HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

ANNUAL STATISTICAL REPORT FOR ANIMALS USED IN IRELAND UNDER SCIENTIFIC ANIMAL PROTECTION LEGISLATION

2015

CONTENTS

1. INTRODUCTION

The Health Products Regulatory Authority (HPRA) is the state agency with responsibility for regulating human and veterinary medicines, medical devices and other health products. 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, i.e. Replacement, Reduction and Refinement:

- **Replacement** means that 'alternative' methods are to be used where possible instead of live animals. Examples of alternative methods would include *in vitro* tests such as the use of cell lines, computer simulation and modelling, video material, or the use of invertebrates such as fruit flies or worms.

- **Reduction** means that it must be ensured that the *appropriate* number of animals is used for *each* project. This allows scientists to obtain statistically robust data without using more animals than are necessary.

- **Refinement** means that animals used are provided with the best possible care and that suffering is reduced to an absolute minimum. Refinement techniques would include, for example, careful handling by trained individuals, the provision of high standards of housing and husbandry to include enrichment materials (e.g. toys and nesting material) and the appropriate use of anaesthesia and pain relief during procedures.

Although complete replacement of animal studies is the ultimate goal of the Directive, this is not currently possible. 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 in order to safeguard human, animal and environmental health. However, the Directive is a significant tool to protect those animals that are still required.

[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 2015, the HPRA performed 29 inspections, and was satisfied with the overall level of care and welfare being provided to the animals in the breeder/supplier/user establishments.
2. **Projects:** Scientific procedures involving animals can only take place following a detailed submission of the planned study 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 based on the 3Rs and requires scientific justification for the research techniques being applied. The likely impact on the animals must be minimised as far as possible by applying refinements and any harms experienced by the animals must be outweighed by the expected benefits of the work. The HPRA checks whether alternative (non-animal) methods are available or appropriate, as alternatives to the use of live animals must be used where possible.

The objective of this report is to present statistical data on the number of animals used for scientific purposes in Ireland during 2015 in accordance with Article 54(2) of the Directive. This is the third 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 and any project which was originally authorised by the Department of Health continues in force until the expiry of the authorisation in question. This may take up to five years (i.e. until the end of December 2017).

As in previous years, the data provided are based on self-declarations by the establishments concerned. The methodology and legal basis for the requirements for data collection were substantially changed with the introduction of the Directive in 2013. For example:

- 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.
- Each use of an animal must now be assigned to a specific category outlined by the legislation, e.g. basic research, translational 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.

This new format meets the requirements for a European database which has been developed by the EU Commission.

2. SUMMARY

a) In 2015, a total of 226,393 naïve animals (not previously used in procedures) were used in procedures, and including animals that were reused, there were a total of 228,975 uses of animals for procedures.

b) Of the total number of naïve animals (226,393), 15,476 were genetically altered, which represents 7% of all animals used. Of these genetically altered animals, 96% did not have a harmful phenotype (i.e. there was no impairment to their well-being from the genetic alteration).

c) Of the total number of uses of animals in procedures (228,975), some 157,872 were used for 'Regulatory and other routine production purposes' which is a necessary requirement (under EU law) to test the safety, quality and potency of medicines (e.g. biological medicines such as vaccines). The vast majority of these tests (94%) were for toxicity and other safety testing including pharmacology, of which 99.6% were mice used for acute and sub-acute toxicity tests.

Note: The following species have not been included in the tables in this document as they were not used in Ireland in 2015:

- Hamsters (Syrian)
- Hamsters (Chinese)
- Mongolian gerbil
- Other rodents
- Other carnivores
- Reptiles
- Rana
- Other amphibians
- Cephalopods
- Non-human primates

3. RESULTS

3.1 Species and numbers of naïve animals

Table 1 shows the number of naïve animals (used for the first time) used in procedures that were completed in 2015. Mice (84%) were by far the most commonly used species. It should be noted that for uses involving dogs and cats, the studies conducted were for research into the development of veterinary medicines, which is expected to be of benefit to those species. Farm animals such as cattle, sheep and pigs were mainly used for agricultural research, and the majority of birds and fish used were for tagging procedures for wildlife monitoring/conservation purposes.

