



Analysis and comments on the statistical survey on the use of animals for scientific purposes in France in 2021, and developments since 2015

April 2023

Data published by the Ministry of Higher Education and Research (MESR) for the year 2021 indicate that the use of animals is not decreasing in France.

1. Data sources and methodological precautions

- a) The survey has been conducted annually since 2014, and the results are made available to the public by the MESR on the page:
<http://www.enseignementsup-recherche.gouv.fr/cid70613/enquete-statistique-sur-l-utilization-des-animals-a-des-fins-scientifiques.html>
- b) This survey includes animals (vertebrates and cephalopods) present in an experimental procedure during the year and removed from this procedure before the end of the year. In accordance with the European directive, these are the uses that are counted, so that an animal can be counted several times when it is "reused".
- c) The survey does not include:
 - animals raised in user establishments and not involved in experimental procedures, including genetically altered animals without a harmful phenotype (breeding animals, animals not presenting the desired characteristics, surplus animals, etc.);
 - animals involved in procedures below the constraint threshold;
 - animals euthanized using regulatory methods for organ or tissue removal (e.g. for alternative methods);
 - Other invertebrate research models such as insects (*Drosophila*) and worms (*C. Elegans*).

The vertebrates concerned by these "outside the scope" categories of the directive are the subject of an investigation every 5 years by the European Commission. In 2017, France used 2.13 million animals for these purposes, including 0.67 million for the creation and maintenance of genetically modified lines. 79% of these animals were mice, 6.6% rats, 8% fish,

3.3% guinea pigs, 1.9% rabbits. 120 dogs and 10 non-human primates were also killed in this way, outside of procedures.

- d) The developments (in France as in other countries) can be studied in principle since the implementation of the new 2013 regulations, therefore from 2014, the first year published in France under this new regime. The data from previous years (in France there was a three-yearly survey, the last data under this method having been published for the year 2010 (2.2 million animals)), although informative, are not entirely comparable since the accounting method was different (in particular, since 2014, uses that ended during the year have been counted).

However, since 2014 was clearly not exhaustive (1,769,118 animals used declared compared to 1.9 million in subsequent years), particularly for certain species (in particular non-human primates), we began the analysis from 2015.

- e) Since the survey is not accompanied by a methodological chapter, we do not know the methods used to collect the data, how many structures are involved, what the completeness rate is, whether there are quality controls on the data communicated by the establishments, etc.

Only once did the Ministry comment on the issue of the number of respondents: it stated, in a commentary on the 2017 data, that the "number of establishments responding to the 2017 survey" was "higher than for the 2016 survey (+8.2%)." Note that no adjustment is made to the data to take this factor into account.

- f) Finally, let us recall that the data from the statistical surveys published on the MESR website do not take into account animals used in military research projects, even though these are not a priori excluded from the scope of the provisions of European Directive 2010/63/EU relating to the protection of animals used for scientific purposes. However, French regulations stipulate that *"The Minister of Defense is the sole recipient of declarations and information concerning establishments under his authority or supervision"* (art R 214.127 of the Rural Code).

2. Results

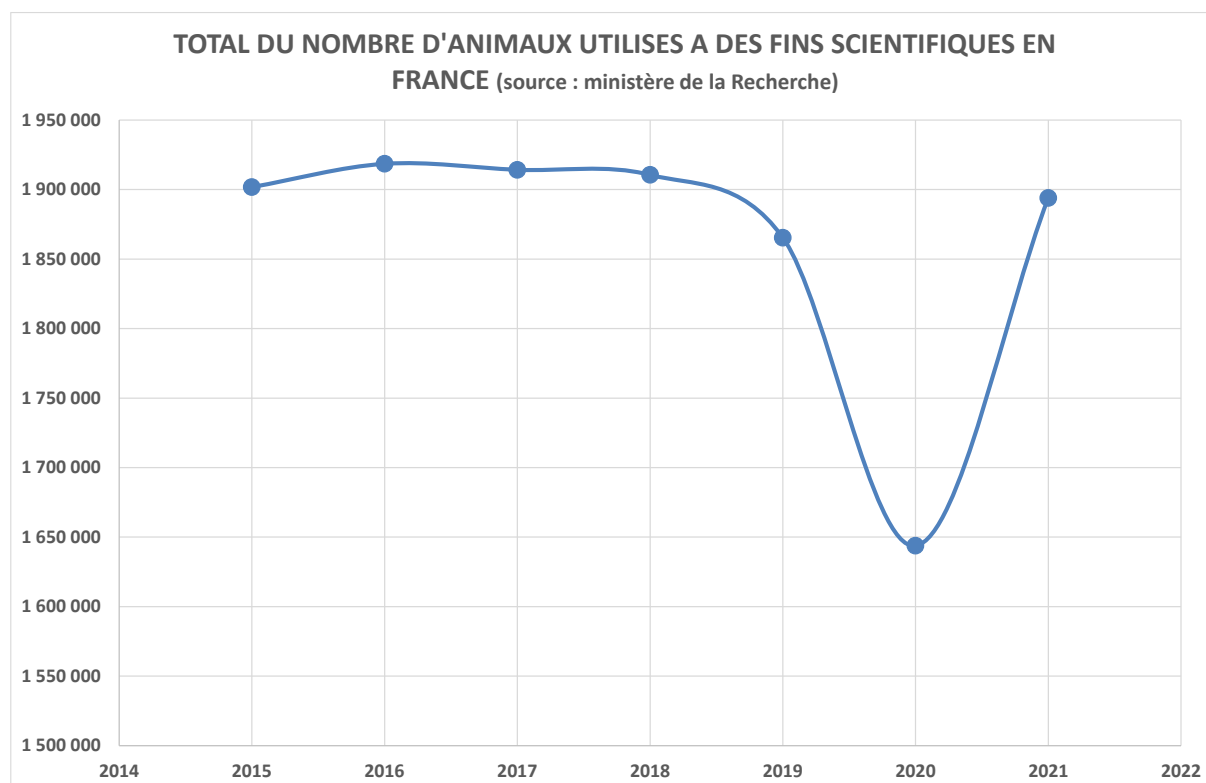
2.1 Global developments

Figure 1 shows the overall evolution of animal use since 2015 in France based on published data.

