Instructions for completion of annual Returns of Procedures in the UK

These instructions have been adapted from the EU Commission Implementing Decision of 14 November 2012:

http://ec.europa.eu/environment/chemicals/lab_animals/home_en.htm

They apply to Returns of Procedures **completed in 2016.**

The Excel form should be completed (one form for each project licence held during the year), saved using the project licence number as the filename in the format:

7001234 (i.e. replacing the '/' in 70/1234 with a zero)

- and sent to the Home Office at: ROPReturns@homeoffice.gsi.gov.uk

Note: In contrast to years prior to 2014, procedures will be counted when they end, not when they begin. **Procedures begun in a previous year, and which have already been reported, but which end in 2016, should be counted again when they end with details of actual severity.**

Complete the preliminary questions on the first page.

Note: The "Procedure Details" spreadsheet will only appear after these questions on the first page have been completed.

Project details:

- Complete name, establishment address and email address as per project licence. Provide a telephone number where you can be contacted if we need to seek further information on this Return.

- Complete the Establishment Licence number. This is shown on your project licence and can be obtained from the Home Office Liaison Contact or the Establishment Licence Holder. This should be in the formal 4001001 (i.e replacing the '/' in 40/1001 with a zero) if you do not have an ASPeL licence. If you do have an ASPeL licence the licence number should be 9 characters long and start with an 'X'.

- Complete project licence number in the format 7001234 (i.e. replacing the '/' in 70/1234 with a zero) if you do not have an ASPeL licence. If you have an ASPeL project licence the licence number should be 9 characters long and start with a 'P'.

- The report year will already be completed. This return should contain details of all procedures **completed** during that year, regardless of when they started.

The following questions must be answered:

1. Were any procedures carried out and completed in the reported year?

   - **If 'No' then there is no need to complete the rest of this form so please return the form to the Home Office as described above.**

   - **If 'Yes' then continue.**

2. Were embryonic forms used exclusively?

   This refers to mammalian embryos between two-thirds of gestation and term (prior to birth), avian and reptile eggs from two-thirds of incubation prior to hatching.

   - **If 'Yes' only embryonic forms were used (you did not use any postnatal forms), there is no need to complete the rest of this form**.

   - **If 'No' and later stages were used then continue to provide further details of those animals but do not provide further details of embryonic forms.**

   - **Note that embryonic forms of amphibian and larval forms of fish fry from the point when they become "protected animals", i.e. from when they are capable of free feeding, should be reported. For zebra fish kept under conventional conditions this means from 5 days post fertilisation.**

3. Endangered species. Were any animals used of species listed in Annex A of Council Regulation (EC) No 338/97 of 9th December 1996. Annex A is based on Appendix 1 of CITES but may contain additional species.

   However, captive bred animals of species listed in Annex A should not be returned as endangered species in the return of procedures.

   - **If 'Yes' please provide details in the additional comments box.**

   Note this does not refer to species listed in CITES appendix 2 (or Annex B).

4. Were neuromuscular blocking agents used in any procedures during the previous year?

- **If 'Yes' please answer the next question. If general anaesthesia was not used throughout the entire period of neuromuscular blockade then please provide details in the additional comments box.**

5. Rodenticide trials. Indicate if rodenticide trials were carried out under this project licence in the year relating to this return. There is no need to provide further details of those trials.

If you answered 'Yes' to question 1 above, please provide further details of procedures in the 'Procedure details' tab.

General

1. Data should be provided on each procedure, i.e. each use of an animal. If an animal has been used in more than one study or experiment, i.e. re-used, provide details on each use in a separate row.
2. Using the drop-down lists, choose one option for each column for each row. If necessary choose the 'best fit' from the drop down list options. If you select 'Other' please provide additional details in the appropriate column.
3. Do not count animals unless used on ***regulated procedures*** (these are procedures authorised on a project licence). Animals killed by Schedule 1 (or other PEL-permitted) methods of killing, for example, for tissue collection, are not counted unless they were genetically altered and bred under project licence authorities.
4. Surplus animals that are killed are not included, unless they have been produced under project licence authority, for example, genetically altered animals.
5. Mammals, birds and reptiles are only counted if they are born alive (including by caesarean section) or hatch.
6. Larval and embryonic forms are counted from when they become capable of free feeding. Zebra fish fry kept under conventional conditions should be counted from five days post-fertilisation.
7. Cephalopods should be counted from the stage at which the animal becomes capable of independent feeding. This will be immediately post-hatching for octopus and squid, and from around seven days post-hatching for cuttlefish.
8. In the case of very small animals, such as fish fry, an estimate of the total numbers used is acceptable.
9. In exceptional cases where a single study involving a large group of animals extends over two calendar years, and data collection is not complete until the end of the entire study (as opposed to at the time of death of each individual subject) it is acceptable to count all procedures in the year in which the last procedure ends, i.e. at the end of the study. This must be agreed with your Home Office Inspector in advance.

Data categories

Do not leave any relevant cells blank.

