research studying oncology should be included here regardless of the target system.

(ii) Nervous system

This category includes neuroscience, peripheral or central nervous system, psychology.

(iii) Sensory Organs (skin eyes and ears)

Studies on nose should be reported under "Respiratory System" and those on tongue should be reported under "Gastrointestinal System including Liver"

(iv) Multisystemic

This should only include research where more than one system is the primary interest, such as on some infectious diseases, and excluding oncology.

(v) Ethology/Animal Behaviour/Animal Biology category covers both animals in the wild and in captivity with the primary goal of learning more about that specific species.

(vi) Other

Research that is not related to an organ/system listed above or is not organ/system specific.

(vii) Remarks

Animals used for the production and maintenance of infectious agents, vectors and neoplasms, animals used for other biological material and animals used for the production of polyclonal antibodies for the purposes of translational/applied research, but excluding production of monoclonal antibodies by ascites method (which is covered under category "Regulatory use and routine production by type") should be reported in the respective fields of categories "Basic research studies" or "Translational and applied research". The purpose of studies needs to be carefully established, because any listings under the two categories could apply and only the main purpose shall be reported.

11. **Translational and applied research**

Human Cancer
Human Infectious Disorders
Human Cardiovascular Disorders
Human Nervous and Mental Disorders
Human Respiratory Disorders
Human Gastrointestinal Disorders including Liver
Human Musculoskeletal Disorders
Human Immune Disorders
Human Urogenital/Reproductive Disorders
Human Sensory Organ Disorders (skin, eyes and ears)
Human Endocrine/Metabolism Disorders
Other Human Disorders
Animal Diseases and Disorders
Animal Welfare
Diagnosis of diseases
Plant diseases
Non-regulatory toxicology and ecotoxicology

(i) Any applied research studying *human cancer* and *human infectious disorders* should be included regardless of the target system.

(ii) Any regulatory use of animals is to be excluded such as regulatory carcinogenicity studies.

(iii) Studies on disorders of the nose should be reported under "Human Respiratory Disorders" and those of the tongue should be reported under "Human Gastrointestinal Disorders including Liver".

(iv) Diagnosis of diseases includes animals used in direct diagnosis of diseases such as rabies, botulism, but excluding those covered under regulatory use.

(v) Non-regulatory toxicology covers discovery toxicology and investigations to prepare for the regulatory submission and method development. This category does not include studies required for regulatory submissions (preliminary studies, MTD (Maximum Tolerated Dose)).

(vi) Animal welfare should include studies as per Article 5(b)(iii) of Directive 2010/63/EU.

(vii) Remarks

Animals used for the production and maintenance of infectious agents, vectors and neoplasms, animals used for other biological material and animals used for the production of polyclonal antibodies for the purposes of translational/applied research, but excluding production of monoclonal antibodies by ascites method (which is covered under category "Regulatory use and routine production by type") should be reported in the respective fields of categories "Basic research studies" or "Translational and applied research". The purpose of studies needs to be carefully established, because any listings under the two categories could apply and only the main purpose shall be reported.

12. **Regulatory use and routine production**

(i) Use of animals in procedures carried out with a view to satisfying legal requirements for producing, placing and maintaining products/substances on the market, including safety and risk assessment for food and feed.

(ii) This includes tests carried out on products/substances for which no regulatory submission is made (i.e. tests performed on those products/substances (for which a regulatory submission was foreseen) that are ultimately deemed unsuitable for the market by the developer, and thus fail to reach the end of the development process).

(iii) This category also includes animals used in the manufacturing process of products if that manufacturing process requires regulatory approval (e.g. animals used in the manufacturing of serum-based medicinal products should be included within this category).

13. **Regulatory use and routine production by type**

Quality control (incl. batch safety and potency testing)
Other efficacy and tolerance testing
Toxicity and other safety testing including pharmacology
Routine production

(i) Efficacy testing during the development of new medicinal product is excluded and should be reported under category "Translational and Applied research".

(ii) Quality control includes animals used in the testing of purity, stability, efficacy, potency and other quality control parameters of the final product and its constituents and any controls carried out during the manufacturing process for registration purposes, to satisfy any other national or international regulatory requirements or to satisfy the in-house policy of the manufacturer. This includes pyrogenicity testing.

(iii) Other efficacy and tolerance testing Efficacy testing of biocides and pesticides is covered under this category as well as the tolerance testing of additives in animal nutrition.