After an increase in 2016 (+0.9%), the number of animal uses in France declined very slightly between 2016 and 2018 (-0.4%), reaching 1,910,519, before decreasing further in 2019 (-2.4%, with 1,865,403 animals). However, in 2021, the number rose to 1,893,897 animals (+1.5% compared to 2019).

The decrease observed in 2020 is linked to the periods of confinement, in particular the first confinement, which led to the cessation of activity in many laboratories, and even to the euthanasia of animals present and not used; a priori if these animals had been included in a procedure (before the period of confinement) and even if they were killed during 2020 before the planned end of the procedure, they should be counted for the year 2020; we cannot know if this is actually the case. If, on the other hand, they had not yet been included in a procedure, they should be counted in the five-yearly report of the European Commission, including statistical data on animals killed outside an experimental procedure (excess numbers, organ removal, etc.).

Figure 1





The figures remain stable; the same number of animals have been used since 2015. Where are the results of applying the principles of replacement and reduction?

Let us remember that these numbers do not include animals killed without having been included in an experimental procedure (animals killed for their tissues and organs, surplus animals, genetically modified animals not developing the expected characteristics, animals that are too old, etc.).

2.2 Distribution by species

Table 1 shows the number of animal uses, by species, between 2015 and 2021 and the changes over this period.

Table 1: Evolution of the number of animal uses by species in France

	2015	2016	2017	2018	2019	2020	2021	Evol 2021/2015	% en 2021
souris	1 007 245	1 144 745	1 134 517	1 192 548	1 131 723	1 048 864	1 150 190	14,2%	60,7%
poissons	424 582	307 482	289 953	256 887	228 296	120 111	198 932	-53,1%	10,5%
rats	157 309	172 288	183 714	159 786	166 245	149 068	165 043	4,9%	8,7%
lapins	108 110	117 531	127 204	131 587	135 608	144 190	172 221	59,3%	9,1%
poules	66 734	56 759	43 144	46 029	76 624	75 108	77 598	16,3%	4,1%
autres oiseaux	46 433	14 633	27 225	29 095	37 982	21 272	24 055	-48,2%	1,3%
cochons d'inde	44 414	44 705	45 034	41 727	37 423	42 841	50 322	13,3%	2,7%
porcs	12 203	11 707	10 346	14 969	12 617	11 843	15 034	23,2%	0,8%
hamsters	10 986	10 768	6 696	5 213	5 929	8 577	12 280	11,8%	0,6%
moutons	3 446	5 763	5 396	4 304	4 895	2 827	4 587	33,1%	0,2%
chiens	3 226	4 204	4 106	4 219	4 898	4 079	4 383	35,9%	0,2%
xénopes	1 644	10 078	4 897	9 289	5 677	3 049	3 824	132,6%	0,2%
macaques	2 820	3 343	3 350	3 071	2 986	3 647	3 352	18,9%	0,2%
bovins	2 203	2 492	1 777	2 256	2 195	1 817	1 906	-13,5%	0,1%
autres amphibiens	3 473	2 117	860	714	833	432	1 866	-46,3%	0,1%
autres rongeurs	755	651	957	2 913	1 582	1 037	1 505	99,3%	0,1%
chats	336	1 067	867	1 185	1 007	970	1 018	203,0%	0,1%
reptiles	1 051	4 958	3 462	2 120	6 151	1 680	839	-20,2%	0,0%
équidés	629	540	305	482	695	483	668	6,2%	0,0%
chèvres	436	1 025	838	710	807	534	579	32,8%	0,0%
gerbilles de Mongolie	1 417	817	429	596	428	342	423	-70,1%	0,0%
furets	155	160	148	28	150	169	251	61,9%	0,0%
autres mammifères	1 772	20	18 525	104	179	181	218	-87,7%	0,0%
marmosets, tamarins	97	41	224	206	172	159	97	0,0%	0,0%
prosimiens	157	1	86	159	109	51	60	-61,8%	0,0%
autres singes	13	8	16	22	20	18	41	215,4%	0,0%
babouins	19	92	32	36	24	84	40	110,5%	0,0%
vervets	56	23	38	16	28	37	3	-94,6%	0,0%
autres carnivores	30	23	27	29	24	18	1 428	4660,0%	0,1%
céphalopodes	1	440	1	219	96	299	1 134		0,1%
TOTAL	1 901 752	1 918 481	1 914 174	1 910 519	1 865 403	1 643 787	1 893 897	-0,4%	
<i>dont primates non humains</i>	<i>3 162</i>	<i>3 508</i>	<i>3 746</i>	<i>3 510</i>	<i>3 339</i>	<i>3 996</i>	<i>3 593</i>	<i>13,6%</i>	

For the main highly represented species, there has been a steady increase in mice (until 2018) and rabbits. However, for a given species, the number of animals used can fluctuate significantly from one year to the next (knowing that the animals used are only counted at the end of the project). For example, in 2017, there was a significant number of animals belonging to the "other mammals"

category, which can be explained by a large project on bats on Réunion Island. These are "non-captive" animals and the purpose of their use was "applied research."

The species with the largest increase between 2015 and 2021 are: cats (203%), xenopus (133%), other rodents (99%), ferrets (62%), rabbits (59%), dogs (36%), sheep (33%), and goats (33%). Other carnivores saw a spike in use in 2021 (1,428 compared to around twenty in previous years), but it is not known which species are affected.

The use of non-human primates has fluctuated, but the trend is increasing (+13.6% between 2015 and 2021). There was a peak in 2020 (nearly 4,000 animals), this increase being linked to experiments concerning the evaluation of treatments and vaccines against Covid-19 (without success, as we know, in France).

Among non-human primates, macaques are by far the most used (from 2,820 in 2015 to 3,352 in 2021).

