HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Annual statistical report for animals used in Ireland under scientific animal protection legislation - 2020

16 DECEMBER 2021

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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.

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 absolutely necessary 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. During 2020, there were 17 inspections completed to monitor animal welfare standards and compliance with legislation. This total incorporated 16 announced inspections and one unannounced inspection. Announced inspections are typically carried out as part of the authorisation renewal process as they allow for a comprehensive review of every aspect of the establishment's activities and operations under the scientific animal protection legislation. In response to challenges arising as a result of the Covid-19 pandemic (such as government restrictions on movement), during 2020 the HPRA developed a remote/on-site hybrid inspection process to enable the inspection of authorised establishments to continue.

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 robust scientific justification for the research techniques being applied. 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. Where non-animal methods to address the specific research question are not available/appropriate, 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. In fulfilment of the HPRA's mandate to promote the 3Rs, in 2020 the HPRA continued its ongoing efforts to enhance awareness and utilisation of non-animal alternatives. The HPRA 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 2020 in accordance with Article 54(2) of the Directive. This is the eighth report to be prepared by the HPRA since it became the competent authority for the protection of animals used for scientific purposes.

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 and including 2018. In line with the EU summary reports under Directive 2010/63/EU on the uses of animals for scientific purposes within the EU and Norway, 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
- numbers and uses of animals for the creation and maintenance of genetically altered animal lines.

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

2 SUMMARY

In 2020, there were a total of 137,988 uses of animals in procedures for research and testing purposes, with reuse representing <1% of this number (670 animals). Some 137,318 animals were reported as being used for the first time for research and testing purposes in 2020. Mice were the most commonly used species at 82% of the total animal use. In addition, 702 mice were reported as having been used to create and maintain colonies of genetically altered animals. These 702 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, 75% 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, 9,564 involved genetically altered animals, which represents 7% 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 58%, followed by moderate at 26%. Of the animals reported as being used for the creation and maintenance of genetically altered lines, 73% 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 (82% 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 animals reported as being used under the category 'other rodents' (<1%) were red squirrels being studied as part of a conservation project aiming to protect their population numbers and habitats. The category 'other fish' (2%) primarily represents wild fish (e.g. salmon and Bluefin tuna) being studied for conservation projects where their movements are closely monitored, as part of efforts to improve the survival of these species. This category also includes some fish species such as lumpfish that are used in aquaculture research. Likewise, the category 'other birds' (<1%)

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

includes wild bird species such as northern gannets and great tits being studied in monitoring and conservation and bird ecology projects. The single animal reported as being used in the category 'other mammals' was a deer used in a study investigating the health and ecology of wild deer populations in Ireland. It should be noted that the following species have been excluded from this table as they were not used in Ireland in 2020: hamsters (Chinese), Mongolian gerbils, cats, 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	113,209	82.44%
Rats	12,330	8.98%
Guinea pigs	228	0.01%
Hamsters (Syrian)	8	0.00%
Other rodents	59	0.04%
Rabbits	1,043	0.76%
Dogs	24	0.02%
Ferrets	186	0.14%
Horses, donkeys and cross-breeds	238	0.17%
Pigs	129	0.09%
Goats	16	0.01%
Sheep	1,239	0.90%
Cattle	2,104	1.53%
Other mammals	1	0.00%
Domestic fowl	129	0.09%
Other birds	87	0.06%
Xenopus	3	0.00%
Zebrafish	3,357	2.44%
Other fish	2,928	2.13%
Total uses	**137,318**	**100.00%**

3.2 Reuse of animals

Table 2 (below) shows the proportion of reuse (see Appendix for definition), which represents 0.49% of total animal use. Under the legislation, 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) and they have been assessed as having returned to full general health between projects.

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 670 represents *uses of animals,* not actual numbers of animals reused). Cats, dogs, horses, sheep, cattle and domestic fowl were the species reused during 2020. In Ireland, cats and dogs are used exclusively for research into animal diseases and disorders, and the development and testing of veterinary medicines for companion animals. The horses that were reused were used for the purposes of training veterinary students, and the severity of the procedures these horses

undergo did not exceed mild. Sheep were reused in studies investigating diseases of sheep and human cardiovascular disorders, and did not exceed mild severity. The reuse of cattle was in agricultural research studies investigating, for example, ways to improve cattle welfare, or protect the environment through the reduction of methane emissions. The overwhelming majority of these types of projects involve only procedures of mild severity. Domestic fowl were reused in a study investigating avian infectious diseases, and again did not exceed mild severity.

