Transparency and Status of The 3Rs Under Directive 2010/63/EU

Openness and transparency are key values of the European society and research. Research may unfortunately still involve – at certain stages – the testing of animals for academic or regulatory purposes (fundamental biological research, pharmaceuticals, immunologicals, infectiology, surgery, medical devices, chemicals, environment, food and feed).

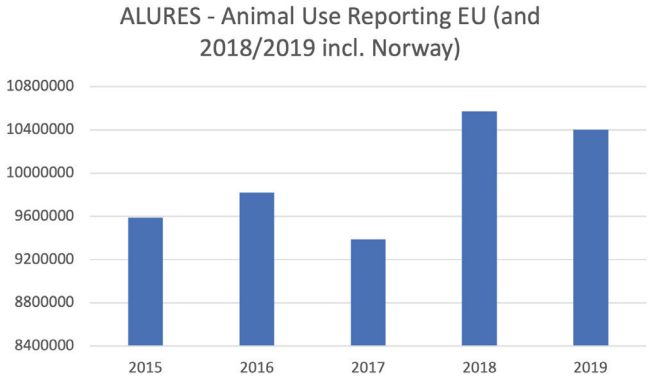
Since 2010 protection of animals which are to be used for scientific purposes is commonly agreed upon and requested legally in Europe as per Directive 2010/63/EU on the protection of animals used for scientific purposes (latest consolidation in 2019). Animal testing on cosmetics and the marketing of such products has even been prohibited in the EU.

The animal protection directive was amended by Regulation 2019/1010 with requirements for the reporting of statistical data on the use of animals for scientific purposes in the EU for which two implementing decisions have been adopted: Commission Implementing Decision 2012/707/EU and Commission Implementing Decision 2020/569/EU. So therefore, transparent data on animals used for scientific purposes in the EU is readily available.

Starting in 2014 the counting methods of the test animals have changed: Since then, all animals had to be counted at the beginning of each experiment and reported at the completion of the trial. With that some animals were counted one, two or even three times, like explained by the German Primate Centre (DPZ). With that it makes sense to start comparing numbers after 2014. Let us have a look and see how experimental animal numbers have developed over the last years (Graph 1: Number of all animals used in the EU (and Norway in 2018/2019) from 2015–2019). As you can clearly see the numbers of all animals used for testing, routine production, education, training purposes, research in the EU has increased and even so the numbers from Norway were included in the last two years, that might not be the only reason why numbers are not dropping as desired and anticipated. On the other hand on ALURES – European Commission (europa.eu) the latest numbers of the past 3 years are not published (yet).

The German BfR (Bundesamt für Risikobewertung) at least published the numbers from 2020 and compared them to 2019. They state that the numbers are clearly decreasing. In the year 2019 round about 3 million animals were used for scientific purposes and in the year 2020 only approx. 2,5 million.[1] But in the published figures of the BfR, only the animals used for scientific purposes were listed. So the animals used for education, routine production, etc. are not included. Therefore again, it is questionable if the numbers are actually decreasing.

Apart from that, Europe and its member states are only a stagnant part of a rapidly growing global scientific community. It is highly questionable, whether animal experiments are not only outsourced to third countries, where animal welfare standards are lower and where competent authorities are less restrictive and faster with granting experimental permits. If this is the case, then even if the European animal numbers were decreasing, this would still be a deterioration of the situation from the perspective of the animals used for scientific purposes. The animals themselves do not care where exactly they contribute to knowledge gain.



Graph 1: Number of all animals used in the EU (and Norway in 2018/2019) from 2015–2019

What exactly is regulated in Directive 2010/63/EU? It lays down the principles of the 3Rs (Replacement, Reduction, Refinement – Table 1). This main idea was developed over 50 years ago by Russell and Burch in their book „The Principles of Humane Experimental Technique". European regulatory assessors, competent authorities, scientists and experimental animal care takers are all morally and legally dedicated to these three principles. Skilful product development and careful study design bear enormous benefits for the sponsor, the academic scientist and the animals simultaneously.