On the other hand, the following are less used in 2021 compared to 2015: amphibians other than xenopus, other birds, fish, gerbils.



A decline in numbers for a given species one year is followed by an increase the next year... Or, while numbers are declining for one species one year, they are increasing for another species. These fluctuations indicate that replacement methods are not sufficiently developed and implemented. If they were, the number of animals would gradually decline for each of the species considered.

2.3 Origin of animals

The origin is only specified for animals not reused (on this notion, see below; the reuse rate is 1.3% of total uses in 2021, decreasing).

The percentage of animals born in an authorized EU farm in France increased from 82.3% in 2015 to 85.7% in 2016, 83.5% in 2017, 84.5% in 2018, 83.4% in 2019 and 85.4% in 2021, excluding reuse. The rate of use of non-authorized farms within the EU therefore remains high in 2021 (9.9%), returning to the 2016 level (12.7% in 2019, 10.4% in 2018, 10.9% in 2017, 9.9% in 2016 and 13.7% in 2015).

Animals born in the "rest of Europe" (outside the EU, including Turkey, Russia, and Israel) numbered 32,127 in 2021 and represented 1.7% of uses. The species concerned are mainly fish (96%), "*used in programs related to environmental studies and species conservation*," according to the MESR.

As for those born in the "rest of the world", they represent 1.7% of uses in 2021, compared to 1.6% in 2018 and 2.9% in 2017. ¹In 2021, the species concerned are, out of 32,330 animals: mice (10,058, including transgenic mice from American farms), fish (13,188), primates (2,557), birds (2,397), other carnivores (1,398), rats and other rodents (1,281), rabbits (697), dogs (603).

In fact, the majority of primates come from Africa (Mauritius) or Asia (Vietnam). Only 9.3% of the primates used come from authorized farms in the European Union.

¹ The data for 2019 and 2020 have a major gap: the provenance is not specified for non-human primates.

- **One may wonder about the consistency of the presence of non-authorized farms within the European Union itself.** The commentary on the table published in 2021 states: *"Animals born in the EU outside authorized farms (10%) come either from user establishments or from occasional suppliers (for example, breeding farms for animals of agronomic interest).*

However, no reference is made in the European Directive to the possibility that certain breeders or suppliers in the EU may not be authorized.

- It is for primates (91% in 2021) and dogs (23%) that the percentage of animals born in "the rest of the world" compared to the total of their species (excluding reuses) is the highest, as in previous years. This is also the case for "other carnivores" (98%), but this is a particularity of the year 2021.



The key fact is that a significant proportion of animals from non-authorized farms within the EU or the "rest of the world" remain, which is the consequence of one of the shortcomings of the Directive (Article 20 on the authorization of breeders, suppliers and users of animals) to the detriment of animals: nothing prevents users from buying animals from non-authorized breeders and suppliers.

The case of primates and, to a lesser extent, dogs is worrying in this regard: excluding reuse, the rate of animals born in EU-authorized breeding facilities is very low. This reality raises questions about the conditions of collection from the wild or breeding in countries where the legislation is much less stringent than European legislation, as well as the conditions of transport of these animals over thousands of kilometers.

2.4 Reuses

In 2021, 24,584 animals were reused; in this case, there is no information on their initial origin. The reuse rate fluctuates: 0.8% of total uses in 2015, 1.9% in 2016, 2.1% in 2017, 2.2% in 2018, 2% in 2019, 2.1% in 2020, 1.3% in 2021.

It is recalled that the regulations set strict conditions for the reuse of animals: animal previously involved in a mild or moderate experimental procedure, animal having fully recovered its state of health and well-being, seriousness of the new procedure of mild, moderate or without recovery, favorable opinion of a veterinarian (see article 16 of European Directive 2010/63/EU).

The species with high reuse rates in 2021 are equines (79.2%), cats (56.9%), xenopus (45.4%), dogs (40.5%), reptiles (36.4%), goats (33%), cattle (31.4%), and non-human primates (21.5%), following the observations of previous years with some variations; for example, in the case of sheep, the reuse rate was high in 2017 (51.2%) and subsequently decreased (19.3% in 2019, 8.3% in 2021). The rate also decreased significantly for reptiles and goats. For primates, the reuse rate fluctuates: 42% in 2015, 33.9% in 2016, 38.5% in 2017, 26.1% in 2018, 37.9% in 2019 and 21.5% in 2021.

The explanation that could be put forward is twofold: on the one hand, most of these species are only subject to mild or moderate procedures (so many of these animals are accessible to reuse) and on the

other hand - as regards non-human primates, bovines, equines or caprines, as well as dogs and cats - the cost of renewing these animals is undoubtedly an "incentive" factor for reuse.

The percentage approach can, however, give a distorted view of reality and must be supplemented by an analysis of the data in absolute value. While the percentage of "reused" mice may indeed appear low (1%), it turns out that since mice represent the majority of animals used in the procedures, they are quantitatively the most reused animals (10,977, or 44.7% of reuses).

It should be noted that this question of reuse makes analysis quite difficult for the species most concerned since there are in fact double counts (the animal is counted as many times as there are uses, and this possibly over several years; we also do not know how many times an animal has been reused).



The reuse of animals means cumulative pain and suffering. The argument often raised by research teams that the practice of reuse is an application of the principle of reduction is unacceptable. Indeed, reuse is never considered in the regulations as a reduction method. Moreover, in accordance with the recommendations of the European directive, it is only possible under strictly regulated conditions (Article 16 of the said directive).

2.5 Non-human primate (NHP) generation

In the case of NHPs, a specific focus is placed on the generation, since the regulations provide for the eventual use of only farm animals. Excluding reused primates, in 2021, 675 are first generation (F1), 2,144 are second generation or later (F2 or higher).

Unlike in previous years, it is mentioned that among these 2,819 animals, 961 come from a "self-sustaining colony" (i.e. 34%)². This data is a break with that of previous years; it would seem that the frame of reference has changed (without any explanation being provided). Indeed, previously only a few dozen animals came from a self-sustaining colony (according to the MESR commentary, this was the breeding of mouse lemurs³ at the CEA / MNHN).