NB. Depending on previous entries, some cells will remain blank and will not allow information to be entered.

Use the drop down lists. Only enter free text in the 'Other ...' columns if this is relevant.

A single row can be completed for any number of procedures if all the details are identical, for example:

- a single animal, one procedure;
- a single experiment, a number of procedures; or
- a group of studies, many procedures.

However, if the number is large (see below) for a single cell you may need to explain the reason in the 'Comments' column.

Column E - Animal species

- Select the species from the drop down list.

- All cephalopods, regardless of species, should be reported under the one heading 'Cephalopod'.

Column F - Other species

- If you selected 'Other' in Column E then you must provide details of the actual species here, otherwise leave blank.

Column G - Number of procedures

- This of the number of uses, i.e. the number of times animals were used in a particular experiment or study.

- If an animal has been used multiple times then the number of procedures is the number of times it was used.

Example: PROCEDURE

10 rats were used in a study involving administration of a drug then 7 separate blood samples and a final surgical intervention, before being killed by a Schedule 1 method.

Number of procedures = 10
Re-use = No

Note: If an animal is used on a long study, extending over more than one calendar year, it should not be counted until that procedure ends.

Example: PROCEDURE OVER TWO CALENDER YEARS

In November 2015 10 rats were used in a study that ended when all of the rats were killed in March 2016.

Number of procedures reported in the 2015 return = 0
All will be returned in the 2016 return.

- If more than 99 non-human primates or 999 of any other species are entered in a single cell then you should add a note in the 'Comments 1' column.

- If the large number applies to a single study then briefly explain why so many animals were used.

- If multiple studies have been combined in one entry, and this is the reason for the large number, simply state e.g. 'Combination of studies'.

- If a large number of animals used on the same breeding protocol has been entered on one line, simply state "breeding".

Column H - Re-use

- Each animal should be reported at the end of each procedure for which it was used. Most animals are used only once, and 'No' should be entered in this column. If an animal has been used before (at any time, not just in the reported year) enter 'Yes' in this column.

- Re-use must have been authorised in the project licence.

Example: RE-USE

10 rats were cannulated and used in a study involving administration of a drug then 7 separate blood samples.
At the end of that study those same rats had a wash out period then were used again to test a separate drug. There was no need to use the same rats for the second study, therefore the second study constitutes "Re-use"

First Row:
Number of procedures = 10 and Re-use = No,
THEN IN A SECOND ROW
Number of procedures = 10 and Re-use = Yes (the place of birth for these re-use procedures is not completed).

Example: RE-USE

100 sheep were used to supply normal blood by being bled repeatedly at approximately monthly intervals.
90 had been used in previous years. 10 were bought in during this reporting year.
Each bleed constitutes a separate procedure, therefore all except the first bleed constitutes "re-use".
Each sheep was bled 10 times, therefore the total number of procedures was 1000 and should be reported in 3 (or possibly 2) separate rows of data, as follows:

Row 1.
The previously used sheep.
Number of procedures = 900, Re-use = Yes and the place of birth column is not completed.

Row 2.
The new sheep, first bleed.
Number of procedures = 10, Re-use = No and the place of birth column is completed.

Row 3 (or added to Row 1)
The second and subsequent bleeds of the new sheep.
Number of procedures = 90, Re-use = Yes and the place of birth column is not completed.

Note: For the purpose of statistical reporting **a single procedure, or use of an animal, extends from the time when the first technique was applied to the animal until the completion of data collection, observations or achievement of the particular purpose**. In most cases this means a single protocol.

'***Continued use*'**, when a single experiment or study extends over more than one licence or protocol, and constitutes a single use; it *is not re-use*. In this case the end user should report the entire procedure, even if it began on another project licence, and the initiator of the study does not report such procedures.

Example: CONTINUED USE

10 rats were surgically prepared under Project Licence 7001234. This had actual severity of Moderate because it involved surgery.

These rats were then moved onto a different Project Licence 7005678 for use in a PK (pharmacokinetics) study. This part of the study has an actual severity of Mild.

PPL 7001234 does not report any of these rats.

PPL7005678 reports all 10 rats when the PK study is completed, and the Actual Severity is reported as Moderate to take account of the severity of the entire procedure which started on a different licence (or protocol).

Note that any subsequent PK studies using the same rats, reported as "Re-use" should have Actual Severity of Mild (if this is what happened on the re-use)

Continued use includes when genetically altered animals are bred under one licence then transferred to a second licence (possibly at a different establishment) for the remainder of the study; the breeder would not report these animals, they would be returned under the end user's project licence return.

If in any doubt as to which classification is correct consult your Home Office Inspector.

Column I - Place of birth: all species except non-human primates

- Only provide details of the place of birth for the first use of an animal. If animals have been re-used, this column is disabled.

Note: The *place of birth, not the source* of the animal, is required. A registered breeder can be any breeder within the EU who is registered under Article 20 of Directive 2010/63 EU. In the UK licensed establishments are registered breeders.

Animals born in your own establishment should be entered as "Animals born in the UK at a licensed establishment".