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	113,209	0	0.00%	113,209
Rats	12,330	0	0.00%	12,330
Guinea pigs	228	0	0.00%	228
Hamsters (Syrian)	8	0	0.00%	8
Other rodents	59	0	0.00%	59
Rabbits	1,043	0	0.00%	1,043
Cats	0	20	100.00%	20
Dogs	24	40	62.50%	64
Ferrets	186	0	0.00%	186
Horses, donkeys and cross-breeds	238	10	4.03%	248
Pigs	129	0	0.00%	129
Goats	16	0	0.00%	16
Sheep	1,239	29	2.29%	1,268
Cattle	2,104	557	20.93%	2,661
Other mammals	1	0	0.00%	1
Domestic fowl	129	14	9.79%	143
Other birds	87	0	0.00%	87
Xenopus	3	0	0.00%	3
Zebrafish	3,357	0	0.00%	3,357
Other fish	2,928	0	0.00%	2,928
Total uses	**137,318**	**670**	**0.49%**	**137,988**

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 (97%) 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 (3%) includes wild animals and farm animals. Animals born in the rest of Europe and the rest of the world (<1%) represents, for example, 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	133,572	97.27%
Animals born in the EU not at a registered breeder	3,553	2.59%
Animals born in rest of Europe	144	0.10%
Animals born in rest of world	49	0. 04%
Total uses	**137,318**	**100.00%**

3.4 Project purposes

Table 4 shows the primary purposes for which animals were used in research and testing. The most common primary purpose at 75% 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 2020.

Table 4: Primary purpose for which animals are used

Primary purpose	Number of uses	Percentage
Basic research	10,455	7.58%
Translational and applied research	21,467	15.56%
Regulatory use and routine production	102,861	74.54%
Protection of the natural environment in the interests of the health or welfare of human beings or animals	2,891	2.10%
Preservation of the species	68	0.05%
Higher education or training for the acquisition, maintenance or improvement of vocational skills	246	0.18%
Total uses	**137,988**	**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 'musculoskeletal system', 'urogenital/reproductive system' and 'other basic research' were excluded from this table as no uses under these sub-fields were reported for 2020.

The most common sub-field of 'Basic research' at 31% was 'immune system', which relates to research investigating the functioning and activities of the immune system in health and disease. The next most common sub-field at 25% 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 third most common sub-field was 'nervous system', making up 22% of all basic research performed. Nervous system research involves studies that investigate how the brain, spinal cord and nerves function in both health and in disease (e.g. Alzheimer's disease or Parkinson's disease). 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	31	0.30%
Cardiovascular, blood and lymphatic system	61	0.58%
Nervous system	2,300	22.00%
Respiratory system	397	3.80%
Gastrointestinal system including liver	64	0.61%
Immune system	3,220	30.80%
Sensory organs (skin, eyes and ears)	590	5.64%
Endocrine system/metabolism	332	3.18%
Multisystemic	824	7.88%
Ethology / animal behaviour /animal biology	2,636	25.21%
Total uses	**10,455**	**100.00%**

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 'human urogenital / reproductive disorders', 'diagnosis of diseases' and 'non-regulatory toxicology and ecotoxicology' were excluded from this table as no uses under these sub-fields were reported for 2020.

The most common sub-field of 'Translational and applied research' at 33% 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 sub-field at 18%, was research into human musculoskeletal disorders. This includes research into conditions such as arthritis, traumatic nerve and bone injury, and genetic muscle diseases. The third most common sub-field was sensory organ disorders (skin, eyes and ears). The large majority of these studies are investigations into treatments for blindness, and the species most commonly used for research of this nature is Zebrafish.

