HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Annual statistical report for animals used in Ireland under scientific animal protection legislation - 2019

07 DECEMBER 2020

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1 INTRODUCTION

The Health Products Regulatory Authority (HPRA) is the state agency with responsibility for the protection of animals used for scientific purposes, the regulation of human and veterinary clinical trials, and the regulation of human and veterinary medicines, medical devices and other health products, amongst other regulatory functions. From 1 January 2013, an EU Directive[1] to protect animals used for scientific purposes came into effect in Ireland. In January 2013, the HPRA became the competent authority responsible for the Directive's implementation, and thus has been publishing statistical data on animals used from 2013 onwards.

The Directive is among the world's most advanced pieces of legislation concerning animal welfare. The restrictions and standards set by the Directive aim to enhance animal welfare and ensure that animals are used in studies only when their use is strongly justified and following independent assessment. The Directive firmly anchors in EU Legislation the 3Rs principles, i.e. Replacement, Reduction and Refinement:

- **Replacement** involves the acceleration of the development and use of models and tools, based on the latest science and technologies, to address important scientific questions without the use of animals. Examples of alternative methods would include *in vitro* tests such as the use of cell lines, computer and mathematical simulation and modelling, video material, or the use of invertebrates such as fruit flies or worms.

- **Reduction** refers to methods that minimise the number of animals used per project or study consistent with the scientific aims. It is essential that studies using animals are appropriately designed and analysed to ensure robust and reproducible findings. Reduction also includes methods that allow the information gathered per animal in a study to be maximised in order to reduce the use of additional animals. Examples of this include the use of some imaging modalities which allow repeated measurements in the same animal to be taken over time (rather than, for example, imaging different animals at each time point) or microsampling of blood, where limiting the amount of blood taken each time to small volumes enables repeat sampling in the same animal.

- **Refinement** refers to methods that minimise the pain, suffering, distress or lasting harm that may be experienced by the animals, and which improve their welfare. Refinement means that animals are provided with the best possible care and this applies to all aspects of animal use, from the animals' housing and husbandry to the scientific procedures performed on them. Examples of refinement include ensuring that animals are provided with housing that allows the expression of species-specific behaviours, using appropriate anaesthesia and analgesia to minimise pain, and training animals to cooperate with procedures to minimise any stress.

Although complete replacement of animal studies is the ultimate goal of the Directive, for the moment the use of live animals continues to be necessary to protect human and animal health and the environment. Where biological processes are not sufficiently understood or are very complex, non-animal research or test methods are often not available. After generating as much information as possible using non-animal alternatives, animal studies can be necessary to fill knowledge gaps. However, the Directive plays a vital role in protecting and improving the welfare of those animals that are required to be used for scientific purposes.

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[1] 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

The HPRA regulates the sector by means of authorisation at three levels:

1. **Breeder/supplier/user establishments:** Breeders and suppliers of animals, as well as establishments where procedures are performed, must be authorised and are subject to HPRA inspections, including unannounced inspections. In 2019, the HPRA performed 31 inspections, of which 32% were unannounced. The HPRA was satisfied with overall levels of compliance nationally.

2. **Projects:** Scientific procedures involving animals can only take place following a detailed submission of the planned study/studies and subsequent approval by the HPRA on the basis of a favourable harm/benefit analysis.

3. **Individuals:** Any person wishing to carry out scientific procedures involving animals, as well as project managers and those conducting euthanasia in an authorised establishment, must be adequately trained to do so and hold a HPRA individual authorisation.

The HPRA aims to improve the welfare of animals used for scientific purposes and to promote the principles of the 3Rs. Every application received for a project involving animals is subject to a detailed evaluation process rooted in the 3R principles, and requires scientific justification for the research techniques being applied. The likely impact on the animals must be minimised in so far as possible by applying all appropriate refinements, and any harms experienced by the animals must be outweighed by the expected benefits of the work. The HPRA considers whether alternative (non-animal) methods are available or appropriate, as alternatives to the use of live animals must be used where possible. In fulfilment of the HPRA's mandate to promote the 3Rs, in 2019 the HPRA continued its ongoing efforts to enhance awareness and utilisation of non-animal alternatives. The HPRA also continued to promote the application of the principles of Replacement, Reduction and Refinement in the conduct of scientific studies in animals through its work, including the regular dissemination of pertinent information to the regulated sector.

The objective of this report is to present statistical data on the number of uses of animals for scientific purposes in Ireland during 2019 in accordance with Article 54(2) of the Directive. This is the seventh report to be prepared by the HPRA since it became the competent authority for the protection of animals used for scientific purposes. The Department of Health published all reports in this area prior to 2013.