- In the case of eggs of birds, reptiles, amphibia and fish the "place of birth" should be the place where the eggs hatched, if this is different from where the eggs were produced.

- In the case of mammals where source of embryos is different from where the embryos are implanted or animals are born, the place of birth is the place where they were born, not the source of the embryos.

- The 'Rest of Europe' means Council of Europe* countries and Israel.

**** Council of Europe Countries***

Albania, Andorra, Armenia, Azerbaijan, Bosnia & Herzegovina, Georgia, Iceland, Liechtenstein, Macedonia, Moldova, Monaco, Montenegro, Norway, Russian Federation, San Marino, Serbia, Switzerland, Turkey, Ukraine

Example: PLACE OF BIRTH

1. Transgenic mice bred in house and used in a study.
Place of Birth "Animals born in the UK at a licensed establishment"

2. Transgenic mice bred at one University in the UK, licensed under ASPA, then moved to a different project licence at a second university for use in an experiment.
The PPL holder at the first university who supplied the mice does not report them at all.
The PPL holder who received and used the mice at the second university reports them all.

If 50 mice were supplied but actually only 40 were used, with the remaining 10 culled as surplus, the return would be as follows:

40 Mice, "Animals born in the UK at a licensed establishment" purpose as appropriate eg "Basic research; Immune system"
AND
10 mice "Animals born in the UK at a licensed establishment" purpose "Maintenance of established lines of GA animals", because the only procedure the surplus 10 were subjected to was being born with a genetic alteration (even if this PPL does not authorise B&M).

3. Mice were bought from supplier, licensed under the EU Directive, in Germany.
Place of birth "Animals born in the EU (non UK) at a registered breeder"

4. Mice were bought from supplier in the USA.
Place of birth "Animals born in the rest of the world"

5. Cattle were sourced from a commercial dairy farm.
Place of birth "Animals born in the UK but not at a licensed establishment"

6. Wild caught animals.
Place of birth "Animals born in the UK but not at a licensed establishment"

Column J - Place of birth: Non-human primates only

- Additional detail is required for non-human primates (NHPs). This column will be disabled for all other species.

- The *place of birth, not the source* of the animal, is required.
    - Asia includes China.
    - America includes North, Central and South America.
    - Africa includes Mauritius.
    - 'Elsewhere' includes Australasia. Provide details of place of birth in the Comments1 column if this category is used.

- For any species other than non-human primates, leave this column blank.

Column K - Non-human primate generation

- Leave blank for any species other than primates.

- If sourced from a colony that is not self-sustaining then ‘F0’, ‘F1’ or ‘F2 or greater’ should be used.

- If the colony has become self-sustaining then you should enter every animal from this colony as ‘Self-sustaining colony’ regardless of generation of the individual animal, and not as ‘F0’, ‘F1’ or ‘F2 or greater’.

Column L - Genetic status

1: ‘Not genetically altered’: includes all wild-type animals, including inbred strains.

- This includes genetically normal parents of genetically altered offspring and genetically normal offspring.

- Triploid fish will generally be regarded as “Not genetically altered” unless induction of triploidy is specifically for a scientific purpose. If part of normal husbandry for the species (e.g. Salmonids) this should be reported as “Not genetically altered”.

‘Genetically altered animals (GAAs)’: includes all genetically modified animals (transgenic, knock-out and other forms of genetic alteration) and mutations, whether naturally occurring or induced.

2: ‘GAAs without a harmful phenotype’: includes all GAAs that do not show an overtly harmful phenotype, or individuals of strains on which a formal welfare assessment has been carried out which showed the strain to have either no phenotype or a phenotype of sub-threshold severity.

This category can apply to any purpose given in Column N. It includes animals used for the creation of new strains, animals used in further procedures and animals used for maintenance of established colonies.

Examples of GAA WITHOUT A HARMFUL PHENOTYPE

- Green fluorescent protein (GFP) expressing lines of mice or fish.
- Cre expressing lines of mice.
- Conditional genetic alterations without induction of conditional gene expression (assuming it is induction of expression that leads to harm, there may be examples where the reverse is the case).
- Transgenic and knockout mice which appear overtly normal

Also

- Strains of mice prone to disease, e.g. tumour development but used or killed prior to the onset of tumour development.

3: Genetically altered animals with a harmful phenotype.

- 'GAAs with a harmful phenotype' includes all GAAs that actually exhibit an overtly harmful phenotype at some time during the procedure. This category can apply to any purpose given in Column N. It includes animals used for the creation of new strains, animals used in further procedures and animals used for maintenance of established colonies, but only if a harmful phenotype manifests.

- If the strain is known to have a harmful phenotype but some individuals do not exhibit that phenotype, then do not use this category for those individuals, use 'Genetically altered animals without a harmful phenotype'.

Example of GAA WITH A HARMFUL PHENOTYPE

Immunocompromised mice, e.g. Nudes, SCID, Rag KO. Although all of this type of strain have potentially harmful phenotypes and must be reported as such, the actual severity is likely to be "Sub-threshold" (if not used in further experiments)

EXAMPLE: Nude mice bred but not used in further studies and culled as surplus.