Table 6: Uses of animals for translational and applied research

Translational and applied research	Number of uses	Percentage
Human cancer	625	2.91%
Human infectious disorders	1,163	5.42%
Human cardiovascular disorders	844	3.93%
Human nervous and mental disorders	7,073	32.95%

Translational and applied research	Number of uses	Percentage
Human respiratory disorders	239	1.11%
Human gastrointestinal disorders including liver	1,115	5.19%
Human musculoskeletal disorders	3,926	18.29%
Human immune disorders	923	4.30%
Human sensory organ disorders (skin, eyes and ears)	3,708	17.27%
Human endocrine/metabolism disorders	285	1.33%
Other human disorders	70	0.33%
Animal diseases and disorders	1,213	5.65%
Animal welfare	271	1.26%
Plant diseases	12	0.06%
Total uses	**21,467**	**100.00%**

Table 7 shows the breakdown of animal uses for 'Regulatory use and routine production'. It should be noted that the sub-field of 'toxicity and other safety testing including pharmacology' was excluded from this table as no uses under this sub-field were reported for 2020. 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)	102,781	99.92%
Other efficacy and tolerance testing	62	0.06%
Routine production	18	0.02%
Total uses	**102,861**	**100.00%**

Table 8 shows a further breakdown of animal use for 'Quality control' tests. 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, 92% 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 (e.g. for some blood and protein-based human medicines), and therefore currently it is necessary to continue to employ animal-based tests in some instances. The 50 animals used under the sub-field 'other quality controls' were cattle used to test the potency of bovine tuberculin, under the relevant veterinary medicines legislation.

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

Quality control	Number of uses	Percentage
Batch safety testing	1,304	1.27%
Pyrogenicity testing	943	0.92%
Batch potency testing	100,484	97.77%
Other quality controls	50	0.05%
Total uses	**102,781**	**100.00%**

Table 9 relates to the use of animals for regulatory testing under the sub-field 'Toxicity and other safety testing' and shows that no animals were used in testing for this purpose in 2020.

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

Toxicity and other safety testing	Number of uses	Percentage
Total uses	**0**	**0.00%**

Since no animals were used in 2020 for Toxicity and other safety testing', no additional breakdown tables in relation to this sub-field have been included within this report.

Table 10 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 sub-fields 'monoclonal antibody by mouse ascites method' and 'other product types' were excluded from this table as no uses were reported in 2020.

Table 10: Routine production uses by product type

Product type	Number of uses	Percentage
Blood based products	18	100.00%
Total uses	**18**	**100.00%**

3.5 Use of animals to meet legislative requirements

Table 11 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. Testing to satisfy medical devices legislation is required to place medical devices on the market. The testing performed under feed legislation, including legislation for the safety of target animals, workers and environment was conducted to confirm the safety of feeding a veterinary food supplement to the target animal species.

Table 11: Regulatory testing by type of legislation

Testing by Legislation	Number of uses	Percentage
Legislation on medicinal products for human use	102,731	99.89%
Legislation on veterinary medicinal products	50	0.05%
Medical devices legislation	2	0.00%
Feed legislation including legislation for the safety of target animals, workers and environment	60	0.06%
Total uses	**102,843**	**100.00%**

Table 12 shows the geographical origin of the legal requirement. All tests were performed to satisfy EU legislative requirements.

Table 12: Origin of legislative requirement

Legislative Requirement	Number of uses	Percentage
Legislation satisfying EU requirements	102,843	100.00%
Legislation satisfying national requirements only [within EU]	0	0.00%
Legislation satisfying non-EU requirements only	0	0.00%
Total uses	**102,843**	**100.00%**

3.6 Use by genetic status for research and testing purposes

Table 13 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 (93%) were not genetically altered, with <2% of all uses involving animals with harmful phenotypes (see Appendix for definitions).

Table 13: Genetic status

Genetic Status	Number of uses	Percentage
Not genetically altered	128,424	93.07%
Genetically altered without a harmful phenotype	7,227	5.24%
Genetically altered with a harmful phenotype	2,337	1.69%
Total uses	**137,988**	**100.00%**

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

Table 14 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, 58% were classified as mild, 26% were moderate and 15% were severe (see Appendix for definitions). Of the animals that were reported as experiencing severe severity in 2020, >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 14: Classification of actual severity

Severity	Number of uses	Percentage
Non-recovery	1,110	0.80%
Mild [up to and including]	79,380	57.53%
Moderate	36,289	26.30%
Severe	21,209	15.37%
Total uses	**137,988**	**100.00%**

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

Table 15 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 2020, hence all other species have been excluded from this table.

