HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

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

2013

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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, a new EU Directive[1] to further protect animals used for scientific purposes came into effect in Ireland. Its aim is to strengthen legislation and improve the welfare of those animals used for scientific purposes and to promote and ensure the application of the principles of the three Rs - Replacement, Reduction and Refinement of the use of animals in scientific studies and which are now embedded in the legislation. In January 2013, the HPRA also became the competent authority responsible for the Directive's implementation. This authority was transferred from the Department of Health which regulated this area until 31 December 2012.

Under the applicable EU and national legislation, the use of animals for scientific or educational purposes should only be considered where a non-animal alternative research technique is unavailable. The HPRA's role is to assess applications to ensure that there are no alternative non-animal methods available that could deliver the expected results; to ensure that where animals are being used that the number of animals is at the lowest level possible; and that each use of an animal is carefully evaluated and the likely harm to the animal is minimised as far as possible and is balanced in any case against the expected benefits of the work. The HPRA aims to improve the welfare of animals used for scientific purposes and to promote the principles of the three Rs (see page 14).

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

1. 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.
2. Projects: Scientific procedures can be performed on an animal only following a detailed submission of the planned study and subsequent approval by the HPRA on the basis of a favourable harm/benefit analysis. Information on the decision taken in respect of individual projects is published on the HPRA website (www.hpra.ie).
3. Individuals: Any person wishing to carry out scientific procedures on 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 new requirements for regulatory oversight of the use of animals for scientific or educational purposes are more rigorous than those which applied historically. However, any project which was originally authorised by the Department of Health continues in force until the expiry of the authorisation in question. This, in many cases, may take up to five years (i.e. until the end of December 2017). The new restrictions and standards are expected to enhance animal welfare and ensure that animals are used in studies only when their use is strongly justified and following independent assessment.

[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

There are several reasons why animals are used for scientific purposes. These may include:

1. to progress the development of new medicines following earlier non-animal tests;
2. to investigate the safety of new medicines or medical devices prior to using them in clinical trials in humans;
3. to ensure the environmental safety of substances that may be released into the environment;
4. to manage risks to human and animal health, particularly relating to the quality, safety and potency of biological substances used in medicines or vaccines.

Every application received for a study involving animals is independently assessed by the HPRA. It requires scientific justification for the research techniques being applied and checks whether alternative (non-animal) methods are available or appropriate. Whenever possible, the HPRA insists on a reduction of the numbers of actual animals required, as well as a refinement of techniques being applied to minimise the impact on animal welfare.

The objective of this report is to present statistical data on the number of animals used for scientific purposes in Ireland during the year 2013 in accordance with Article 54(2) of the Directive. This is the first 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 previous reports in this area.

As the methodology and legal basis for the requirements for data collection were substantially changed with the introduction of the new Directive, the type and format of the data being collected has also changed. 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 new format is designed to meet the requirements for a European database which is being developed currently by the EU Commission.

The effect of the new data requirements means that like-for-like comparisons between this year's information and the statistical data previously provided by the Department of Health would not be meaningful or accurate. Thus it is inadvisable to compare the current data and numbers from 2013 with those of preceding years as it would not provide accurate comparisons. For example, previous data reported only on the first use of each animal, whereas this report includes any subsequent uses of the same animals. In addition, the breeding of genetically modified animal lines was not required to be included in previous reporting years. This is now a requirement of the legislation. As in previous years, the data provided are based on self-declarations by the establishments concerned. For the year 2013, all establishments submitted self-declared returns.

Based on experiences with collecting other categories of national data, the HPRA expects that it will take at least three years using the new reporting format before meaningful trends can be interpreted with reasonable accuracy.

2. SUMMARY

a) In 2013, a total of 277,559 naive animals (not previously used in procedures) were used in procedures, and including animals that were reused, there were a total of 279,379 uses of animals for procedures.

b) Of the total number of naive animals (277,559), 9,970 genetically modified animals were used in procedures, which represent 4% of all animals used. Of these genetically modified animals, 88% did not display any impairment to their well-being.

c) Of the total number of uses of animals in procedures (279,379), some 205,751 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 the tests conducted (94% or 193,197) were for acute and sub-acute toxicity testing.