All will be reported under "'Breeding/maintenance of colonies of established genetically altered animals, not used in other procedures" in column N.

Heterozygous offspring
"Genetically altered without a harmful phenotype", Actual severity "Sub-threshold".

Homozygous Nude offspring:
Genetically altered with a harmful phenotype", Actual severity "Sub-threshold".

Wild type offspring. Not reported (unless genotyped by a regulated method, e.g. tail biopsy).

Column M - Creation of a new genetically altered animal line

- This category includes all animals involved in the creation of a novel line up to the point where a new line is considered 'established'.

- This category includes the offspring from crossing of established lines of genetically altered animals; this is considered to lead to the creation of a new line. Crossing of a genetically altered animal with a wild type will not normally be considered to create a new line unless it is expected that the change of background will adversely affect the phenotype.

- Wild-type offspring that are not subjected to regulated procedures (for example, regulated genotyping methods) should not be reported.

- If "Yes" is used in this column, the purpose given in Column N **should not** be "Breeding/maintenance of colonies of established genetically altered animals, not used in other procedures"'. The purpose given in Column N should be the primary scientific purpose for which the new strain was being created.

- It **excludes** animals of established strains on which a formal welfare assessment has been carried out and excludes long-standing strains of GAAs even if no formal welfare assessment has been carried out. These are reported as "No" in column M and as "Breeding/maintenance of colonies of established genetically altered animals, not used in other procedures" in column N.

- Rederivation and archiving of lines is reported in column N as "Breeding/maintenance of colonies of established genetically altered animals, not used in other procedures" .

Columns N and O - Purpose

- Classification of purpose is divided into two columns.

- **Column N** for the high level purpose, e.g. "Basic research", "Translational/Applied research","Breeding/maintenance of colonies of established genetically altered animals, not used in other procedures".

- **Column O** Sub purpose is for the sub-category of "Basic research", "Translational/applied research" or "Regulatory use" only. The choices available in this column will be restricted to those relevant to the high level purpose given in column N. For example, if "Regulatory Use" is entered in column N then only the associated sub-categories will be available in column O.

- If "Breeding/maintenance of colonies of established genetically altered animals, not used in other procedures", "Higher education or training

for the acquisition, maintenance or improvement of vocational skills", "Forensic enquiries", "Protection of the natural environment in the interests of the health or welfare of human beings or animals" or "Preservation of species" is entered in column N then the drop-lists in Column O will be disabled and this column should be left blank.

- Choose the best fit for the purpose of the study. This will generally be the purpose given in the project licence.

1. Basic research includes studies of a fundamental nature, including physiology.

Studies that are designed to add knowledge about the normal and abnormal structure, functioning and behaviour of living organisms and the environment. These include 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.

Any animals used for the creation of a new genetically altered animal (GAA) line (including the crossing of two established lines) intended to be used for the purposes of basic research should be recorded according to the purpose they are being created for and should be reported as 'Yes' in Column M 'Creation of a new genetic line'.

Basic research categories

i. 'Oncology'. Any research studying oncology regardless of target system.
ii. 'Nervous system'. Includes neuroscience, peripheral or central nervous system, psychology.
iii. 'Sensory organs' (skin, eyes, ears).
You should report studies on the nose under 'Respiratory system' and those on the tongue under 'Gastrointestinal system including liver'.
iv. 'Multisystemic'. Should only include research where more than one system is the primary interest, for example, some infectious diseases. This category excludes 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. Dentistry should be reported under 'dentistry' not 'musculoskeletal system' ('dentistry' is a new sub-category included for the first time).
vii. 'Other'. Research not related to an organ/system listed above or is not organ/system specific.

Animals used for the production and maintenance of infectious agents, vectors and neoplasms or other biological material, and animals used for the

production of antibodies, but excluding production of monoclonal antibodies by ascites method (which is covered under purpose "Regulatory use" and sub-purpose "Routine production …"), should be reported under "Basic research" or 'Translational/applied research". Where the purpose could be reported under the two categories you should only report the main purpose.

2. Translational/applied research includes discovery toxicology, investigations prior to formal regulatory studies and method development. It includes efficacy testing during the development of new medicinal products. It **does not** include studies required for regulatory submissions.

Any animals used for the creation of a new genetically altered animal line (including the crossing of two established lines) intended to be used for the purposes of translational and applied research should be recorded according to the purpose they are being created for and should be reported as 'Yes' in Column L 'Creation of a new genetic line'.