There have been no non-human primates used that have been taken from the wild since 2017 (F0). However, no information is provided by the Ministry on the controls carried out on these farms, which are mostly located in distant countries (Vietnam, Mauritius, etc.). The 2017 European Commission report on this topic⁴ indicated that while the animals used (and therefore transported by plane) in European laboratories did not include F0, the farms themselves did not prohibit themselves from taking animals from the wild for breeding purposes.

Table 2 shows how these data have evolved since 2015.

² colony in which animals are bred only within the colony or sourced from other colonies but not taken from the wild, and where the animals are kept in a way that ensures that they are accustomed to humans

³ endemic to the island of Madagascar. Their longevity characteristics (7-12 years) allow for research on the aging process. The colony at the National Museum of Natural History (MNHN) includes nearly 500 animals: <https://www.mecadev.cnrs.fr/index.php?post/elevage-microcebe-Brunoy>

⁴ Feasibility study as required in Article 10 of Directive 2010/63/EU on the protection of animals used for scientific purposes, 31st July 2017

Tableau 2 - Génération des primates non humains utilisés (hors réutilisations)

	2015		2016		2017		2018		2019		2020		2021	
F0	1	0,1%	5	0,2%	0	0,0%	0	0,0%	0	0,0%	0	0,0%	0	0,0%
F1	1171	63,8%	1030	44,4%	885	38,4%	709	27,4%	607	29,3%	641	28,7%	675	23,9%
F2 ou plus	451	24,6%	1272	54,9%	1285	55,8%	1733	66,9%	1370	66,0%	1540	69,0%	2144	76,1%
colonie autonome	211	11,5%	11	0,5%	134	5,8%	150	5,8%	98	4,7%	51	2,3%		0,0%
TOTAL	1834		2318		2304		2592		2075		2232		2819	

Note: in 2021, among F2 and above, 961 come from "self-sustaining colonies".



There is a trend towards increasing use of F2 or more (knowing that the European objective was to reach 100% by the end of 2022) but with "breaks" in 2017 and 2019.

The still high rate of F1 indicates that these uses have given rise upstream to collections in the wild for the capture of the "parents" of the NHP used.

The methods of monitoring breeding and transport conditions would need to be clarified.

2.6 The purposes of the studies

Table 3 details the evolution of the purposes of studies using animals.

Tableau 3 - Objet des études entre 2015 et 2021 en France

	2015		2016		2017		2018		2019		2020		2021	
Recherche fondamentale	785 617	41,3%	819 181	42,7%	731 041	38,2%	691 468	36,2%	761 701	40,9%	602 561	36,7%	718 550	37,9%
Etudes toxicologiques ou	579 121	30,5%	507 864	26,5%	574 030	30,0%	517 169	27,1%	538 993	29,0%	507 414	30,9%	528 471	27,9%
Recherches appliquées	432 417	22,7%	482 097	25,1%	479 372	25,0%	543 468	28,4%	424 278	22,8%	443 405	27,0%	489 701	25,9%
Maintenance de colonies d'animaux génétiquement	71 824	3,8%	57 646	3,0%	70 507	3,7%	76 426	4,0%	59 205	3,2%	42 677	2,6%	69 561	3,7%
Enseignement, formation	28 271	1,5%	34 280	1,8%	35 512	1,9%	41 510	2,2%	36 632	2,0%	27 314	1,7%	34 460	1,8%
Conservation des espèces	1 122	0,1%	16 750	0,9%	18 786	1,0%	36 807	1,9%	35 084	1,9%	19 483	1,2%	49 443	2,6%
Protection de l'environnement	3 380	0,2%	635	0,0%	4 918	0,3%	3 665	0,2%	5 542	0,3%	1 187	0,1%	3 711	0,2%
Enquêtes médico-légales		0,0%	28	0,0%	8	0,0%	6	0,0%	8	0,0%	2	0,0%	-	0,0%
TOTAL	1 901 752		1 918 481		1 914 174		1 910 519		1 861 443		1 644 043		1 893 897	100,0%

Note: The total indicated for 2019 does not correspond to the total indicated above of 1,865,403 animals used, because the MESR table concerning the objects of use contains an error: it is missing 3,960 zebrafish!

A minor error is also noted in 2020.

Basic research, toxicological or regulatory studies and applied research constitute between 92% and 94% of all studies for the period studied, with basic research being the primary reason.

It should be noted that the use of animals for teaching and training, after a steady increase from 2015 to 2018, experienced a slight decline in 2019 and 2021 compared to previous years, returning to the 2016 level (2020 not being a significant year in this area); this result is disappointing compared to what can be observed in other European countries where the reduction in the number of animals used is much more marked. Especially since alternative methods exist (videos, 3D simulations, mannequins, etc.) and some of them are also used in human medicine for the training of health personnel and even surgeons in most university hospitals (for example within the virtual hospital of Lorraine: <http://hopital-virtuel.univ-lorraine.fr/le-cuesim/>) as well as for the training of veterinary students (example of VetSim at the National Veterinary School of Alfort).

87% of these training uses concern mice or rats in 2021, but we also find pigs (6.4%), rabbits, guinea pigs, dogs.

There has also been a considerable increase in the number of uses of animals for "species conservation", from 1,122 uses in 2015 to 35,084 in 2019 and 49,443 in 2021, a 44-fold increase. Details are lacking on the context in which these procedures are carried out; but it would be shocking if thousands of individuals of unprotected species were sacrificed for this reason, especially since the species currently in danger are, for the most part, endangered as a result of human activities.

A greater level of detail is provided for toxicological and regulatory studies for human and veterinary medicinal products and for food products (Table 4). However, in 2021, the classification of categories was modified, creating a break in the series, with the identification of quality controls for products of animal origin, which impact all other sections.