Table 15: 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	104	0	0.00%	104
Total uses	**104**	**0**	**0.00%**	**104**

Table 16 shows the uses of animals for the creation of new genetically altered lines by severity. 86% of animals used in 2020 for the creation of a new genetically altered line were reported as having experienced mild severity.

Table 16: Uses of animals for the creation of new genetically altered animal lines by severity

Severity	Number of uses	Percentage
Non-recovery	3	2.88%
Mild [up to and including]	89	85.58%
Moderate	0	0.00%
Severe	12	11.54%
Total uses	**104**	**100.00%**

Table 17 shows the uses of animals for the creation of new genetically altered lines by genetic status of the animals. 43% of animals used in 2020 for the creation of a new genetically altered line were reported as genetically altered without a harmful phenotype whereas 57% were reported as genetically altered with a harmful phenotype.

Table 17: 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	45	43.27%
Genetically altered with a harmful phenotype	59	56.73%
Total uses	**104**	**100.00%**

Table 18 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 'Musculoskeletal system', therefore since the remaining basic research purposes had no animals reported, they are excluded from this table.

Table 18: Uses of animals for the creation of new genetically altered animal lines by type of basic research purposes

Basic research	Number of uses	Percentage
Musculoskeletal	3	100.00%
Total uses	**3**	**100.00%**

Table 19 shows the uses of animals for the creation of new genetically altered lines by type of translational and applied research purposes. The only translational and applied sub-field categories under which animals were reported as being used for the creation of a new genetically altered line were 'human musculoskeletal disorders' and 'human immune disorders'. Since the remaining translational and applied research sub-fields had no animals reported, they are excluded from this table.

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

Translational and applied research	Number of uses	Percentage
Human musculoskeletal disorders	45	44.55%
Human immune disorders	56	55.45%
Total uses	**101**	**100.00%**

Table 20 shows the uses of animals for the maintenance of established genetically altered lines by species. Mice and zebrafish were the only species of animal reported as being used for the maintenance of established genetically altered lines in 2020 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	491	0	0.00%	491
Zebrafish	107	0	0.00%	107
Total uses	**598**	**0**	**0.00%**	**598**

Table 21 shows the uses of animals for the maintenance of established genetically altered lines by severity. 71% of animals used for the maintenance of established genetically altered lines in 2020 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]	424	70.90%
Moderate	162	27.09%
Severe	12	2.01%
Total uses	**598**	**100.00%**

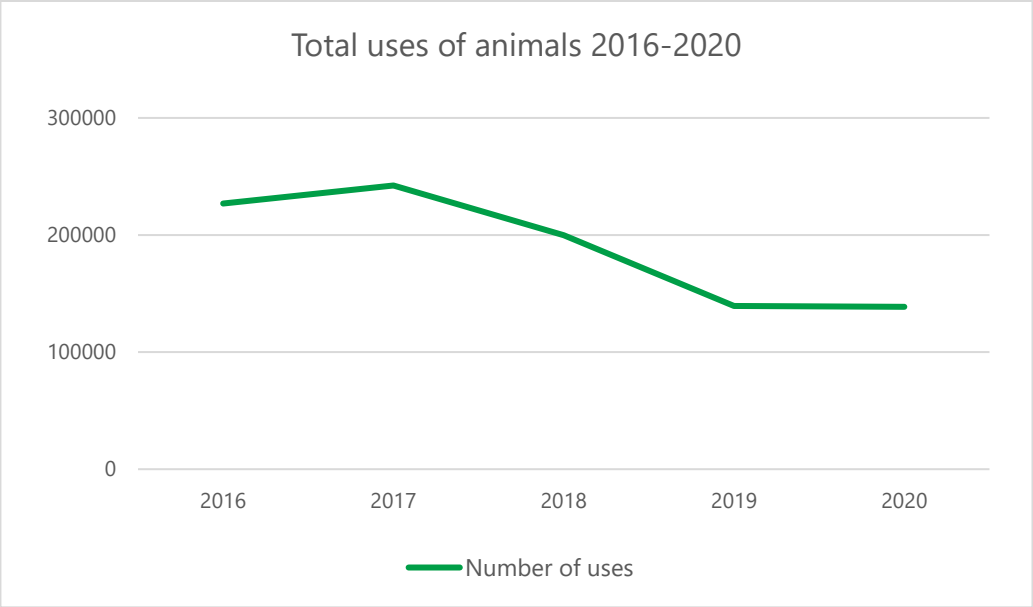
Table 22 shows the uses of animals for the maintenance of established genetically altered lines by genetic status of the animals. 45% of animals used for the maintenance of established genetically altered lines in 2020 were reported as not genetically altered, with 37% reported as genetically altered 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	270	45.15%
Genetically altered without a harmful phenotype	107	17.89%
Genetically altered with a harmful phenotype	221	36.96%
Total uses	**598**	**100.00%**