As in previous years, the data provided are based on self-declarations by the establishments concerned. The data are presented in this report in accordance with the Commission Implementing Decision 2020/569//EU, which sets out a common format for the submission of information to the European Commission. As a result of this new implementing decision, there are changes to the format of this report in comparison with the annual reports published by the HPRA for the years up to 2018. In line with the first EU summary report under Directive 2010/63/EU (published in February 2020) on the statistics on the use of animals used for scientific purposes by the Member states of the Union from 2015 – 2017, data has been categorised in this report as follows:

- number of animals used in research, testing, routine production and educational (including training) purposes[2]
- details of all uses (first and any subsequent reuse) of animals for research and testing

[2] Hereafter referred to as 'research and testing'

- numbers and uses of animals for the creation and maintenance of genetically altered animal lines

There are significant differences in the reporting requirements under Directive 2010/63/EU versus those under earlier legislation. The newer requirements provide significantly more detailed and tailored information on animal use. They include aspects of animal use, which have not previously been available, for example, on the genetic status of animals and the actual severity experienced by the animals during their use in procedures.

The main differences from reports published under legislation prior to the Directive are:

- Previous data (i.e. prior to 2013) reported only on the first use of each animal, whereas this report includes any subsequent uses of the same animals (reuse).
- Each use of an animal must now be assigned to a specific project purpose outlined by the legislation, e.g. basic research, translational and applied research, regulatory use etc.
- The breeding of genetically altered animal lines was not required to be included in previous reporting years and this is now a requirement of the legislation.
- The actual severity experienced by the animals must now be reported under four categories: non-recovery, mild, moderate or severe.

Please refer to the Appendix for definitions relating to some of the terminology used in this report.

2 SUMMARY

In 2019, there were a total of 138,439 uses of animals in procedures for research and testing purposes, with reuse representing <2% of this number (2,275 animals). 136,164 animals were reported as being used for the first time for research and testing purposes in 2019. Mice were the most commonly used species at 69% of the total animal use. In addition, 904 mice were reported as having been used to create and maintain colonies of genetically altered animals. These 904 mice are not considered by the European Commission to have been directly used in research and testing.

Of the total number of uses of animals in procedures for research and testing purposes, 70% were used for regulatory purposes, which refers to legal requirements to test the safety, quality and potency of medicines (e.g. biological medicines such as vaccines). Of the total number of uses of animals in procedures for research and testing purposes, 11,604 involved genetically altered animals, which represents 8% of all animal use.

The most frequently reported actual severity experienced by animals during their uses in procedures for research and testing purposes was mild at 56%, followed by moderate at 29%. Of the animals reported as being used for the creation and maintenance of genetically altered lines, 83% were reported as having experienced an actual severity of mild.

3 DATA ON THE USES OF ANIMALS FOR RESEARCH AND TESTING PURPOSES

3.1 Species and numbers of uses of animals for research and testing purposes

Table 1 shows the number of animals used (by species) for the first time in procedures performed for research and testing purposes. Each use of an animal extends from the time when

the first intervention is applied to the animal until the completion of data collection under a project, or when the animal is removed from the project.

Mice (70% of total first uses of animals) were by far the most commonly used species. The next most commonly used species was rats, followed by fish. The category 'other fish' (4%) primarily represents wild fish being studied for conservation projects. For example, European eels are a critically endangered species and Irish salmon stocks are critically low, so monitoring projects are required to improve the survival of these species. Likewise, the category 'other birds' (<1%) represents wild bird species such as brent geese being studied in monitoring and conservation projects. The category 'other mammals' includes deer, and badgers (used in studies researching diseases in these species), and grey seals, which were studied in a conservation project. It should be noted that the following species have been excluded from this table as they were not used in Ireland in 2019: hamsters (Chinese), Mongolian gerbils, other rodents, cats, dogs, other carnivores, reptiles, rana, other amphibians, cephalopods and non-human primates.

Table 1: Numbers animals used for the first time by species

Animal species	Number of uses	Percentage
Mice	95,596	70.21%
Rats	22,994	16.89%
Guinea pigs	603	0.44%
Hamsters (Syrian)	6	0.00%
Rabbits	552	0.41%
Ferrets	403	0.30%
Horses, donkeys and cross-breeds	19	0.01%
Pigs	323	0.24%
Goats	26	0.02%
Sheep	703	0.52%
Cattle	3,417	2.51%
Other mammals	28	0.02%
Domestic fowl	80	0.06%
Other birds	673	0.49%
Xenopus	16	0.01%
Zebrafish	5,219	3.83%
Other fish	5,506	4.04%
Total uses	**136,164**	**100.00%**

Table 2 shows the total numbers of all uses of animals (first time and reuse) in procedures performed for research and testing purposes, broken down by species.