Translational and applied research categories

i. "Human cancer". You should include any applied research studying human cancer, regardless of the target.
ii. "Human infectious disorders". You should include any applied research studying human infectious disorders, regardless of the target.
iii. Any regulatory use of animals is to be excluded, such as regulatory carcinogenicity studies.
iv. You should report studies on disorders of the nose under "Human respiratory disorders" and those of the tongue under "Human gastrointestinal disorders including liver".
v. Human dentistry should be reported under 'human dentistry' not 'musculoskeletal system' ('human dentistry' is a new sub-category included for the first time).
vi. Renal disease should be reported under "Human urogenital/reproductive disorders".
vii. "Diagnosis of diseases" includes animals used in direct diagnosis of diseases such as rabies, botulism, but excludes those covered under regulatory use.
viii. Non-regulatory toxicology' covers discovery toxicology and investigations prior to formalising the regulatory studies and method development. This category does not include studies required for regulatory submissions (preliminary studies, maximum tolerated dose).
ix. Animal welfare should include studies as per Article 5(b)(iii) of Directive 2010/63 EU i.e. "the welfare of animals and the improvement of the production conditions for animals reared for agricultural purposes"

3. 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 the regulatory use of animals used for ecotoxicology purposes.

4. Preservation of species. This includes research where the primary purpose is the preservation of a species.

5. Higher education or training for the acquisition, maintenance or improvement of vocational skills in the tertiary educational setting.

This includes training to acquire and maintain practical competence in techniques as required under Article 23(2) of Directive 2010/63 EU.

6. Forensic enquiries. This includes tests as part of forensic investigations and the production of materials, for example, antisera, for use in forensic investigations where this is not being carried out to meet a regulatory requirement.

7. Breeding/maintenance of colonies of established genetically altered animals, not used in other procedures.

This includes the animals required for the maintenance of colonies of genetically altered animals (GAAs); the intended purpose for which the line is being bred is not recorded (in contrast to “creation of new genetic lines”).

It includes genetically altered breeding stock and surplus animals unless killed for use of tissues post mortem, i.e. all of the GAA that are bred but not used for a further scientific purpose, whether regulated or not.

This category should be used for established or long-standing strains of GAAs, i.e. those that have had a welfare assessment carried out, or those that are generating animals being used in experimental procedures. The latter can be considered effectively “established”. You should report the creation of new strains under the purpose for which they are being created.
Breeding/maintenance of colonies of established genetically altered animals, not used in other procedures excludes:

- Genetically altered animals bred under project authorisation but killed using Schedule 1 listed methods whose tissues are then used for research: these should be reported under the purpose for which their tissues were used.
- Live animals that go on to be used in further regulated procedures.

Examples: HOW TO RETURN BREEDING AND MAINTENANCE OF COLONIES OF ESTABLISHED LINES OF GAA (B&M)

If the phenotype of offspring of a newly created line is not yet known, return under “Creation of new genetic line” (Column M) = Yes, then under appropriate purpose for which the new line was created, e.g. Basic Research (Column N) Oncology (Column O). **Do not record under Column N as B&M.**

If the line has been bred for more than 2 generations and its phenotype is known, further breeding should be reported under purpose as B&M. “Creation of new genetic line” = NO.
The line has no phenotype when heterozygous but homozygotes show paralysis from 6 months of age.
A heterozygous transgenic mouse is mated with a wild type mouse, and produces offspring:
- The transgenic parent is reported when it dies under: purpose B&M, genetic status “Genetically altered without a harmful phenotype” and actual severity “Sub-threshold”.
- The wild type parent is not reported
- All heterozygous offspring’s (F1) genetic status are reported as “Genetically altered without a harmful phenotype” and their actual severity are reported as “Sub-threshold”.
- Wild type offspring are not reported
- Occasional offspring have to have a second biopsy to confirm genotype. This cannot be considered identification and so must be included in the severity assessment. These will be reported as actual severity = “Mild”, reflecting the biopsy procedure, whether transgenic or wild type.

The next generation is bred by crossing 2 heterozygous offspring:
- Parents (F1) are returned under genetic status as “Genetically altered without a harmful phenotype”, under purpose as B&M and under actual severity as “Sub-threshold”, when they are eventually culled.
- Homozygous offspring (F2) culled at 3 months of age, before appearance of phenotype: are recorded under genetic status as “Genetically altered without a harmful phenotype” and under actual severity as “Sub-threshold”
- Some of these were used for tissues following Schedule 1 killing, these should be reported under the purpose for which the tissues were used, not under B&M.
- Some offspring were kept and culled because they developed paralysis. If these mice were discarded and tissues not used return under: purpose B&M, genetic status “Genetically altered with a harmful phenotype” and actual severity “Severe”.

8. Regulatory use and routine production - 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 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.

This category also includes animals used in the manufacturing process of products *if that manufacturing process requires regulatory approval* (for example, animals used in the manufacturing of serum-based medicinal products should be included within this category). This includes quality assurance and potency testing of biologicals.

The efficacy testing during the development of new medicinal products is excluded and you should report this under "Translational/applied research".

Categories of regulated use and routine production:

- **Routine production**. Applies to manufacturing processes requiring regulatory approval.
    - PR51 Routine production/blood-based products: Blood products including serum and polyclonal antisera by established methods.
    - PR52 Routine production/monoclonal antibodies: Covers the production of monoclonal antibodies by ascites. This excludes immunisation of animals for hybridoma production, which should be captured under 'Basic research' or 'Translational and applied research' under the appropriate category.
    - PR53 Other forms of production of biological material to meet regulatory standards or requirements that use live animals.