Table 1: Numbers of naïve animals used in procedures by species

Animal Species	Number of Animals	%
Mice	190585	84%
Rats	9876	4%
Guinea-Pigs	1929	<1%
Rabbits	1343	<1%
Cats	76	<1%
Dogs	122	<1%
Ferrets	621	<1%
Horses, donkeys & cross-breeds	112	<1%
Pigs	2840	1%
Goats	71	<1%
Sheep	1112	<1%
Cattle	10420	5%
Other Mammals	20	<1%
Domestic fowl	113	<1%
Other birds	572	<1%
Xenopus	420	<1%
Zebra fish	1489	<1%
Other Fish	4672	2%
Total	226393	

3.2 Species and numbers of uses of animals

Table 2 shows the number of *uses* of animals in procedures, rather than the total numbers of animals used (as shown in Table 1). It shows both the first, and all the subsequent uses of the animals that were completed in the year 2015. The number of uses of animals exceeds the number of new animals used because it includes reuse. The species most frequently 'reused' are farm animals, dogs and cats.

Table 2: Numbers of uses of animals by species

Animal Species	Number of Animals	%
Mice	190585	83%
Rats	9876	4%
Guinea-Pigs	1929	<1%
Rabbits	2490	1%
Cats	164	<1%
Dogs	587	<1%
Ferrets	621	<1%
Horses, donkeys & cross-breeds	127	<1%
Pigs	2840	1%
Goats	71	<1%
Sheep	1112	<1%
Cattle	11287	5%
Other Mammals	20	<1%
Domestic fowl	113	<1%
Other birds	572	<1%
Xenopus	420	<1%
Zebra fish	1489	<1%
Other Fish	4672	2%
Total	228975	

3.3 Origin of animals

Table 3 shows the birthplace of naïve animals used in procedures. 99% of all animals were born in the EU. In accordance with the legislation, animal species listed in Annex I to the Directive (e.g. rodents, cats and dogs) must be obtained from a registered breeder unless an exemption is granted by the HPRA. Animals born outside a registered breeder include wild animals and farm animals.

Table 3: Place of birth of all naïve animals

Animal species	Animals born in the EU at a registered breeder	Animals born in the EU but not at a registered breeder	Animals born in rest of Europe	Animals born in rest of the world	Total
Mice	189311	1140		134	190585
Rats	9782	70		24	9876
Guinea-Pigs	1929				1929
Rabbits	1263	80			1343
Cats	76				76
Dogs	122				122
Ferrets	621				621
Horses, donkeys & cross-breeds		112			112
Pigs	64	2776			2840
Goats	4	67			71
Sheep	292	820			1112

Animal species	Animals born in the EU at a registered breeder	Animals born in the EU but not at a registered breeder	Animals born in rest of Europe	Animals born in rest of the world	Total
Cattle	2255	8165			10420
Other Mammals		20			20
Domestic fowl	110	3			113
Other birds	2	215	129	226	572
Xenopus	409			11	420
Zebra fish	1489				1489
Other Fish	1858	2014		800	4672
Total	209587	15482	129	1195	226393

3.4 Species and classification of severity

Table 4 shows the reported actual severity experienced by the animals during procedures, grouped by species. Overall, 2% of animals were involved in procedures that were classified as non-recovery, 50% were classified as mild, 22% were moderate and 27% were severe. This is a reduction in severe procedures from the 2014 data, when 40% were reported as severe. Of the animals that were involved in severe procedures in 2015, 99% were mice. It should be noted that animals involved in procedures classified as 'severe' cannot be reused.