Table 2: Numbers animals used (first time and reuse) by species

Animal species	First uses	Reuses	Percentage of reuses	Total uses (first use + reuse)
Mice	95,596	0	0.00%	95,596
Rats	22,994	0	0.00%	22,994
Guinea pigs	603	0	0.00%	603
Hamsters (Syrian)	6	0	0.00%	6
Rabbits	552	0	0.00%	552
Ferrets	403	0	0.00%	403
Horses, donkeys and cross-breeds	19	10	34.48%	29
Pigs	323	0	0.00%	323
Goats	26	0	0.00%	26
Sheep	703	259	26.92%	962
Cattle	3,417	2,003	36.96%	5,420
Other mammals	28	3	9.68%	31
Domestic fowl	80	0	0.00%	80
Other birds	673	0	0.00%	673
Xenopus	16	0	0.00%	16
Zebrafish	5,219	0	0.00%	5,219
Other fish	5,506	0	0.00%	5,506
Total uses	**136,134**	**2,275**	**1.64%**	**138,439**

3.2 Reuse of animals

Table 2 (above) shows the proportion of reuse (see Appendix for definition), which represents 1.64% of total animal use. Animals are only permitted to be reused on second or subsequent projects if the severity they have experienced to date is mild or moderate (see Appendix for definition of severity categories). It should be noted that the true number of animals that are reused cannot be deduced from this data due to the fact that some animals may be reused more than once (i.e. the figure 2,275 represents *uses of animals,* not actual numbers of animals reused). Horses, sheep, cattle and badgers were the species reused during 2019. In Ireland, sheep and cattle are used only for agricultural research studies (for the benefit of the species, the environment or the agricultural sector). The overwhelming majority of projects of this nature are of overall mild severity, with only a tiny minority reaching moderate severity. In 2019, horses were used exclusively in projects with the purpose of higher education or training of veterinary medicine or equine science undergraduate students, all of which are of overall mild severity. Three badgers were reused in a project related to badger health, again of overall mild severity. Since the severity experienced by each of the species on previous studies is strictly limited to mild or moderate, and they return to full general health between projects, their reuse in further projects is permissible under the legislation.

3.3 Origin of animals at the first use

Table 3 shows the number of animals according to their place of birth, but only includes animals used for the first time as the place of birth is not recorded for animals on their second

(or subsequent) use(s). The majority (95%) of animals were born in the EU at a registered breeder, which means that they were born at breeding establishments authorised under the Directive. Animals born in the EU but not at a registered breeder (4%) include wild animals and farm animals. Animals born in the rest of Europe and the rest of the world (<1%) includes animals that have been obtained from breeding establishments outside the EU (e.g. specific strains of mice not available in the EU) as well as wild animals that have travelled into Ireland from other regions (e.g. migratory birds).

Table 3: Origin of animals at the first use

Place of Birth	Number of uses	Percentage
Animals born in the EU at a registered breeder	129,395	95.03%
Animals born in the EU not at a registered breeder	6,007	4.41%
Animals born in rest of Europe	10	0.01%
Animals born in rest of world	752	0. 55%
Total uses	136,164	100.00%

3.4 Project purposes

Table 4 shows the primary purposes for which animals were used for research and testing purposes. The most common primary purpose at 70% was 'Regulatory use and routine production'. This is defined as the 'use of animals in procedures 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'.

The primary purposes are further sub-divided in Tables 5-11. It should be noted that the primary purpose 'Forensic enquiries' was excluded from this table as no uses were reported under this purpose in 2019.

Table 4: Primary purpose for which animals are used

Primary purpose	Number of uses	Percentage
Basic research	13,910	10.05%
Translational and applied research	22,341	16.14%
Regulatory use and routine production	96,810	69.93%
Protection of the natural environment in the interests of the health or welfare of human beings or animals	5,043	3.64%
Preservation of the species	18	0.01%
Higher education or training for the acquisition, maintenance or improvement of vocational skills	317	0.23%
Total uses	**138,439**	**100.00%**

Table 5 shows the number of uses of animals in more specific categories of 'Basic research'. 'Basic research' refers to studies of a fundamental nature, which are designed to add knowledge about the structure, functioning or behaviour of organisms. It should be noted that the sub-fields of 'urogenital/reproductive system' and 'other basic research' were excluded from this table as no uses under these sub-fields were reported for 2019.

The most common sub-field of 'Basic research' at 31% was 'ethology/animal behaviour/animal biology'. In Ireland, this is mainly accounted for by agricultural research (e.g. nutrition and reproduction studies in farm animals) or research into the behaviour of wild animals (e.g. fish or bird tracking studies).

The next most common purpose was research into the nervous system (30%). Nervous system research involves studies that look at particular cells and disorders related to diseases of the brain and spinal cord, e.g. Alzheimer's, Parkinson's, and multiple sclerosis. These types of studies most commonly use mice and rats.

Table 5: Uses of animals for basic research

Basic Research	Number of uses	Percentage
Oncology	193	1.39%
Cardiovascular, blood and lymphatic system	71	0.51%
Nervous system	4,203	30.22%
Respiratory system	338	2.43%
Gastrointestinal system including liver	433	3.11%
Musculoskeletal system	38	0.27%
Immune system	2,724	19.58%
Sensory organs (skin, eyes and ears)	898	6.46%
Endocrine system/metabolism	294	2.11%
Multisystemic	429	3.08%
Ethology / animal behaviour /animal biology	4,289	30.83%
Total uses	**13,910**	**100%**

Table 6 shows the number of uses of animals in more specific categories of 'Translational and applied research', which refers to studies which aim to prevent, diagnose, detect or treat disease in animals or humans as well as studies which aim to improve animal welfare. It should be noted that the sub-fields of 'other human disorders' and 'non-regulatory toxicology and ecotoxicology' were excluded from this table as no uses under these sub-fields were reported for 2019.