Note that production of antibodies, antigens etc. using routine or standard methods but not to meet a regulatory requirement should be reported under "Basic research", "Translational/applied research" etc.

- **Quality control (including batch safety and potency testing)** 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. It also includes 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.

- PR61 (Quality control) Batch safety testing. Batch safety testing excludes pyrogenicity testing.
- PR62 (Quality control) Pyrogenicity testing.
- PR63 (Quality control) Batch potency testing.
- PR64 (Quality control) Other quality controls.

- **PR71 (Regulatory use) 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.

  Combined tolerance/efficacy studies, dose range finding studies and maximum tolerated dose studies when being carried out to support regulatory submissions should be reported under this category.

- **Toxicity and other safety testing including pharmacology by test type -** Includes safety evaluation of products and devices for human medicine and dentistry and veterinary medicine. This 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, as a result of its manufacture or as a potential or actual contaminant in the environment.

  - Choose the most appropriate test description.

  - Immunotoxicology studies should be reported under "Repeated dose toxicity".

  - Kinetics (pharmacokinetics, toxicokinetics, residue depletion): If toxicokinetics is performed as part of the regulatory repeat dose toxicity study, you should report it under 'Repeated dose toxicity'.

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

  - Target animal safety: This is testing to ensure that a product for a specific animal can be used safely on that species (excluding batch safety testing, which is covered under "Quality control").

Column P - Other

- If you have chosen any of the "Other"' categories of testing you should provide details in this column.

Column Q - Testing by legislation

- The legislative requirement should be entered as per the *intended primary* use. For example, in relation to water quality, if it is concerning tap water for drinking you should report it under "Food legislation".

Column R

- If you have entered “Other” in Column P provide details in this column.

Column S - Legislative requirements (origin of the legislation)

- 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.

- Where national legislation is derived from EU legislation, only ”Legislation satisfying EU requirements” should be chosen. “Legislation satisfying EU requirements” also includes any international requirement that at the same time satisfies EU requirements (such as testing to the guidelines of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH), the Organisation for Economic Cooperation and Development (OECD), and European Pharmacopoeia monographs).

- “Legislation satisfying UK requirements only” is to be chosen only when the test is carried out to satisfy UK requirements and there is no equivalent requirement in the EU.

- “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.

Column T - Severity

You should give the actual severity that animals used on the procedure experienced, **not** the severity classification or limit of the protocol.

Refer to the Home Office document “Advisory notes on recording and reporting the actual severity of regulated procedures” for detailed guidance on this:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/276014/NotesActualSeverityReporting.pdf

and on severity assessment for breeding and maintenance of genetically altered animals:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/276015/AdviceSeverityAssessmentGA.pdf

Assign the severity to one of the categories:

- sub-threshold;
- mild;
- moderate;
- severe; or
- non-recovery.

If different animals on a study suffered different levels of severity you should enter a separate line for each class of severity.

Sub-threshold severity is chosen when a procedure was regulated, and therefore it was considered that the procedure might have caused mild, moderate or severe suffering, but which in retrospect did not.

Whenever the severe classification is exceeded*, whether pre-authorised or not, you should report these animals and their use normally like any other use, and under the “severe” category. You should add further details in the Comments1 column (column W) explaining:

- whether prior exemption was authorised;
- the details of the use; and
- the reasons why the severe classification was exceeded.

*This would be if an animal was suffering severe prolonged pain that was not alleviated.

Reporting of wild animals used in procedures under ASPA.

- Procedures should be reported and severity assessed at the end of a procedure; this poses challenges for work in the wild.

- The procedures should be reported in the best way practicable, following guidance given in separate documents on “Work in the Wild” and on Severity, available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/535574/working-with-wild-animals-160706.pdf

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/276014/NotesActualSeverityReporting.pdf

- Where possible animals should be reported when the procedure ends or the animal is known to have died. If this is not practicable then:

    1. At the end of the study when attempts to recapture are no longer made
    2. At the end of the relevant project licence when the work will not continue on another licence

- There will often be uncertainty as to the fate of animals in the wild. Refer to the above guidance and discuss this with your local inspector.

Column V - Techniques of special interest

- Household product testing. Choose this option only if the work involved safety testing of substances used in the household.

- Use of ascites models for monoclonal antibody production. Choose this option only if monoclonal antibodies were harvested from ascites fluid. Do not use this option for immunisation of animals to provide tissues to generate monoclonal antibodies *in vitro*.

- Tobacco. Choose this option only for the safety testing of products containing tobacco, not for use of nicotine or other compounds found in tobacco and not for use of tobacco in disease models.

- Alcohol. Choose this option only for the safety testing of products containing alcohol, not for the use of alcohol as a research tool or in disease models.

Column W - Comments 1

Use this column to add comments for the attention of the Home Office, e.g. the reason for using large numbers of animals.

