HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

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

2014

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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, an EU Directive[1] to protect animals used for scientific purposes came into effect in Ireland. In January 2013, the HPRA also 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 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. The Directive firmly anchors in EU Legislation the 3Rs, i.e. Replacement, Reduction and Refinement:

- **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, etc. Where replacement is not possible, animal use most 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 to minimise pain, suffering, distress and lasting harm (e.g. use of pain-killers, use of nesting material, etc.).

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 are often 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.

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.

[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

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 authorisation.

The HPRA aims to improve the welfare of animals used for scientific purposes and to promote the principles of the 3Rs. In 2014, the HPRA inspected each establishment at least once, and was satisfied with the level of care and welfare being provided to the animals in the establishments. Every application received for a project involving animals requires scientific justification for the research techniques being applied and was independently evaluated by the HPRA using these principles. The likely impact to the animals is minimised as far as possible by applying refinements and is balanced in any case against the expected benefits of the work. The HPRA checks whether alternative (non-animal) methods are available or appropriate; 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 the year 2014 in accordance with Article 54(2) of the Directive. This is the second 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, in many cases, 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 modified 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.

The effect of the new data requirements means that like-for-like comparisons between the HPRA's statistical data from 2013 and 2014 with that of the data previously provided by the Department of Health would not be meaningful or accurate. The HPRA expects that it will take at least three years using the new reporting format before any trends could be interpreted with reasonable accuracy.

2. SUMMARY

a) In 2014, a total of 224,249 naive animals (not previously used in procedures) were used in procedures, and including animals that were reused, there were a total of 226,684 uses of animals for procedures.

b) Of the total number of naive animals (224,249), 8,961 genetically modified animals were used in procedures, which represent 4% of all animals used. Of these genetically modified animals, 94% did not display any impairment to their well-being.

c) Of the total number of uses of animals in procedures (226,684), some 144,037 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 (95% or 137,491) were for toxicity and other safety testing including pharmacology, of which 98% 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 2014:

- 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 naive animals

Table 1 shows the number of naive animals (used for the first time) used in procedures. Mice (89%) were by far the most commonly used species. It should be noted that for uses involving dogs and cats, the only studies conducted were for research into the development of veterinary medicines, which is expected to be of benefit to those species.

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

Animal species	Number of animals
Mice	200160
Rats	10465
Guinea-Pigs	2107
Rabbits	1539
Cats	53
Dogs	69
Ferrets	367
Horses, donkeys & cross-breeds	66
Pigs	698
Goats	2
Sheep	1765
Cattle	3153
Other Mammals	22
Domestic fowl	96
Other birds	318
Xenopus	25
Zebra fish	127
Other Fish	3217
Total	224249

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). It shows both the first, and all the subsequent uses of the animals that were completed in the year 2014. It also includes animals that were used for the first time (i.e. were naive) in years *prior* to 2014.

Table 2: Numbers of uses of animals by species

Animal species	Number of uses
Mice	200160
Rats	10465
Guinea-Pigs	2107
Rabbits	2124
Cats	444

Animal species	Number of uses
Dogs	807
Ferrets	367
Horses, donkeys & cross-breeds	76
Pigs	698
Goats	2
Sheep	1774
Cattle	3849
Other Mammals	22
Domestic fowl	102
Other birds	318
Xenopus	25
Zebra fish	127
Other Fish	3217
Total	226684

3.3 Origin of animals

Table 3 shows the birthplace of naive animals used in procedures. 95.7% 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 the rest of Europe	Animals born in rest of the world	Total
Mice	189995	1054		9111	200160
Rats	10449			16	10465
Guinea-Pigs	2107				2107
Rabbits	1511			28	1539
Cats	53				53
Dogs	69				69
Ferrets	325			42	367
Horses, donkeys & cross-breeds	1	65			66
Pigs	37	661			698
Goats		2			2
Sheep	835	930			1765
Cattle	894	2259			3153
Other Mammals		4	10	8	22
Domestic fowl	91	5			96
Other birds	2	4		312	318
Xenopus				25	25
Zebra fish	127				127

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 the rest of Europe	Animals born in rest of the world	Total
Other Fish	2246	953	18		3217
Total	208742	5937	28	9542	224249

3.4 Species and classification of severity

Table 4 shows the reported actual severity experienced by the animals during uses in procedures, grouped by species. Overall, 40% of animals were involved in procedures that were classified as 'severe', and of these, 98.5% were mice. Amongst the other species (i.e. excluding mice), the majority of animals (65.6%) 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	Moderate	Severe	Total
Mice	619	45312	65543	88686	200160
Rats	1236	4788	3337	1104	10465
Guinea-Pigs		2107			2107
Rabbits		1400	688	36	2124
Cats		29	415		444
Dogs		19	788		807
Ferrets		367			367
Horses, donkeys & cross-breeds		76			76
Pigs	35	641	22		698
Goats			2		2
Sheep	24	1491	259		1774
Cattle	11	3830	8		3849
Other Mammals		22			22
Domestic fowl		102			102
Other birds		318			318
Xenopus	5	19	1		25
Zebra fish	50	77			127
Other Fish	1	2118	852	246	3217
Total	1981	62716	71915	90072	226684

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 2014. The most common purpose at 64% 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 21%.