(iv) Toxicity and other safety testing (including safety evaluation of products and devices for human medicine and dentistry and veterinary medicine) covers studies carried out on any product or substance to determine its potential to cause any dangerous or undesirable effects in humans or animals as a result of its intended or abnormal use, manufacture or as a potential or actual contaminant in the environment.

(v) Routine production covers the production of monoclonal antibodies (by ascites) and blood products including polyclonal antisera by established methods. This excludes immunisation of animals for hybridoma production which should be captured under basic or applied research under the appropriate category.

14. **Testing by legislation**

Legislation on medicinal products for human use
Legislation on medicinal products for veterinary use and their residues
Medical devices legislation
Industrial chemicals legislation
Plant protection product legislation
Biocides legislation
Food legislation including food contact material
Feed legislation including legislation for the safety of target animals, workers and environment
Cosmetics legislation
Other

(i) The legislative requirement should be entered as per the *intended primary* use.

(ii) Water quality; if concerning e.g. tap water to be reported under food legislation.

15. **Legislative requirements**

Legislation satisfying EU requirements
Legislation satisfying national requirements only (within EU)
Legislation satisfying Non-EU requirements only

(i) This category allows identification of the level of harmonisation between different legislative requirements. The determining factor is not *who* requests the test to be carried out but which legislation is satisfied, giving priority to the widest level of harmonisation.

(ii) Where national legislation is derived from EU legislation, only Legislation satisfying EU requirements is to be chosen.

(iii) Legislation satisfying EU requirements also includes any international requirement which at the same time satisfies EU requirements (such as testing to ICH, VICH, OECD guidelines, European Pharmacopoeia monographs).

(iv) Legislation satisfying national requirements only (within EU) is to be chosen only when the test is carried out to satisfy the requirements of one or more Member State; not necessarily the one in which the work is being carried out. However, there is no equivalent requirement in the EU.

(v) Legislation satisfying Non-EU requirements only is to be chosen when there is no equivalent requirement to carry out the test to satisfy EU requirements.

16. **Quality control (incl. batch safety and potency testing)**

Batch safety testing
Pyrogenicity testing
Batch potency testing
Other quality controls

Batch safety testing excludes pyrogenicity testing. These are reported under a separate category Pyrogenicity testing.

17. **Toxicity and other safety testing by test type**

Acute (single dose) toxicity testing methods (including limit test)
Skin irritation/corrosion
Skin sensitisation
Eye irritation/corrosion
Repeated dose toxicity
Carcinogenicity
Genotoxicity
Reproductive toxicity
Developmental toxicity
Neurotoxicity
Kinetics (pharmacokinetics, toxicokinetics, residue depletion)
Pharmaco-dynamics (including safety pharmacology)
Phototoxicity
Ecotoxicity
Safety testing in food and feed area
Target animal safety
Other

(i) Immunotoxicology studies should be covered under Repeated dose toxicity.

(ii) Kinetics (pharmacokinetics, toxicokinetics, residue depletion) if toxicokinetics is performed as part of the regulatory repeat dose toxicity study, it should be reported under repeated dose toxicity.

(iii) Safety testing in the food and feed area includes testing of drinking water (including target animal safety testing).

(iv) Target animal safety this is testing to ensure a product for a specific animal can be used safely on that species (excluding batch safety testing which is covered under quality control).

18. **Acute and subacute toxicity testing methods**

LD50, LC50
Other lethal methods
Non-lethal methods

19. **Repeated dose toxicity**

< and 28 days
29-90 days
> 90 days

20. **Use of animals for regulated production by product type**

Blood based products
Monoclonal antibodies
Other

21. **Ecotoxicity**

Acute toxicity
Chronic toxicity
Reproductive toxicity
Endocrine activity
Bioaccumulation
Other

C. MEMBER STATE NARRATIVE

1. General information on any changes in trends observed since the previous reporting period.

2. Information on significant increase or decrease in use animals in any of the specific areas and analysis of the reasons thereof.

3. Information on any changes in trends in actual severities and analysis of the reasons thereof.

4. Particular efforts to promote the principle of replacement, reduction and refinement and its impacts on statistics if any.

5. Further breakdown on the use of "other" categories if a significant proportion of animal use is reported under this category.

6. Details on cases where the "severe" classification is exceeded, whether pre-authorised or not, covering the species, numbers, whether prior exemption was authorised, the details of the use and the reasons why "severe" classification was exceeded.'