Column X - Comments 2

Use this column to add comments that are not relevant to the Home Office but are for your own reference/information only e.g. study reference numbers.

Annex - Code lists

PLEASE NOTE: These lists are for information only. To ensure that the data you provide is correct, please select the options available to you in the drop-down lists in the data collection template. What appears in the drop-down lists, in some instances, will depend on what was selected in the preceding columns.

Animal Species (Column E)

[A1] Mice (Mus musculus)
[A2] Rats (Rattus norvegicus)
[A3] Guinea-Pigs (Cavia porcellus)
[A4] Hamsters (Syrian) (Mesocricetus auratus)
[A5] Hamsters (chinese) (Cricetulus griseus)
[A6] Mongolian gerbil (Meriones unguiculatus)
[A7] Other Rodents (other Rodentia)
[A8] Rabbits (Oryctolagus cuniculus)
[A9] Cats (Felis catus)
[A10_1] Beagles (Canis lupus familiaris)
[A10_2] Other dogs (Other Canis)
[A11] Ferrets (Mustela putorius furo)
[A12] Other carnivores (other Carnivora)
[A13] Horses, donkeys & cross-breeds (Equidae)
[A14] Pigs (Sus scrofa domesticus)
[A15] Goats (Capra aegagrus hircus)
[A16] Sheep (Ovis aries)
[A17] Cattle (Bos primigenius)
[A18] Prosimians (Prosimia)
[A19] Marmoset and tamarins (eg. Callithrix jacchus)
[A20] Cynomolgus monkey (Macaca fascicularis)
[A21] Rhesus monkey (Macaca mulatta)
[A22] Vervets Chlorocebus spp. (usually either pygerythrus or sabaeus)
[A23] Baboons (Papio spp.)
[A24] Squirrel monkey (eg. Saimiri sciureus)
[A25-1] Other species of Old World Monkeys (Cercopithecoidea)
[A25-2] Other species of New World Monkeys (Ceboidea)
[A26] Apes (Hominoidea)
[A27] Other Mammals (other Mammalia)
[A28] Domestic fowl (Gallus gallus domesticus)
[A29_1] Quail (Coturnix coturnix)
[A29_2] Other birds (other Aves)
[A30] Reptiles (Reptilia)
[A31] Rana (Rana temporaria and Rana pipiens)
[A32] Xenopus (Xenopus laevis and Xenopus tropicalis)
[A33] Other Amphibians (other Amphibia)
[A34] Zebra fish (Danio rerio)

[A35] Other Fish (other Pisces)

[A36] Cephalopods (Cephalopoda)

Place of birth (Column I)

[O1_1] Animals born in the UK at a licensed establishment

[O1_2] Animals born in the EU (non UK) at a registered breeder

[O2_1] Animals born in the UK but **NOT** at a licensed establishment

[O2_2] Animals born in the EU (non UK) but **NOT** at a registered breeder

[O3] Animals born in rest of Europe

[O4] Animals born in rest of world

Non-human Primate Source (Column J)

[NHPO1_1A] Animals born in the UK at a licensed establishment

[NHPO1_2A] Animals born in the EU (non UK) at a registered breeder

[NHPO1_1B] Animals born in the UK but **NOT** at a licensed establishment

[NHPO1_2B] Animals born in the EU (non UK) but **NOT** at a registered breeder [NHPO2] Animals born in rest of Europe

[NHPO3] Animals born in Asia

[NHPO4] Animals born in America

[NHPO5] Animals born in Africa

[NHPO6] Animals born elsewhere

NHP Generation (Column K)

[NHPG1] F0

[NHPG2] F1

[NHPG3] F2 or greater

[NHPG4] Self-sustaining colony

Genetic status (Column L)

[GS1] Not genetically altered

[GS2] Genetically altered without a harmful phenotype

[GS3] Genetically altered with a harmful phenotype

Purpose (Columns N and O)

[PB1] (Basic Research) Oncology

[PB2] (Basic Research) Cardiovascular Blood and Lymphatic System

[PB3] (Basic Research) Nervous System

[PB4] (Basic Research) Respiratory System

[PB5] (Basic Research) Gastrointestinal System including Liver

[PB6_1] (Basic Research) Musculoskeletal System

[PB6_2] (Basic Research) Dentistry

[PB7] (Basic Research) Immune System

[PB8] (Basic Research) Urogenital/Reproductive System

[PB9] (Basic Research) Sensory Organs (skin, eyes and ears)