The most common purpose at 28% was research into human nervous and mental disorders, which includes research into diagnostics and treatments for diseases such as epilepsy, autism, and depression, using mice and rats. The next most common purpose, at 24%, was research into human sensory organ disorders (skin, eyes and ears). The large majority of these studies are investigations into treatments for blindness, and zebrafish represent 95% of the animals used for this type of research.

Table 6: Uses of animals for translational and applied research

Translational and applied research	Number of uses	Percentage
Human cancer	695	3.11%
Human infectious disorders	588	2.63%
Human cardiovascular disorders	964	4.31%
Human nervous and mental disorders	6,349	28.42%
Human respiratory disorders	248	1.11%
Human gastrointestinal disorders including liver	1,366	6.11%
Human musculoskeletal disorders	2,034	9.10%
Human immune disorders	587	2.63%
Human urogenital/reproductive disorders	136	0.61%
Human sensory organ disorders (skin, eyes and ears)	5,387	24.11%
Human endocrine/metabolism disorders	901	4.03%
Animal diseases and disorders	2,275	10.18%
Animal welfare	410	1.84%
Diagnosis of diseases	398	1.78%
Plant diseases	3	0.01%
Total uses	**22,341**	**100%**

Table 7 shows the breakdown of animal uses for 'Regulatory use and routine production'. It should be noted that the sub-field of 'other efficacy and tolerance testing' was excluded from this table as no uses under this sub-field were reported for 2019. Regulatory testing refers to procedures carried out with a view to satisfying legal requirements for producing, placing and maintaining products/substances on the market. The majority of reported uses (>99%) can be attributed to quality control testing.

Table 7: Uses of animals for regulatory testing

Regulatory use	Number of uses	Percentage
Quality control (including batch safety and potency testing)	96,172	99.34%
Toxicity and other safety testing including pharmacology	200	0.21%
Routine production	438	0.45%
Total uses	**96,810**	**100%**

Table 8 shows a further breakdown of animal use for 'Quality control' tests. It should be noted that 'other quality controls' were excluded from this table as no uses were reported under this purpose for 2019. Quality control refers to animals used in the testing of purity, stability, efficacy, and potency parameters of a final medicinal product, in order to satisfy regulatory requirements. The majority of quality control tests were for batch potency (97%), and of these tests, 81% were performed on mice. Batch potency testing is required for biological products, which are products made in a living system such as a microorganism, or plant or animal cells, as opposed to being manufactured through chemical synthesis. The nature of biological products is that they can be inherently variable, and therefore it is necessary to perform batch potency testing to ensure that each manufactured batch of product is of a consistent strength, and therefore both safe and effective for patients. It is also required as a safety/efficacy test for

certain types of vaccine. In relation to pyrogenicity testing (<1%), non-animal alternatives have been developed to replace this type of testing for certain medicines. However, there are still some limited circumstances in which it is not possible to use a non-animal alternative to test for pyrogenicity, and therefore it is necessary to continue to employ animal-based tests in some instances.

Table 8: Uses of animals for regulatory testing - quality control

Quality control	Number of uses	Percentage
Batch safety testing	2,765	2.88%
Pyrogenicity testing	525	0.55%
Batch potency testing	92,882	96.58%
Total uses	**96,172**	**100.00%**

Table 9 shows a further breakdown of animal use for 'Toxicity and other safety testing'. All of these tests were for ecotoxicity testing.

Table 9: Uses of animals for regulatory testing - toxicity and other safety testing including pharmacology

Toxicity and other safety testing	Number of uses	Percentage
Acute and sub-acute testing	0*	0%
Skin irritation/corrosion	0	0%
Skin sensitisation	0	0%
Eye irritation/corrosion	0	0%
Repeated dose toxicity	0**	0%
Carcinogenicity	0	0%
Genotoxicity	0	0%
Reproductive toxicity	0	0%
Developmental toxicity	0	0%
Neurotoxicity	0	0%
Kinetics	0	0%
Pharmaco-dynamics (incl safety pharmacology)	0	0%
Phototoxicity	0	0%
Ecotoxicity	200	100%
Safety testing in food and feed area	0	0%
Target animal safety testing	0	0%
Other toxicity/safety testing	0	0%
Total uses	**200**	**100%**

*No uses were reported for 'Acute and sub-acute testing', therefore no additional 'Acute and sub-acute toxicity testing methods' table provided in this report.
**No uses were reported for 'Repeated dose toxicity', therefore no additional 'Repeated dose toxicity' table provided in this report.

Table 10 shows a further breakdown of animal use for 'Ecotoxicity'. All tests performed were reported under the category 'Acute toxicity', therefore the other categories were excluded from this table as no uses were reported. All of the ecotoxicity tests reported were conducted using fish.