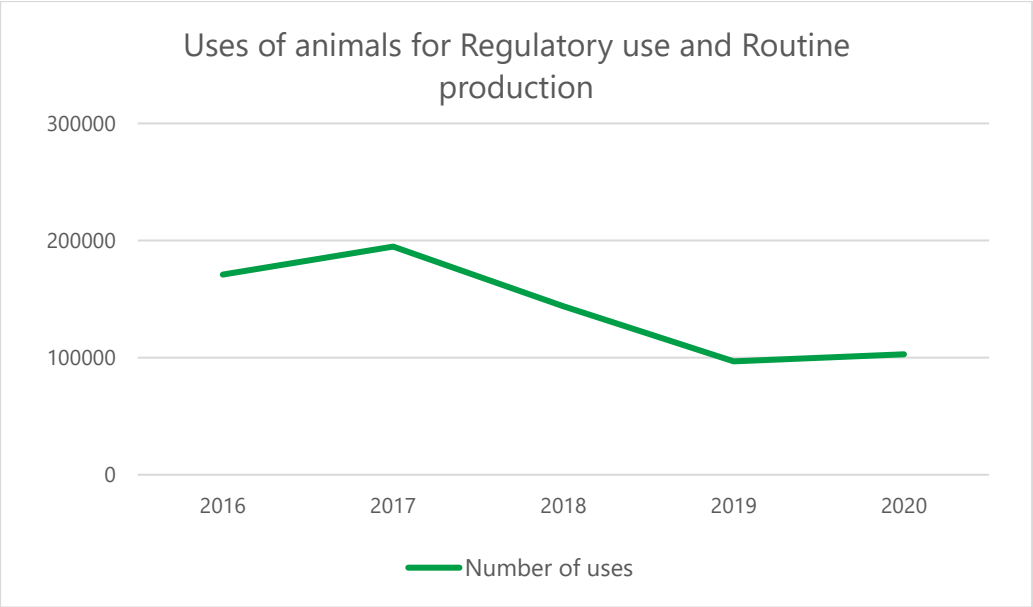
5 TRENDS

a) In 2020, there were a total of 138,690[3] uses of animals. This figure is broadly in line with the number of uses of animals reported for 2019 (139,343). The number of uses of animals in 2020 is significantly lower than the number of uses in the years preceding 2019. For example, in 2018 there were 199,800 uses of animals reported, with the total number of uses reported in 2020 some 31% lower than in 2018. The below graph illustrates the total number of uses of animals over the past five years.



b) The decrease in total animal use seen in 2019 and 2020 versus earlier years is mainly accounted for by a significant reduction in the use of animals for the purpose of regulatory testing. For example. 29% fewer animals (absolute decrease of 41,034 animals) were used for regulatory testing in 2020 than in 2018, with 47% fewer animals (absolute decrease of 91,955 animals) being used for regulatory testing in 2020 versus in 2017. This is due to the ongoing transition from animal tests to non-animal alternatives. The following graph illustrates the pattern of use of animals for regulatory testing 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.



c) Mice remain the most commonly used species at 82% of all animal uses. A significant decrease in the numbers of rats used was noted in 2020, with 46% fewer rats used than in 2019. There was also a large reduction in the numbers of guinea pigs used, with 62% fewer guinea pigs used in 2020 than in 2019, as well as in the numbers of ferrets used, with usage of ferrets 54% lower in 2020 versus 2019. These decreases are due to a reduction in the use of these species for the regulatory testing of certain types of human medicinal products (e.g. influenza vaccine products). The number of animals reported under the species category 'other rodents' has increased from 0 in 2019 to 59 in 2020 as a result of a wildlife conservation study investigating the habitats and behaviour of wild squirrels. The use of rabbits has increased by almost two-fold since 2019 due to the relocation of regulatory testing using this species from a Contract Research Organisation in another Member State to Ireland.