Tableau 4 - Détail des utilisations d'animaux pour obligation législative et réglementaire en France

	2015		2016		2017		2018		2019		2020		2021	
Production d'origine animale, contrôle qualité													238 269	45,1%
Produits à usage médical	369 620	63,8%	345 748	66,0%	334 865	58,3%	354 337	68,5%	322 990	59,9%	319 737	63,0%	213 141	40,3%
Appareils médicaux	40 300	7,0%	66 231	12,6%	64 309	11,2%	44 898	8,7%	109 936	20,4%	101 371	20,0%	25 496	4,8%
Produits à usage vétérinaire	115 003	19,8%	79 254	15,1%	82 088	14,3%	75 675	14,6%	75 159	13,9%	50 192	9,9%	30 744	5,8%
Industrie chimique	14 804	2,6%	13 141	2,5%	12 737	2,2%	15 723	3,0%	21 226	3,9%	22 385	4,4%	14 662	2,8%
Autres	3 599	0,6%	767	0,1%	775	0,1%	16 373	3,2%	3 025	0,6%	6 988	1,4%	1 120	0,2%
Produits phytosanitaires	7 026	1,2%	3 996	0,8%	4 541	0,8%	4 010	0,8%	3 334	0,6%	3 071	0,6%	3 079	0,6%
Produits alimentaires	29 004	5,0%	14 271	2,7%	73 958	12,9%	4 973	1,0%	2 037	0,4%	2 055	0,4%	547	0,1%
Biocides	394	0,1%	569	0,1%	757	0,1%	1 180	0,2%	1 286	0,2%	1 615	0,3%	1 413	0,3%
TOTAL	579 750		523 977		574 030		517 169		538 993		507 414		528 471	

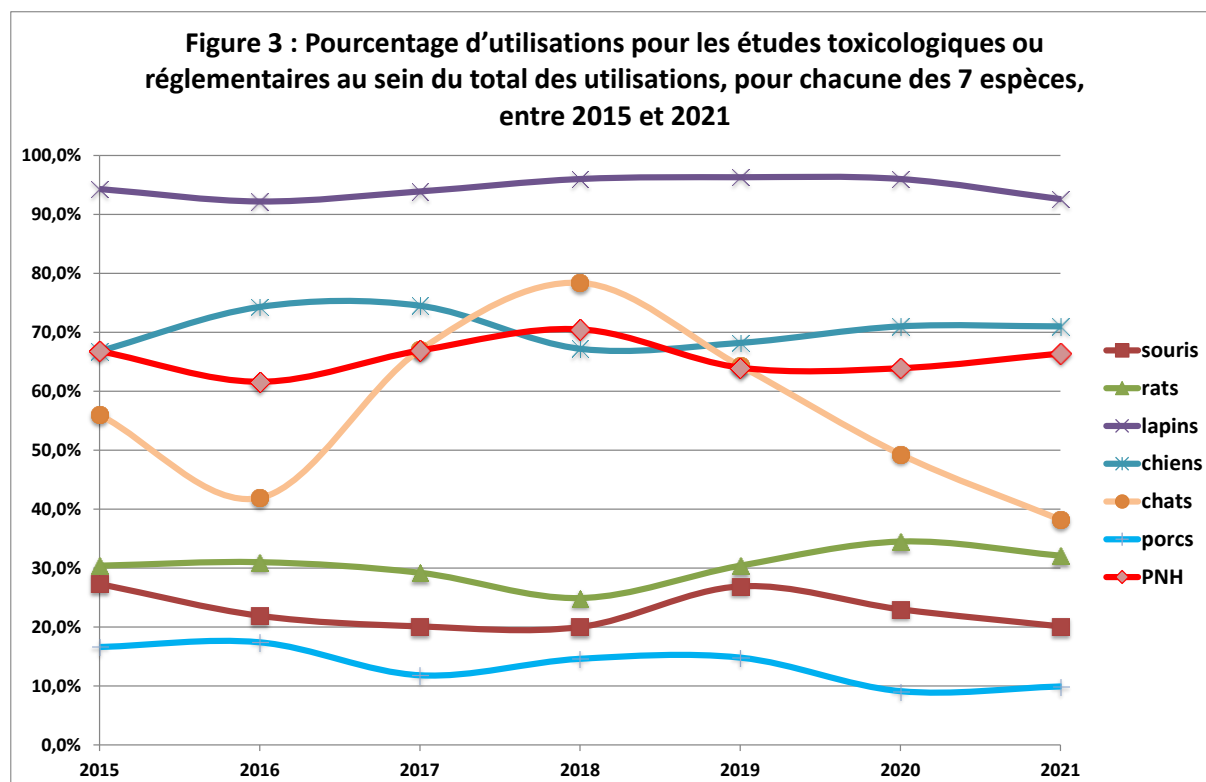
Note : in 2015 and especially in 2016, there was a discrepancy with the "toxicological and regulatory studies" line in table 3 (e.g.: in 2016, 523,977 animals in table 4 compared to 507,864 in table 3); this discrepancy is mainly linked to a discrepancy in the number of mice and rats.

The main reasons for these toxicological or regulatory studies concern by far medical products and medical devices: more than 80% of uses in this category.

The number of animals used for food product studies varies greatly but is on the decline.

The chemical industry represents only a small proportion of experiments for toxicological or regulatory purposes (3.9% in 2019, 4.4% in 2020, 2.8% in 2021), but the number of animals, which tended to decrease slightly until 2017, rose again in 2018 and especially in 2019 and 2020, to decrease again in 2021, raising doubts about the rigor in the application of the REACH regulation on limiting the use of experiments on vertebrates.

The situation varies greatly depending on the species. Without going into too much detail, let's look at the toxicological and regulatory studies for seven different species (Figure 3).



Rabbits are primarily used in toxicological or regulatory studies (mainly for medical products): these represent between 93 and 96% of rabbit uses depending on the year. Also mainly used for this type of study are:

- dogs: between 66 and 75% (within these regulatory uses, 61% concern products for medical use and 29% products for veterinary use);
- cats: between 42 and 78% (for veterinary studies or food product testing);
- NHPs: between 62 and 71% (for products for medical use or quality controls).