Table 10: Regulatory uses – Toxicity and other safety testing including pharmacology – Ecotoxicity

Regulatory uses - Toxicity and other safety testing including pharmacology - Ecotoxicity	Number of uses	Percentage
Acute toxicity	200	100.00%
Total uses	**200**	**100.00%**

Table 11 shows a further breakdown of animal use for 'Routine production uses by product type'. Animals reported under this category were all used for the production of blood based products. This refers to the collection of animal blood for use in other regulatory tests required under legislation for human medicinal products (the other categories were excluded from this table as no uses were reported).

Table 11: Routine production uses by product type

Product type	Number of uses	Percentage
Blood based products	438	100.00%
Total uses	**438**	**100.00%**

3.5 Use of animals to meet legislative requirements

Table 12 shows which type of legislation is being satisfied in the performance of the regulatory tests for which animals were used. Only categories of legislation under which animal use was reported are included in this table. The vast majority (>99%) were performed on medicinal products manufactured for use in humans. <1% of uses were to satisfy legislation on medicinal products for veterinary use and their residues. The category 'other legislation' is accounted for by ecotoxicity testing (also <1%) performed under pollution control legislation. **Table 13** shows the geographical origin of the legal requirement. All tests were performed to satisfy EU legislative requirements.

Table 12: Regulatory testing by type of legislation

Testing by Legislation	Number of uses	Percentage
Legislation on medicinal products for human use	96,062	99.68%
Legislation on veterinary medicinal products	110	0.11%
Other legislation	200	0.21%
Total uses	**96,372**	**100.00%**

Table 13: Origin of legislative requirement

Legislative Requirement	Number of uses	Percentage
Legislation satisfying EU requirements	96,372	100.00%
Legislation satisfying national requirements only [within EU]	0	0%
Legislation satisfying non-EU requirements only	0	0%
Total uses	93,372	100.00%

3.6 Use by genetic status for research and testing purposes

Table 14 shows the number of uses of animals for research and testing purposes that had a genetic alteration, broken down by whether the animal exhibited a harmful phenotype at the time of the study or not. The majority of animals (92%) were not genetically altered, with <4% of all uses involving animals with harmful phenotypes (see Appendix for definitions).

Table 14: Genetic status

Genetic Status	Number of uses	Percentage
Not genetically altered	126,835	91.62%
Genetically altered without a harmful phenotype	6,761	4.88%
Genetically altered with a harmful phenotype	4,843	3.50%
Total uses	**138,439**	**100.00%**

3.7 Actual severity of uses of animals for research and testing purposes

Table 15 shows the reported actual severity experienced by the animals during their uses for research and testing purposes. Overall, 1% of uses were classified as non-recovery, 56% were classified as mild, 29% were moderate and 13% were severe (see Appendix for definitions). Of the animals that were reported as experiencing severe severity in 2019, >99% were mice. It should be noted that there were no reports received of the severe classification being exceeded, nor did the HPRA grant any exemptions for the severe classification to be exceeded.

Table 15: Classification of actual severity

Severity	Number of uses	Percentage
Non-recovery	1,991	1.44%
Mild [up to and including]	77,452	55.95%
Moderate	40,453	29.22%
Severe	18,543	13.39%
Total uses	**138,439**	**100%**

4 DATA ON THE USES OF ANIMALS FOR THE CREATION AND MAINTENANCE OF GENETICALLY ALTERED ANIMAL LINES

Table 16 shows the uses of animals for the creation of new genetically altered lines by species, first uses, and reuses. Mice were the only species reported as being used for the creation of new genetically altered animal lines in 2019, hence all other species have been excluded from this table.

Table 16: Uses of animals for the creation of new genetically altered animal lines by species, first uses and reuses

Animal species	First uses	Reuses	Percentage of reuses	Total uses
Mice	175	0	0	175
Total uses	**175**	**0**	**0**	**175**

Table 17 shows the uses of animals for the creation of new genetically altered lines by severity. 100% of animals used in 2019 for the creation of a new genetically altered line were reported as having experienced mild severity.

Table 17: Uses of animals for the creation of new genetically altered animal lines by severity

Severity	Number of uses	Percentage
Non-recovery	0	0.00%
Mild [up to and including]	175	100.00%
Moderate	0	0.00%
Severe	0	0.00%
Total uses	**175**	**100.00%**

Table 18 shows the uses of animals for the creation of new genetically altered lines by genetic status of the animals. 100% of animals used in 2019 for the creation of a new genetically altered line were reported as genetically altered without a harmful phenotype.

Table 18: Uses of animals for the creation of new genetically altered animal lines by genetic status

Genetic status	Number of uses	Percentage
Not genetically altered	0	0.00%
Genetically altered without a harmful phenotype	175	100.00%
Genetically altered with a harmful phenotype	0	0.00%
Total uses	**175**	**100.00%**

Table 19 shows the uses of animals for the creation of new genetically altered lines by type of basic research purposes. 100% of animals used for the creation of a new genetically altered line were reported under the basic research purpose 'Multisystemic', therefore since the remaining basic research purposes had no animals reported, they are excluded from this table. It should be noted that no animals were reported as being used for the creation of new genetically altered lines for translational and applied research purposes therefore no table listing these purposes has been included in this report.