d) There has been an eight-fold increase from 2019 in the numbers of horses used. This is a result of a large equine disease surveillance study being performed in 2020.

e) In relation to agricultural species, the use of pigs has decreased by 60% from 2019, and uses of cattle have decreased by 51% from 2019, primarily due to the conclusion of several projects using these species in 2019. The COVID-19 pandemic, and government restrictions on movement prohibiting travel to commercial farms for the purpose of performing agricultural research may also have been a factor in this reduction. Uses of sheep have increased by 32% from 2019 due to several studies being performed in 2020 for the purpose of investigating methane emissions from sheep. The number of uses of domestic fowl has increased by 79% from 2019 as a result of a large project performed for the purpose of avian disease surveillance and the protection of the health of the national poultry flock. The use of birds reported in the species category 'other birds' has seen an 87% decrease from 2019, as there were fewer conservation projects studying wild birds performed in 2020 than in 2019 (most likely as a result of pandemic-related public health measures restricting movement and travel).

f) There has been a 33% reduction in the numbers of uses of zebrafish reported; the reasons for this decrease are not known. There has also been a 47% reduction in the numbers of uses of fish reported under the species category 'other fish'. This is thought

to be due to the COVID-19 pandemic and logistical difficulties in travelling to locations (rivers/sea) where wildlife studies are performed, due to government restrictions on movement in place at various periods throughout 2020.

g) There was a significant reduction in the number of animals reused in 2020 versus 2019 (71% decrease). This is largely due to the fact that cattle are one of the species that are most commonly reused, and there was a notable decrease in the total number of uses of cattle in procedures in 2020 due to the conclusion of several projects using large numbers of cattle in 2019. The COVID-19 pandemic, and government restrictions on movement prohibiting travel to commercial farms for the purpose of performing agricultural research may also have been a contributing factor.

h) 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 many 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 confirm quality, safety and efficacy through 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.

   There was a 96% reduction in the numbers of animals used for the purpose of 'Regulatory use and routine production – blood based products'. This is a result of a decrease in the numbers of animals being used for antisera production. There was an 80% increase in the number of rabbits used for pyrogenicity testing in 2020 versus 2019. As referenced above, this is as a result of the relocation of regulatory testing using this species from a Contract Research Organisation in another Member State to Ireland. Alternative testing methods to determine the pyrogenicity of medicinal products are recognised under the legislation of the Union. However these methods are not suitable for certain classes of medicinal products, for example some blood/protein based medicines. Therefore, in order to meet the necessary regulatory safety requirements for release of certain medicinal products onto the market there is currently no alternative to the use of the rabbit pyrogen test.

i) The distribution of animal numbers across the four severity categories in 2020 is broadly similar to that of 2019, with no significant changes noted.

To Note: In addition to routine year-on-year variation in the number and nature of projects authorised, annual trend data can be impacted by a range of other factors which can lead to variation in the overall number of animals used. Decreases, for example, may arise as a result of the ongoing application of the 3Rs principles while certain extraneous developments may result in increases in the levels of animal use. Among the factors that should be considered when assessing annual trend data include:

- The relocation of existing regulatory testing either to or from Ireland;
- The regulatory requirement for the use of animal tests to determine the safety and effectiveness of new human medicines and vaccines developed in response to emerging and significant public health developments;
- The adoption, following regulatory approval, of alternative testing methods including in vitro tests.

6 CONCLUSION

In the year 2020, there were 138,690 reported uses of animals in procedures in Ireland. The distribution of animal numbers across the four severity categories in 2020 is broadly similar to that of 2019, and as with previous years, the most commonly reported actual severity remains at mild.

The HPRA's focus will continue to be on promoting the replacement of tests using animals with suitable non-animal alternative tests, ensuring that the principle of Reduction is applied appropriately when animals are used in procedures, and refining both the care and use of animals in procedures. In addition, the HPRA will ensure that animals are used only when there is no equivalent alternative (non-animal) technique available, and the harm-benefit analysis of the proposed use is favourable.

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.