Thus, primates are not primarily used for research into the causes and treatments of human diseases, but for the assessment of the health and toxicological risks of chemical and pharmacological substances.



The number of animals used for toxicological or regulatory testing is not decreasing (remaining around 27-30% since 2015), which raises questions about the effectiveness of the validation process for alternative tests and the implementation of validated tests.

However, many alternative methods (*in vitro*, *in silico*, *in chimico*) can replace the use of animals in studies on the assessment of health and environmental safety. But it turns out that the validation procedure is very long (it can last up to 10 years) and very expensive (several hundred thousand euros). ECVAM (European laboratory responsible for validation) does not validate more than 2 or 3 alternative tests per year.

All chemicals must be registered at the EU level before they can be marketed. To prove the safety of substances, manufacturers must—under the REACH regulation—prioritize the use of non-animal methods, with animal testing only permitted as a last resort. However, for reproductive toxicity or carcinogenicity, in particular, animal testing is still required.

When a validated non-animal alternative exists, research teams or manufacturers are free to use it or not, while the directive states in its recital 12: "*the use of animals for scientific or educational purposes should therefore only be considered where a non-animal alternative is unavailable.*" It is therefore regrettable that alternative tests are not promoted by public authorities, which do not help to develop their use.

The growing increase in the use of NHPs – 2/3 for toxicological or regulatory purposes since 2015 – also poses an ethical problem, as the European legislator noted in one of the recitals of the European Directive (recital 17): "*Due to their genetic proximity to human beings and to their highly developed social skills, the use of non-human primates in scientific procedures raises specific ethical and practical problems [...]. Therefore the use of non-human primates should be permitted only in those biomedical areas essential for the benefit of human beings, for which no other alternative replacement methods are yet available. Their use should be permitted only for basic research, the preservation of the respective non-human primate species or when the work, including xenotransplantation, is carried out in relation to potentially life-threatening conditions in humans or in relation to cases having a substantial impact on a person's day to day functioning, i.e. debilitating conditions [...]*".

It should also be noted that 15 NHPs were used in 2018 for education and vocational training projects (compared to 16 in 2017, 49 in 2016, and 21 in 2015), even though the use of NHPs for this purpose is not authorized by the European directive. These projects therefore benefited from illegal authorizations issued by the MESR services. This use was stopped from 2019, following litigation initiated by associations, including Transcience.

2.7 Genetic status of animals

In 2021, in France, 487,971 animals used were carriers of a genetic alteration, or 25.8% of the total. This rate has increased slightly since 2015 and genetic alterations therefore concern more than a quarter of the animals used, which is a very significant proportion since we observed 21.7% in 2015 and 2016, 22.4% in 2017, 25.4% in 2018, 22.4% in 2019, 26.8% in 2020.

The most affected species are the mouse (89% of animals with genetic alteration), the rabbit (3.9%), the zebrafish (2.8%), the rat (2.7%).

For the first three species, the proportion of animals carrying a genetic alteration out of the total uses for these species is high: 37.8% in mice, 11% in rabbits, 20.4% in zebrafish.

It should also be noted that 16 dogs used in 2021 were genetically altered (compared to 27 dogs in 2020, 45 in 2019, and 86 in 2018), as well as 15 primates (prosimians). This is the first time that primates that have undergone genetic alterations have appeared in France.

Among these animals, those with a harmful phenotype are distinguished (i.e. the genetic alteration causes diseases, disabilities, pain): 82,842 animals were affected in 2021; this number is a sharp increase compared to previous years (61,357 animals were affected in 2019, 56,412 in 2018, 53,076 in 2017). Among these animals undergoing these alterations, there are 78,258 mice, 2,499 rats, 2,070 zebrafish, 15 dogs.