Table 19: Uses of animals for the creation of new genetically altered animal lines by type of basic research purposes

Basic research	Number of uses	Percentage
Multisystemic	175	100.00%
Total uses	**175**	**100.00%**

Table 20 shows the uses of animals for the maintenance of established genetically altered lines by species. Mice were the only species of animal reported as being used for the maintenance of established genetically altered lines in 2019 and therefore other species have been excluded from this table.

Table 20: Uses of animals for the maintenance of established genetically altered animal lines by species

Animal species	First uses	Reuses	Percentage of reuses	Total uses
Mice	729	0	0.00%	729
Total uses	**729**	**0**	**0.00%**	**729**

Table 21 shows the uses of animals for the maintenance of established genetically altered lines by severity. 79% of animals used for the maintenance of established genetically altered lines in 2019 were reported as having experienced mild severity.

Table 21: Uses of animals for the maintenance of established genetically altered animal lines by severity

Severity	Number of uses	Percentage
Non-recovery	0	0.00%
Mild [up to and including]	576	79.01%
Moderate	146	20.03%
Severe	7	0.96%
Total uses	**729**	**100.00%**

Table 22 shows the uses of animals for the maintenance of established genetically altered lines by genetic status of the animals. 71% of animals used for the maintenance of established genetically altered lines in 2019 were reported as not genetically altered, with 29% reported as genetically altered with a harmful phenotype.

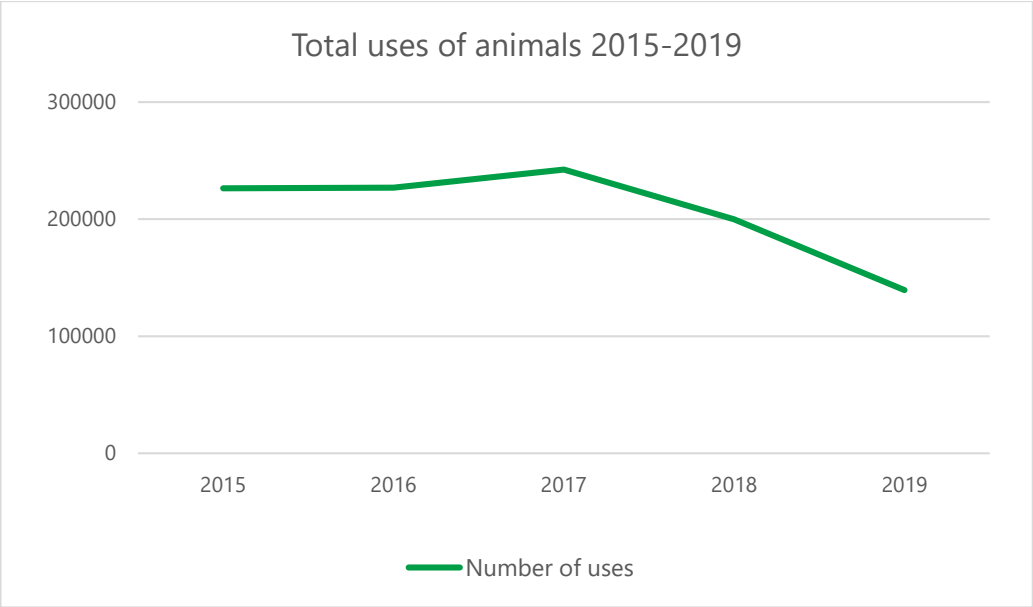
Table 22: Uses of animals for the maintenance of established genetically altered animal lines by genetic status

Genetic status	Number of uses	Percentage
Not genetically altered	520	71.33%%
Genetically altered without a harmful phenotype	0	0.00%
Genetically altered with a harmful phenotype	209	28.67%
Total uses	**729**	**100.00%**

5 TRENDS

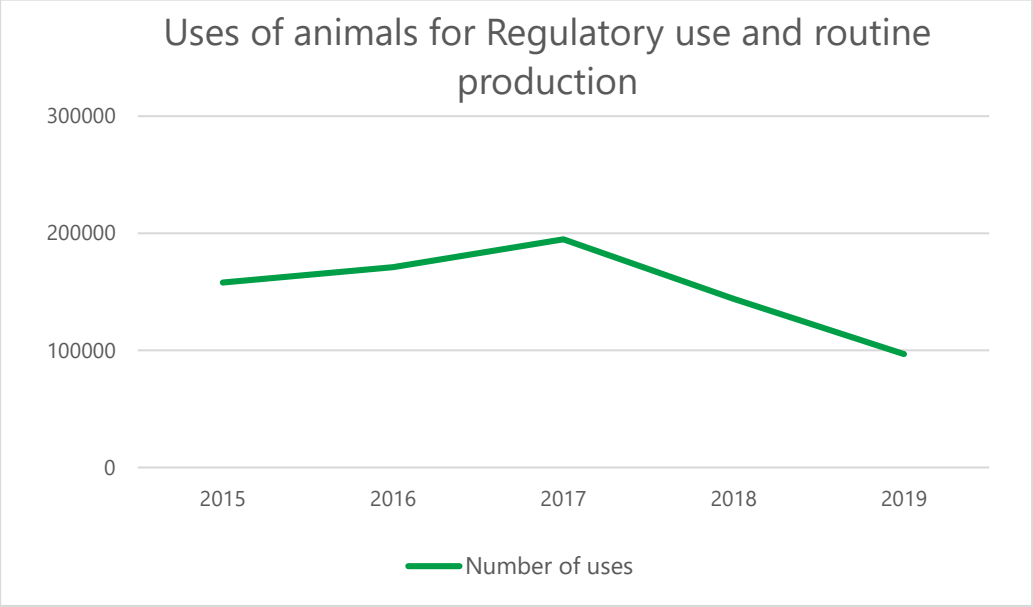
a) In 2019, there were a total of 139,343[3] uses of animals, which represents a 30% decrease on the total number of uses reported for 2018 (199,800). In 2017, there were 242,302 uses of animals reported, so the total number of uses reported in 2019 is 42% lower than in 2017. The below graph illustrates the total number of uses of animals over the past five years.