[PB10] (Basic Research) Endocrine System/Metabolism

[PB11] (Basic Research) Multisystemic
[PB12] (Basic Research) Ethology / Animal Behaviour /Animal Biology
[PB13] (Basic Research) Other
[PT21] (Trans/Appl Research) Human Cancer
[PT22] (Trans/Appl Research) Human Infectious Disorders
[PT23] (Trans/Appl Research) Human Cardiovascular Disorders
[PT24] (Trans/Appl Research) Human Nervous and Mental Disorders
[PT25] (Trans/Appl Research) Human Respiratory Disorders
[PT26] (Trans/Appl Research) Human Gastrointestinal Disorders including Liver
[PT27_1] (Trans/Appl Research) Human Musculoskeletal Disorders
[PT27_2] (Trans/Appl Research) Human Dentistry
[PT28] (Trans/Appl Research) Human Immune Disorders
[PT29] (Trans/Appl Research) Human Urogenital/Reproductive Disorders
[PT30] (Trans/Appl Research) Human Sensory Organ Disorders (skin, eyes and ears)
[PT31] (Trans/Appl Research) Human Endocrine/Metabolism Disorders
[PT32] (Trans/Appl Research) Other Human Disorders
[PT33] (Trans/Appl Research) Animal Diseases and Disorders
[PT34] (Trans/Appl Research) Animal Welfare
[PT35] (Trans/Appl Research) Diagnosis of diseases
[PT36] (Trans/Appl Research) Plant diseases
[PT37] (Trans/Appl Research) Non-regulatory toxicology and ecotoxicology
[PE40] Protection of the natural environment in the interests of the health or welfare of human beings or animals
[PS41] Preservation of species
[PE42] Higher education or training for the acquisition, maintenance or improvement of vocational skills
[PF43] Forensic enquiries
[PG43] Breeding/maintenance of colonies of established genetically altered animals, not used in other procedures
[PR51] (Regulatory use/ Routine production) Blood based products
[PR52] (Regulatory use/ Routine production) Monoclonal antibodies
[PR53] (Regulatory use/ Routine production) Other
[PR61] (Regulatory use/ Quality control) Batch safety testing

[PR62] (Regulatory use/ Quality control) Pyrogenicity testing
[PR63] (Regulatory use/ Quality control) Batch potency testing
[PR64] (Regulatory use/ Quality control) Other quality controls
[PR71] (Regulatory use) Other efficacy and tolerance testing
[PR81] (Regulatory use/Toxicity and../Acute and sub-acute) LD50, LC50
[PR82] (Regulatory use/Toxicity and../Acute and sub-acute) Other lethal methods
[PR83] (Regulatory use/Toxicity and../Acute and sub-acute) Non lethal methods
[PR84] (Regulatory use/Toxicity and..) Skin irritation/corrosion
[PR85] (Regulatory use/Toxicity and..) Skin sensitisation
[PR86] (Regulatory use/Toxicity and..) Eye irritation/corrosion
[PR87] (Regulatory use/Toxicity and../Repeated dose toxicity) up to 28 days
[PR88] (Regulatory use/Toxicity and../Repeated dose toxicity) 29 - 90 days
[PR89] (Regulatory use/Toxicity and../Repeated dose toxicity) > 90 days
[PR90] (Regulatory use/Toxicity and..) Carcinogenicity
[PR91] (Regulatory use/Toxicity and..) Genotoxicity
[PR92] (Regulatory use/Toxicity and..) Reproductive toxicity
[PR93] (Regulatory use/Toxicity and..) Developmental toxicity
[PR94] (Regulatory use/Toxicity and..) Neurotoxicity
[PR95] (Regulatory use/Toxicity and..) Kinetics
[PR96] (Regulatory use/Toxicity and..) Pharmaco-dynamics (incl safety pharmacology)
[PR97] (Regulatory use/Toxicity and..) Phototoxicity
[PR98] (Regulatory use/Toxicity and../Ecotoxicity) Acute toxicity
[PR99] (Regulatory use/Toxicity and../Ecotoxicity) Chronic toxicity
[PR100] (Regulatory use/Toxicity and../Ecotoxicity) Reproductive toxicity
[PR101] (Regulatory use/Toxicity and../Ecotoxicity) Endocrine activity
[PR102] (Regulatory use/Toxicity and../Ecotoxicity) Bioaccumulation
[PR103] (Regulatory use/Toxicity and../Ecotoxicity) Other
[PR104] (Regulatory use/Toxicity and..) Safety testing in food and feed area

[PR105] (Regulatory use/Toxicity and..) Target animal safety

[PR106] (Regulatory use/Toxicity and..) Other

Testing by legislation (Column Q)

[LT1] Legislation on medicinal products for human use

[LT2] Legislation on medicinal products for veterinary use and their residues

[LT3] Medical devices legislation

[LT4] Industrial chemicals legislation

[LT5] Plant protection product legislation

[LT6] Biocides legislation

[LT7] Food legislation including food contact material

[LT8] Feed legislation including legislation for the safety of target animals, workers and environment

[LT9] Cosmetics legislation

[LT10] Other

Legislative requirements (Column S)

[LO1] Legislation satisfying EU requirements

[LO2] Legislation satisfying national requirements only [within EU]

[LO3] Legislation satisfying Non-EU requirements only

Actual severity (Column T)

Sub-threshold

[SV1] Non-recovery

[SV2] Mild

[SV3] Moderate

[SV4] Severe

Techniques of Special Interest (Column V)

None

Household product testing

Use of ascites models for monoclonal antibody production

Tobacco

Alcohol