Table 4: Classification of actual severity

Animal species	Non-recovery	Mild	Moderate	Severe	Total
Mice	1368	84510	43251	61456	190585
Rats	1664	2946	4715	551	9876
Guinea-Pigs	695	1234			1929
Rabbits		1863	617	10	2490
Cats		29	135		164
Dogs		201	386		587
Ferrets		621			621
Horses, donkeys & cross-breeds		119	8		127
Pigs	21	2717	100	2	2840
Goats			71		71
Sheep		1106	6		1112
Cattle		11200	86	1	11287
Other Mammals		20			20
Domestic fowl	28	85			113
Other birds		572			572
Xenopus		37	171	212	420
Zebra fish		1489			1489
Other Fish	2	4497	159	14	4672
Total	3778	113246	49705	62246	228975

3.5 Animal species and project purpose

Table 5 shows the general project purposes for which animals were used based on species. It shows both the first and all subsequent uses of the animals completed in the year 2015. The most common purpose at 69% was 'Regulatory use and routine production'. This includes animals used in procedures for pre-clinical safety testing of medicines or safety testing for possible pollutants, as well as studies on the quality and potency of production batches of certain categories of medicines (e.g. those of biological origin). The next most common purpose was 'Basic research' at 18%. Basic research is fundamental research performed to improve understanding of the structure, functioning and behaviour of living organisms and the environment. 'Translational and applied research', which is research conducted for the benefit of human or animal health (e.g. in the development of medicines), accounted for 10% of procedures.

Table 6 (broken into two separate parts) shows the breakdown of the categories of 'Basic research' purposes by species, the most common purpose being research involving the immune system at 31%, followed by research into ethology/animal behaviour/animal biology at 22%. Immune system research involves studies that look at particular cells in the immune system, such as the cells involved in autoimmune diseases and cancer. The majority of animals used for ethology/animal behaviour and animal biology were cattle, in studies investigating reproduction and fertility in Irish cows.

Table 7 (also broken into two separate parts) shows the breakdown of the categories of 'Translational and applied research' purposes by species. The most common category was animal diseases and disorders at 44%, followed by human nervous and mental disorders at 18%. Cattle accounted for the majority of animals used for research into animal diseases and disorders, which included, for example, studies investigating diseases of newborn calves. The research into human nervous and mental disorders in Ireland included research into treatments for diseases such as epilepsy and autism.

Table 5: Uses of animals by general project purpose and species

Animal species	Basic Research	Translational and applied research	Regulatory use and Routine production	Protection of the natural environment in the interests of the health or welfare of human beings or animals	Higher education or training for the acquisition, maintenance or improvement of vocational skills	Maintenance of colonies of established genetically altered animals, not used in other procedures	Total
Mice	22506	9628	153730		153	4568	190585
Rats	5997	2562	1263		54		9876
Guinea-Pigs		949	980				1929
Rabbits	12	1869	609				2490
Cats		152	12				164
Dogs		547	40				587
Ferrets			621				621
Horses, donkeys & cross-breeds	90	9	16		12		127
Pigs	1699	1114	18		9		2840
Goats		68	3				71
Sheep	691	369			52		1112
Cattle	7246	3911	21		109		11287
Other Mammals		20					20
Domestic fowl	3	110					113
Other birds	570	2					572
Xenopus	420						420
Zebra fish	1414	75					1489
Other Fish	1699	1599	559	815			4672
Total	42347	22984	157872	815	389	4568	228975

Table 6 (part 1): Uses of animals for basic research by species and category

Animal species	Oncology	Cardiovascular Blood and Lymphatic System	Nervous System	Respiratory System	Gastrointestinal System including Liver	Musculoskeletal System	Immune System
Mice	1058	119	3293	433	2558	153	12967
Rats		305	5249	40	72	113	198
Rabbits						12	
Horses, donkeys & cross-breeds							
Pigs	3	5					
Goats							
Sheep					249		
Cattle					64		
Domestic fowl							3
Other birds							
Xenopus							
Zebra fish							
Other Fish							
Cephalopods							
Total	1061	429	8542	473	2943	278	13168
%	3%	1%	20%	1%	7%	<1%	31%

Table 6 (part 2): Uses of animals for basic research by species and category

Animal species	Urogenital/Reproductive System	Sensory Organs (skin, eyes and ears)	Endocrine System/Metabolism	Multisystemic	Ethology / Animal Behaviour /Animal Biology	Total
Mice	40	1123	573	167	22	22506
Rats				20		5997
Rabbits						12
Horses, donkeys & cross-breeds					90	90
Pigs					1691	1699
Goats						
Sheep					442	691
Cattle	2338		5		4839	7246
Domestic fowl						3
Other birds					570	570
Xenopus		420				420
Zebra fish				1414		1414
Other Fish					1699	1699
Cephalopods						
Total	2378	1543	578	1601	9353	42347
%	6%	4%	1%	4%	22%	