Note: The following species have not been included in the tables in this document as they were not used in Ireland in 2013:

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

3. RESULTS

3.1 Species and numbers of naive animals

Table 1 shows the number of naive animals (used for the first time) used in procedures. Mice (92%) were by far the most commonly used species. Please note that for uses involving cats and horses, the only studies conducted were for research into the development of veterinary medicines, which is expected to be of benefit to those species. The uses of cattle related to improving animal health, husbandry production and farming techniques.

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

Animal species	Number of animals
Mice	255754
Rats	12029
Guinea-Pigs	3262
Rabbits	1843
Cats	54
Dogs	0
Ferrets	109
Horses, donkeys & cross-breeds	49
Pigs	606
Sheep	1189
Cattle	2315
Other Mammals	198
Domestic fowl	42
Xenopus	17
Zebra fish	50
Other Fish	42
Total	277559

3.2 Species and numbers of uses of animals

Table 2 shows the number of *uses* of animals in procedures, rather than the numbers of animals used (as shown in Table 1).

Table 2: Numbers of uses of animals by species

Animal species	Number of uses
Mice	256029
Rats	12047
Guinea-Pigs	3262
Rabbits	2217
Cats	288
Dogs	696*
Ferrets	109
Horses, donkeys & cross-breeds	59

Animal species	Number of uses
Pigs	625
Sheep	1189
Cattle	2505
Other Mammals	198
Domestic fowl	42
Xenopus	21
Zebra fish	50
Other Fish	42
Total	279379

*There were no new (naive) dogs used in 2013. This figure relates to dogs that were also used in studies prior to 2013. Please note that for uses involving dogs, the only studies conducted were for research into the development of veterinary medicines.

3.3 Origin of animals

Table 3 shows the birthplace of naive animals used in procedures. 99.9% of all animals were born in the EU. In accordance with the legislation only the 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.

Table 3: Place of birth of all naive 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 the world	Total
Mice	255109	379	266	255754
Rats	12029			12029
Guinea-Pigs	3262			3262
Rabbits	1843			1843
Cats	54			54
Dogs				
Ferrets	109			109
Horses, donkeys & cross-breeds		49		49
Pigs	285	321		606
Sheep	1009	180		1189
Cattle	211	2104		2315
Other Mammals		198		198
Domestic fowl	37	5		42
Xenopus			17	17
Zebra fish	50			50
Other Fish		40	2	42
Total	273998	3276	285	277559

3.4 Species and classification of severity

Table 4 shows the reported actual severity experienced by the animals used in procedures. Overall, 44% of animals were involved in procedures that were classified as 'severe', and of these, 99.6% were mice. Amongst the other species (i.e. excluding mice), the majority of animals (60%) were involved in procedures that were classified as 'mild'. It should be noted that animals involved in procedures classified as 'severe' cannot be reused.

Table 4: Classification of actual severity

Species	Non-recovery	Mild [up to and including]	Moderate	Severe	Total
Mice	11962	39414	82635	122018	256029
Rats	1518	4758	4958	813	12047
Guinea-Pigs	835	2427			3262
Rabbits	16	1527	643	31	2217
Cats		272	16		288
Dogs		631	65		696
Ferrets	109				109
Horses, donkeys & cross-breeds		59			59
Pigs	24	529	72		625
Sheep	30	1159			1189
Cattle		2387	112	6	2505
Other Mammals		198			198
Domestic fowl		42			42
Xenopus	14	6		1	21
Zebra fish	50				50
Other Fish		3	39		42
Total	14558	53412	88540	122869	279379

3.5 Animal species and project purpose

Table 5 shows the general project purposes for which animals were used based on their species. The most common purpose at 74% was 'Regulatory and other routine production purposes'. This includes animals used in procedures for pre-clinical 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 'Translational and applied research' at 15%.

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 35%, followed by research involving the nervous system at 23%.

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 human musculo-skeletal disorders at 51% followed by human nervous and mental disorders (26%).

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 natural environment in interests of health or welfare of human beings or animals	Higher education for training for the acquisition, maintenance or improvement of vocational skills	Maintenance of colonies of genetically altered animals not used in other procedures	Total
Mice	23360	28935	203577			157	256029
Rats	3913	8104			30		12047
Guinea-Pigs	110	2093	1059				3262
Rabbits	49	1521	647				2217
Cats		147	141				288
Dogs		588	108				696
Ferrets			109				109
Horses, donkeys & cross-breeds	49		10				59
Pigs	554	52	14		5		625
Sheep	156	1033					1189
Cattle	2330	41	86	48			2505
Other Mammals		198					198
Domestic fowl	5	37					42
Xenopus	21						21
Zebra fish	50						50
Other Fish	24			18			42
Total	30621	42749	205751	66	35	157	279379