[3] Total uses of animals represents the sum of uses of animals for research and testing purposes and for the creation and maintenance of genetically altered animals.



b) There was a significant increase in the total number of reuses of animals in 2019 (2,275 reuses) versus 2018 (180 reuses). This increase is largely due to the reuse of a significant number of cattle. In Ireland, cattle are used only for agricultural research studies (for the benefit of the species, the environment or the agricultural sector).

c) The 30% decrease in total animal use (from 2018 to 2019) is mainly accounted for by a 33% decrease in the use of animals for regulatory testing. This follows a decrease in regulatory testing of 26% between 2017 and 2018. The shift downwards seen in 2019 (mirroring that of 2018) is likely due to the ongoing transition from animal tests to non-animal alternatives. The numbers of animals being used for regulatory testing has reduced from 194,816 in 2017 to 96,810 in 2019, representing a decrease of 50% over the two-year period. The below graph illustrates the pattern of use of animals for regulatory testing over the past five years.



d) The project purpose 'Regulatory use and routine production' continues to account for the majority of animal use in Ireland. Although non-animal alternative tests have replaced the need to use animals for regulatory testing for a number of human and veterinary medicinal products, these non-animal alternatives are not yet available/approved for all medicinal products that require regulatory testing. Consequently, there remains in some instances a requirement to perform regulatory testing of medicinal products using animals. In addition, non-animal tests can occasionally fail or malfunction, thereby resulting in unreliable results and necessitating the use of an animal test.

e) The project purpose 'Translational and applied research' remains the second most common project purpose under which the use of animals is reported (16% of all reported uses). The number of uses of animals reported under the project purpose 'Translational and applied research' has however decreased from 38,477 in 2018 to 22,341 in 2019. This decrease may be due to the overall reduction in animal numbers used in this year. The number of animals reported as being used under the project purpose 'Basic research' increased by 79% from 2018. 31% of basic research performed in 2019 was reported under the sub-field 'ethology/animal behaviour/animal biology, which in Ireland is mainly accounted for by agricultural research e.g. into animal nutrition.

f) The use of animals for the project purpose 'Maintenance of colonies of established genetically altered animals, not used in other procedures' increased by 60% from 2018. This increase is potentially as a result of two main factors:

   (i) increased familiarity of users with the reporting requirements in respect of genetically altered animals,

   (ii) increased selection of genetically altered animals over non-genetically altered lines in order to more effectively answer particular scientific questions.

g) Uses of animals for other project purposes remained relatively stable.

h) The use of mice has dropped by one third from the previous year but mice remain the most commonly used species at 69% of all animal uses. The decrease in the use of mice in 2019 is a reflection of the large reduction in the total number of animals used for regulatory testing. The use of rabbits has increased by greater than two-fold since 2018, from 171 uses to 552 uses. This one-year increase in the numbers of rabbits being used is due to the relocation of a number of rabbit studies to Ireland from elsewhere in the EU in 2019. The use of ferrets has increased from 288 uses in 2018 to 403 uses in 2019. The increase in the number of ferrets used is a result of increased levels of regulatory testing that require the use of this species (mainly human vaccine testing).

i) In relation to agricultural species, the total number of uses of pigs has reduced from 1,662 uses in 2018 to 323 uses in 2019. The HPRA is not aware of any significant factor underlying the reduction in the numbers of pigs undergoing procedures in 2019. Conversely, the total number of uses of sheep has increased from 644 uses in 2018 to 962 uses in 2019, and the total number of uses of cattle has increased from 3,137 uses in 2018 to 5,420 uses in 2019. The increases in the numbers of cattle and sheep being used in 2019 versus 2018 are due to the authorisation of several agricultural studies requiring large numbers of these species (for example epidemiological and nutritional studies).

j) There was a 71% increase in the use of zebra fish compared with 2018. The increase in zebra fish numbers relates to the expanding interest in using zebra fish as a model species within the scientific community, and in particular the authorisation of one project that required the use of a large number of fish. There was a 69% decrease in the use of 'other fish' compared with 2018. This is as a result of a marked decrease in the number of fish reported as being tagged for wildlife conservation and monitoring studies in 2019 versus 2018. The HPRA is not aware of the factors underlying the decreased number of wild fish tagged in 2019.

k) There was a 33% decrease from 2018 in the number of animals used that were reported as not genetically altered. However, there was a 39% increase in the number of animals used reported as being genetically altered with a harmful phenotype. The significant decrease in the numbers of non-genetically altered animals used in 2019 relates to the marked reduction in the numbers of animals used for regulatory testing.