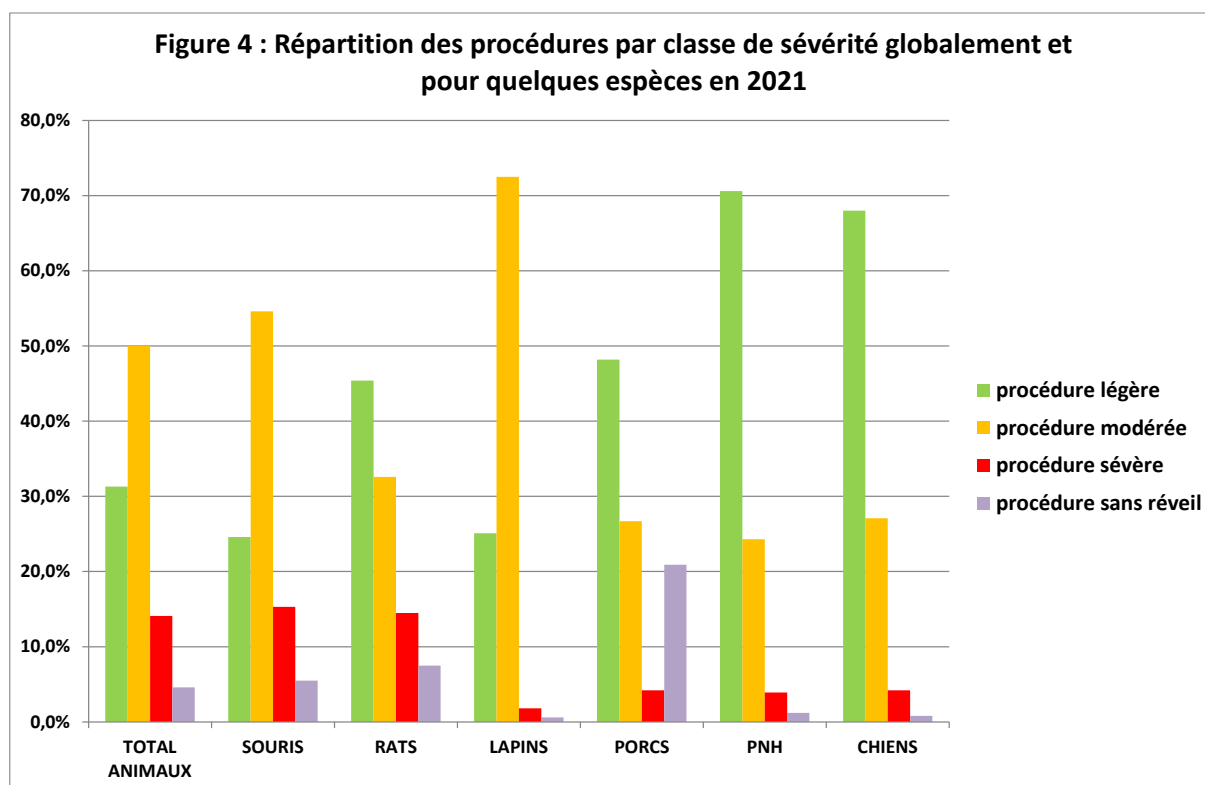


The increase in the use of genetically altered animals with harmful phenotypes poses a major ethical problem because the suffering of these animals is permanent, from birth, regardless of the procedures that may otherwise be applied to them.

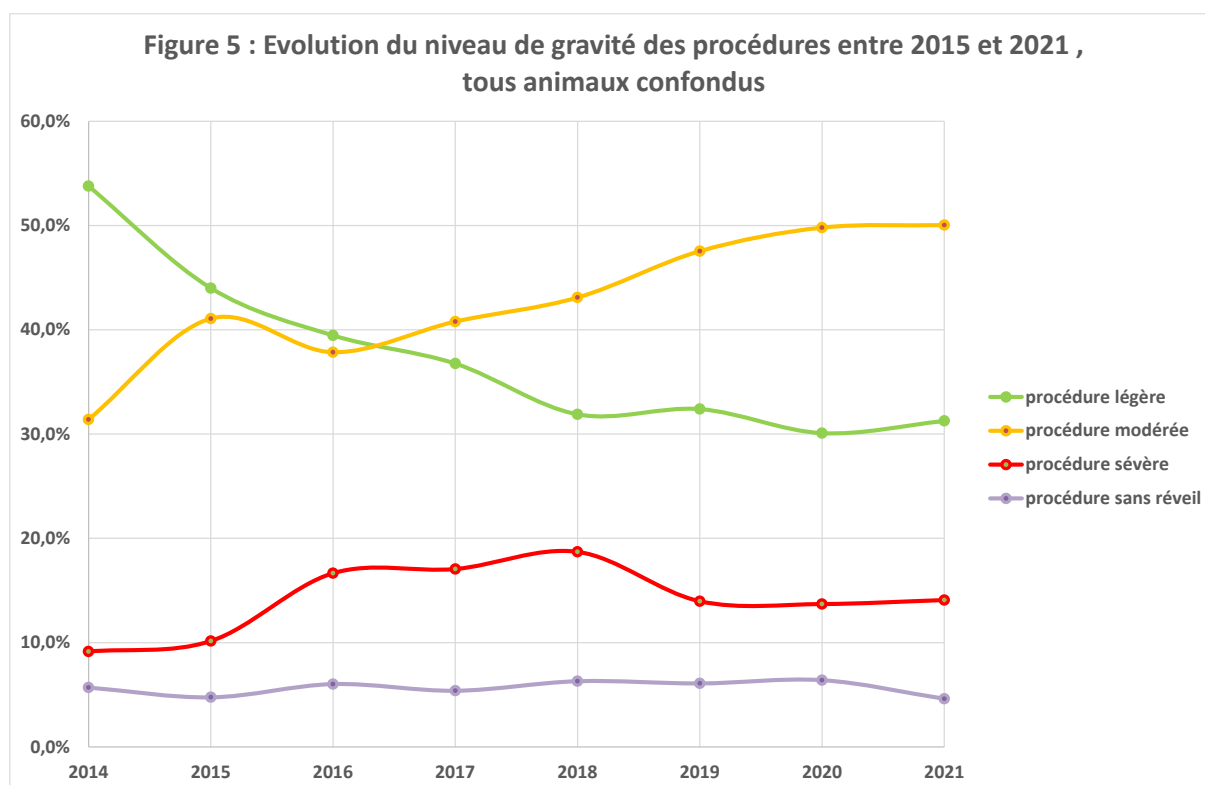
But whether the phenotype is harmful or not, genetic manipulation represents an obvious attack on the integrity of the species in question, and is also incompatible with the requirement to consider animals as "sentient beings", affirmed in the European Directive which recognizes their "intrinsic value" (recital 10). In addition, all genetically modified individuals that do not develop the expected characteristics are eliminated, as are surplus animals (those that do not find a "buyer"), over-aged breeders, etc., these animals being thus reduced to the state of simple laboratory "material".

2.8 Severity classes of experimental procedures

Figure 4 details the distribution observed by severity classes in 2021, overall and for some species.