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	Musculo-skeletal system	Immune system
Mice	2272	876	4627	295	819	45	10600
Rats	16	12	2554	40	165		99
Guinea Pigs							
Rabbits		20					2
Cats							
Dogs							
Ferrets							
Horses, donkeys & cross-breeds						10	
Pigs		71			273		
Sheep					132		
Cattle					1900		90
Domestic fowl							5
Xenopus							
Zebra fish							
Other Fish							
Total	2288	979	7181	335	3289	55	10796

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	Multi-systemic	Ethology / animal behaviour / animal biology	Other	Total
Mice	77	755	1170	1710	6	108	23360
Rats	223	190	20	274	162	158	3913
Guinea Pigs						110	110
Rabbits		11				16	49
Cats							
Dogs							
Ferrets							
Horses, donkeys & cross-breeds				39			49
Pigs						210	554
Sheep					24		156
Cattle	236				56	48	2330
Domestic fowl							5
Xenopus		3				18	21
Zebra fish		50					50
Other Fish					23	1	24
Total	536	1009	1190	2023	271	669	30621

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 Musculo-skeletal Disorders	Human Immune Disorders
Mice	114	451	71	6354	240		18887	1239
Rats	10	41	24	4516	389	53	2824	
Guinea Pigs								
Rabbits					18			3
Cats								
Dogs								
Ferrets								
Horses, donkeys & cross-breeds								
Pigs						3		
Sheep			24					
Cattle								
Other Mammals								
Domestic fowl								
Xenopus								
Zebra fish								
Other Fish								
Total	124	492	119	10870	647	56	21711	1242

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	Other Human Disorders	Animal Diseases and Disorders	Animal Welfare	Diagnosis of diseases	Total
Mice	1199		380				28935
Rats		127	6	18	56	40	8104
Guinea-Pigs				2093			2093
Rabbits				1500			1521
Cats				131	16		147
Dogs				588			588
Ferrets							
Horses, donkeys & cross-breeds							
Pigs	1			48			52
Sheep				1009			1033
Cattle				16	15	10	41
Other Mammals				198			198
Domestic fowl						37	37
Xenopus							
Zebra fish							
Other Fish							
Total	1200	127	386	5601	87	87	42749

3.6 Animals used for regulatory use and other routine production purposes

In relation to animals used for 'Regulatory and other routine production purposes' all the tests were performed to satisfy requirements emanating from EU and from national legislation. No tests were performed in order to satisfy non-EU legislation.

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. Of these, dogs and cats (249 animals) were solely used for the development of veterinary medicines (e.g. pharmacokinetic tests) which are ultimately for the benefit of the species.

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	10380		193197		203577
Rats					
Guinea-Pigs	1059				1059
Rabbits	643			4	647
Cats			141		141
Dogs			108		108
Ferrets	109				109
Horses, donkeys & cross-breeds	10				10
Pigs		14			14
Sheep					
Cattle	86				86
Other Mammals					
Domestic fowl					
Xenopus					
Zebra fish					
Other Fish					
Total	12287	14	193446	4	205751

4. CONCLUSION

As this is the first year of reporting under the new Directive (2010/63/EU) on the protection of animals used for scientific purpose the data collation, criteria and detail are not comparable to that related to the years pre-2013. The HPRA anticipates that as the years progress more meaningful comparative analysis will be apparent.

The level of research undertaken within the State fundamentally influences the data, and in the future if there is an increase or decrease in the number of breeder/supplier/user establishments and studies undertaken, this will impact on the data acquired by the HPRA. The HPRA will continue to place the emphasis of its regulatory remit on the protection of animals used in research and the application of the 3Rs by establishments as now embedded in the legislation:

Replacement refers to the use of alternative methods which substitute the use of animals for scientific purposes e.g. *in vitro* test methods, use of computer simulations and modelling, use of video material. Where replacement is not possible, animal use must only be permitted where justified and where the expected benefits outweigh the potential adverse effects experienced by the animals.

Reduction refers to measures that must be applied so as to minimise the number of animals used in each research project (e.g. better study designs).

Refinement refers to measures that must also be applied to enable procedures to be carried out in the most humane manner possible and to minimise pain, suffering, distress and lasting harm (e.g. use of pain-killers, use of nesting material etc).

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 adverse effects.