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 58%, followed by research involving the nervous system at 24%.

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 61% followed by animal diseases and disorders (17%).

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	Total
Mice	26911	32221	141028			200160
Rats	3691	6733			41	10465
Guinea-Pigs		1037	1070			2107
Rabbits	8	1474	642			2124
Cats		344	100			444
Dogs		635	172			807
Ferrets			367			367
Horses, donkeys & cross-breeds	51	3	12		10	76
Pigs	160	534			4	698
Goats		2				2
Sheep	440	1262	24		48	1774
Cattle	2712	987	98		52	3849
Other Mammals	8	4		10		22
Domestic fowl	5	97				102
Other birds	4	2		312		318
Xenopus	25					25
Zebra fish	50	77				127
Other Fish	447	2246	524			3217
Total	34512	47658	144037	322	155	226684

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	1428	135	2687	674	1139	239	19433
Rats		128	2215	3	131	9	98
Guinea Pigs							
Rabbits							8
Cats							
Dogs							
Ferrets							
Horses, donkeys & cross-breeds							
Pigs		7			123		
Goats							
Sheep					349		52
Cattle					989		448
Other mammals							
Domestic fowl							5
Other birds							
Xenopus							
Zebra fish							
Other Fish							
Total	1428	270	4902	677	2731	248	20044

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	127	608	127		230	84	26911
Rats	252			71	717	67	3691
Guinea Pigs							
Rabbits							8
Cats							
Dogs							
Ferrets							
Horses, donkeys & cross-breeds				51			51
Pigs				15		15	160
Goats							
Sheep	23				16		440
Cattle	826		124		188	137	2712
Other mammals						8	8
Domestic fowl							5
Other birds					4		4
Xenopus		20				5	25
Zebra fish		50					50
Other Fish					447		447
Total	1228	678	251	137	1602	316	34512

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	740	862	338	1478	219	148	25825	903
Rats	52	30		2780	220	28	3347	75
Guinea Pigs								
Rabbits								
Cats								
Dogs								
Ferrets								
Horses, donkeys & cross-breeds								
Pigs	1		22			53		
Goats							2	
Sheep			77					
Cattle								
Other Mammals								
Domestic fowl								
Other birds								
Xenopus								
Zebra fish	28							
Other Fish								
Total	821	892	437	4258	439	229	29174	978

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	681		983	44			32221
Rats			201				6733
Guinea-Pigs				1037			1037
Rabbits	76			1392		6	1474
Cats				344			344
Dogs				635			635
Ferrets							
Horses, donkeys & cross-breeds				2	1		3
Pigs				458			534
Goats							2
Sheep				1075	110		1262
Cattle				875	72	40	987
Other Mammals				4			4
Domestic fowl						97	97
Other birds						2	2
Xenopus							
Zebra fish	49						77
Other Fish				2246			2246
Total	806		1184	8112	183	145	47658

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	3213	1376	136439		141028
Rats					
Guinea-Pigs	784		286		1070
Rabbits	597			45	642
Cats			100		100
Dogs			142	30	172
Ferrets	367				367
Horses, donkeys & cross-breeds	12				12
Pigs					
Goats					
Sheep	24				24
Cattle	98				98
Other Mammals					
Domestic fowl					
Other birds					
Xenopus					
Zebra fish					
Other Fish			524		524
Total	5095	1376	137491	75	144037

4. CONCLUSION

As this is only the second year of reporting under the Directive (2010/63/EU) on the protection of animals used for scientific purposes, the data collation, criteria and detail are not comparable to previous reports from the Department of Health. The HPRA also advises that in respect of the HPRA's 2013 data, it would be unsound to directly compare this data as it is only the second year of a new reporting structure to which reporters are getting better acquainted to the changed reporting requirements and provisions required. Extreme caution should be applied therefore in any attempt to draw comparisons to previous years' figures. The HPRA anticipates that it will take at least three years for more meaningful comparative analysis and trends to be apparent.

The level of research undertaken within the state fundamentally influences the data. In the future, if there is an increase or decrease in the number of breeder/supplier/user establishments and studies undertaken, this will impact accordingly 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 (Replacement, Reduction and Refinement) by establishments as embedded in the legislation. 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.