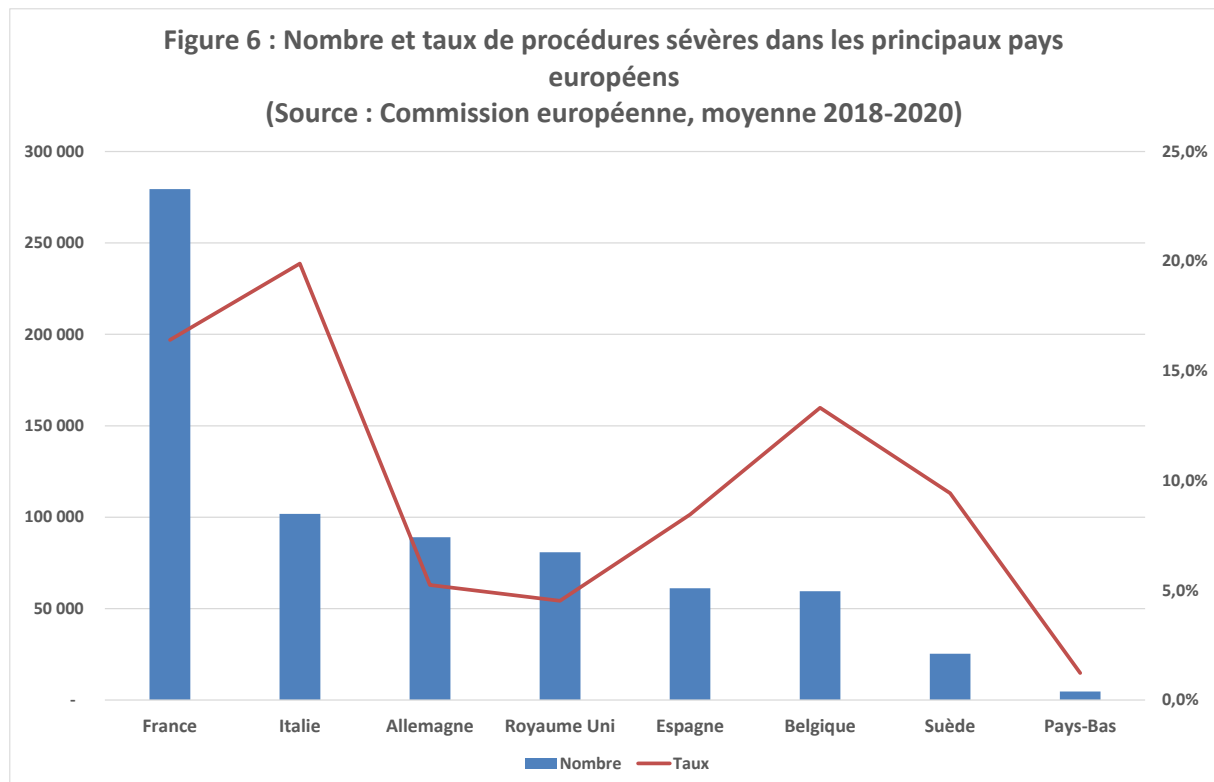
For all animals, the proportion of severe procedures was 14% in 2021, as in 2019 and 2020, down from 2018, which had peaked (Figure 5); it was higher in mice (15.3%) and lower in rabbits, pigs, NHPs and dogs; however, in pigs, there was a very high rate of procedures without recovery (21%). Note the high proportion of mild procedures in NHPs and dogs.



Over this period, the rate of mild procedures has steadily decreased (from 54% in 2015 to 31% in 2021) while moderate procedures have steadily increased (from 31% in 2015 to 50% in 2021) knowing that in this category of procedures, some are very severe (see Annex 8 of the European directive). The crossing of the lines between mild and moderate procedures took place in 2016. Furthermore, the rate of severe procedures (see examples in the annex to this document) has also increased sharply to stabilize at 14%, a rate well above the European average which is around 11% (see below). Procedures without recovery remain at fairly stable levels, around 5-6%.

This trend is the same as observed for mice and rats. For dogs, the trend is different: the rate of severe procedures has decreased, from 7.5% in 2015 to 4.2% in 2021. For NHPs, this rate is fluctuating: while it decreased from 7.7% in 2015 to 3.9% in 2020 and 2021, it peaked at 8.1% in 2018.

However, there is reason to be concerned about the number of severe procedures in France, which is significantly higher than in other EU countries, as shown in Figure 6, which is based on the average for the years 2018 to 2020, based on statistical surveys by the European Commission.



The number of "severe" class procedures is higher than it was in 2015. As for the number of "moderate" class procedures, it has been constantly increasing since 2015. Overall, the rate of moderate and severe class procedures increased from 51.3% in 2015 to 64.1% in 2021.

These data cast serious doubt on the consideration of the principle of refinement (3R rule). Such a development is unjustifiable in light of the very principles of the European Directive.

France is well ahead of all EU Member States in the number of animals used in severe class procedures (the European average being 11%), which means that our European neighbors know how to do things "differently" and that France is not respecting the spirit of the regulations.

APPENDIX

Examples of different types of procedures defined for the severe class based on factors related to the type of procedure (source: European directive, annex VIII):

- (a) toxicity testing where death is the end-point, or fatalities are to be expected and severe pathophysiological states are induced. For example, single dose acute toxicity testing (see OECD testing guidelines);
- (b) testing of device where failure may cause severe pain, distress or death of the animal (e.g. cardiac assist devices);
- (c) vaccine potency testing characterised by persistent impairment of the animal's condition, progressive disease leading to death, associated with long-lasting moderate pain, distress or suffering;
- (d) irradiation or chemotherapy with a lethal dose without reconstitution of the immune system, or reconstitution with production of graft versus host disease;
- (e) models with induction of tumours, or with spontaneous tumours, that are expected to cause progressive lethal disease associated with long-lasting moderate pain, distress or suffering. For example tumours causing cachexia, invasive bone tumours, tumours resulting in metastatic spread, and tumours that are allowed to ulcerate;
- (f) surgical and other interventions in animals under general anaesthesia which are expected to result in severe or persistent moderate postoperative pain, suffering or distress or severe and persistent impairment of the general condition of the animals. Production of unstable fractures, thoracotomy without adequate analgesia, or trauma to produce multiple organ failure;
- (g) organ transplantation where organ rejection is likely to lead to severe distress or impairment of the general condition of the animals (e.g. xenotransplantation);
- (h) breeding animals with genetic disorders that are expected to experience severe and persistent impairment of general condition, for example Huntington's disease, Muscular dystrophy, chronic relapsing neuritis models;
- (i) use of metabolic cages involving severe restriction of movement over a prolonged period;
- (j) inescapable electric shock (e.g. to produce learned helplessness);
- (k) complete isolation for prolonged periods of social species e.g. dogs and non-human primates;
- (l) immobilisation stress to induce gastric ulcers or cardiac failure in rats;
- (m) forced swim or exercise tests with exhaustion as the end-point.