   The increase in the number of animals used being reported as genetically altered with a harmful phenotype is thought to be due to three main factors:

   (i) increased familiarity of users with the reporting requirements in respect of genetically altered animals,

   (ii) increased awareness and recognition of the impacts of genetic alterations on the phenotypes of animals, with lines of animals that may not have been previously recognised as having a harmful phenotype, now being classified as harmful lines, and

   (iii) increased selection of genetically altered animals over non-genetically altered lines for scientific studies, in order to more effectively answer particular scientific questions.

l) The percentage of animals reported as experiencing non-recovery severity increased from 0.53% of the total in 2018, to 1.43% of the total in 2019, representing an increase of almost three-fold between the two years. The rationale behind this increase is uncertain, but it may be as a result of improved understanding among the user community of each of the severity categories, and therefore more accurate reporting year-on-year. The percentage of animals reported as experiencing severe severity in 2019 dropped to 13% of total, down from 17% in 2018. In absolute terms, the number of animals reported as having experienced severe severity reduced from 33,746 in 2018 to 18,550 in 2019. Over the two-year period from 2017 to 2019, the percentage of animals reported as experiencing an actual severity of severe has reduced from 29% to 13%. The reduction in the proportion of procedures reported as severe is attributed to the reduction in regulatory use of animals, as well as efforts made by the HPRA, animal welfare bodies, and animal users to reduce the severity of procedures through the implementation of refinements and earlier humane endpoints.

6 CONCLUSION

In the year 2019, there were 139,343 reported uses of animals in procedures in Ireland. This represents a 30% decrease on the number of uses reported for 2018, and follows an 18% decrease between 2017 and 2018. The proportion of animals that experienced a

severe severity in 2019 is lower than previous years, and as with previous years, the most commonly reported actual severity remains at mild.

The HPRA's focus will continue to be the reduction of severe suffering, for example, with the continued application of early humane endpoints, as well as ensuring that the 3Rs are applied to all authorised projects. In addition, the HPRA will ensure that procedures are only performed where there is no alternative (non-animal) technique available and where the expected benefits outweigh any potential harms.

7 APPENDIX: DEFINITIONS

Procedures

The Directive defines a procedure as: "any use of an animal for scientific or educational purposes, which may cause the animal a level of pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice". This includes the creation and maintenance of any genetically altered animal lines that may result in pain or distress as per the above definition. Each procedure may consist of several stages or techniques for a single scientific purpose, which is then counted as *one* procedure and reported in the year it was completed.

Reuse

Reuse means that following a full recovery from a completed procedure, and having been certified by a veterinarian as being returned to full health, that animal can then be enrolled on another project.

Genetically altered animals

Genetically altered animals are those that have been genetically modified, for example, by the introduction (into an animal) of genetic material from another animal, or by 'knocking out' or disrupting an existing gene. Statistics are only collected on genetically altered animals that have an impairment to their well-being from the genetic alteration (a harmful phenotype), or when a new genetic line of animals is being created and the effect on the animals is not yet known.

Actual severity

At the end of the use of an animal on a procedure, the impact of the procedure must be determined and reported as 'actual severity'. This means that the *highest severity* that an animal may have experienced throughout the course of their time on procedure (rather than the severity at the end or the average severity throughout) must be recorded. Therefore, it is based on the real impact of the procedure, rather than any predicted impact. The legislation defines four categories of actual severity, in order of least to most harmful, as: non-recovery, mild, moderate and severe.

Non-recovery: This means the entire procedure is carried out under general anaesthesia and, at the end, the animal is humanely euthanised rather than being allowed to wake up.

Mild: Any pain or suffering experienced by the animal is only slight, minor or temporary and so the animal recovers in a short period of time. This would include an injection, a short period of social isolation, or non-invasive imaging under sedation or anaesthesia (e.g. MRI scanning).

Moderate: Any suffering experienced by the animal is short-term moderate pain, suffering or distress; long-lasting mild pain, suffering or distress; or involves a moderate impairment to their well-being. This would include surgery performed under general anaesthesia, repeated injections or blood tests, or the induction of tumours that cause moderate impairment to well-being.

Severe: Severe procedures indicate a major departure from the animal's usual state of health or well-being, and cause long-lasting moderate pain, suffering or distress, or short-term severe pain. This might include toxicity testing under legislation where fatalities may occur, surgical procedures that cause severe post-operative pain, or the breeding of animals with serious genetic disorders.

It should also be noted that procedures that involve severe pain, suffering or distress that are *long-lasting* are prohibited under the legislation.