Table 7 (part 1): Uses of animals for translational and applied research by species and category

Animal species	Human Cancer	Human Infectious Disorders	Human Cardiovascular Disorders	Human Nervous and Mental Disorders	Human Respiratory Disorders	Human Gastrointestinal Disorders including Liver	Human Musculoskeletal Disorders	Human Immune Disorders
Mice	1134	1413	779	2786	317	3	1494	481
Rats			159	1387	245	297	186	53
Guinea-Pigs								
Rabbits							24	
Cats								
Dogs								
Horses, donkeys & cross-breeds							8	
Pigs			46					6
Goats							64	
Sheep			18					
Cattle								
Other Mammals								
Domestic fowl								
Other birds								
Zebra fish	75							
Other Fish								
Cephalopods								
Total	1209	1413	1002	4173	562	300	1776	540
%	5%	6%	4%	18%	2%	1%	8%	2%

Table 7 (part 2): Uses of animals for translational and applied research by species and category

Animal species	Human Sensory Organ Disorders (skin, eyes and ears)	Human Endocrine/Metabolism Disorders	Animal Diseases and Disorders	Animal Welfare	Diagnosis of diseases	Total
Mice	1029	65			127	9628
Rats	91	64			80	2562
Guinea-Pigs			949			949
Rabbits	3	10	1832			1869
Cats			152			152
Dogs			547			547
Horses, donkeys & cross-breeds			1			9
Pigs	10		1046		6	1114
Goats			4			68
Sheep			111	240		369
Cattle			3863		48	3911
Other Mammals			20			20
Domestic fowl					110	110
Other birds					2	2
Zebra fish						75
Other Fish			1599			1599
Cephalopods						
Total	1133	139	10124	240	373	22984
%	5%	<1%	44%	1%	2%	

3.6 Animals used for regulatory use and other routine production purposes

Table 8 breaks down the types of tests performed for 'Regulatory purposes and other routine production purposes' by species, showing that toxicity and other safety testing including pharmacology was the most commonly performed category of test. It should be noted that the dogs and cats were solely used for the development of veterinary medicines (pharmacokinetics and target animal safety), and not for toxicity testing.

Table 8: Uses of animals by regulatory purpose and species

Animal species	Quality control (incl batch safety and potency testing)	Other efficacy and tolerance testing	Toxicity and other safety testing including pharmacology	Routine production	Total
Mice	5062	608	148060		153730
Rats	1263				1263
Guinea-Pigs	980				980
Rabbits	609				609
Cats			12		12
Dogs			40		40
Ferrets	621				621
Horses, donkeys & cross-breeds	2	14			16
Pigs		18			18
Goats	3				3
Sheep					
Cattle	21				21
Other Fish			559		559
Total	8561	640	148671		157872
%	5%	<1%	94%	0%	

4. CONCLUSION

In the year 2015, there were 228,975 reported uses of animals in procedures in Ireland. This is a 1% increase on the number of uses reported for 2014 and follows a 19% reduction between 2013 and 2014. These figures highlight the difficulty in observing clear trends at this point with data available for only three years under the new reporting system. Nevertheless, there does appear to have been an overall reduction in severity during 2015, with a 31% drop in procedures reported as severe when compared to the 2014 report.

The HPRA will continue to work to reduce severe suffering, and place the emphasis of its regulatory remit on the application of the 3Rs (Replacement, Reduction and Refinement). In addition, the HPRA will continue to apply its influence and judgement in all applications to ensure that studies are only permitted where there is no alternative research technique available and the expected benefits outweigh any possible harms.

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 having fully recovered from a completed procedure, and having been certified by a veterinarian as having returned to full health, that animal can then be enrolled on another project.

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 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, or 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 and 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 and 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.