Replacement is obviously restricted by the replacement methods being actually „fit for the purpose". In the end, scientists and regulatory bodies depend on obtaining „the same information". The scientific community is working on this constantly and many grants are available for the development, the validation and verification of alternative methods (e.g. Felix-Wankel-Tierschutz-Forschungspreis (felix-wankel-forschungspreis.de)). The European Food safety Authority (EFSA) for example clearly states on its website:

"EFSA supports risk assessment approaches which minimise and refine the use of experimental animals (*in-vivo* testing) and that promote use of data derived from alternative approaches, where possible. These alternatives include lab tests in tubes, flasks, petri dishes, etc. (*in vitro*) or performed via computer simulation (*in silico*)."

Refinement is constantly developed by associations like FELASA (Federation of European Laboratory Animal Science Assessment) and commercial providers of experimental animals in their guidance documents (e.g. diet recommendations, enrichment recommendations etc.). When experiments with farm animals are to be carried out, the European farm animal welfare laws have of course also to be considered. The latter evolve constantly to higher levels.

But why does Reduction not seem to function? The answer to this question might be multifold and lies in the field of substance regulation:

- „long history of safe use" is not an accepted principle for substance assessment. This may lead to the necessity of generation of a lot of new toxicological data especially for substances which have in the past been generally acknowledged as „safe". For these substances, nobody in the past ever generated scientifically sound safety data. New tests may involve the use of new animals.
- „One substance one assessment" is not consequently established. EFSA for example wants to see toxicological raw data, even if ECHA has assessed the substance already and robust summaries are publicly available. This may lead to the situation that experiments have to be duplicated.
- European consumer expectations: „I just want safe food". The scientific approach to the very high standards of European food and feed safety requires hugh efforts by the food and feed industry and by the European Regulatory bodies. Testing also involves animal experiments.
- „Analytical overkill". The possibilities of substance measurement have evolved in the last decades to brilliant methods with extraordinary possibilities of substance detection and quantification. Ironically this seems to rather lead to the impression of the European consumers that feed, food or pharmaceuticals are often contaminated. This puts public pressure on the EU regulatory bodies, who request more and more testing – partly also in animal models.
- Most grants for research projects are given for alternative methods, so mostly for the replacement strategy. It is hard to find promotions for good ideas to "only" reduce animal testing and it is even harder to get foundation if the ideas are coming from the industry. The BfR published some common grants for research in the field of alternative methods (https://www.bf3r.de/de/externe_forschungsfoerderungsmoeglichkeiten_auf_dem_gebiet_der_alternativmethoden-283335.html). Under all applicants those doing research at an university are usually preferred. Only the so called SET ("Stiftung zur Förderung von Ersatz- und Ergänzungsmethoden zur Einschränkung von Tierversuchen") project promotes alternative and supplementary methods to limit animal testing. One of its main goal is to support "Scientific communication and international activities related to the 3Rs".

3Rs	Explanation
Replacement	It should be considered to do some kind of research without any animal testing – if possible with the alternative methods.
Reduction	The animals used for testing should be reduced to that point that the outcome of the research is still obtaining the same information.
Refinement	The experiment shall be planned that the distress of the animals is at the lowest level and the welfare of the animals is at the highest level.
VISION: Reuse	As seen under REACH: The Reuse of test results should be considered and possible at different levels in the field of research, authorisation

Table 1; 3Rs + Vision of Reuse

But which strategy out of this self-enforcing cycle could reduce the demand for animal testing systems? A vision would be to re-use study data packages for different regulatory purposes by making data sets ready to trade them in a transparent market. Results from similar substances could also be referred to by read-across. Having a look at the REACH[2] regulation from 2007 it is already requested by law that the outcome of similar animal testings for the safety of chemicals need to be shared: „Adequate and reliable studies with animal experiments must not be repeated. Companies are also encouraged to share all data available in their possession."

Professional data sharing could not only positively affect animal welfare and industry budgets, but is also highly sustainable.

Now that the transparency regulation (Regulation (EU) 2019/1381 on the transparency and sustainability of the EU risk assessment in the food chain for food and feed) is in place, it will become visible how many animals – here often farm animals – are used for authorizations of regulated feed and food products in Europe. Let us see what conclusions the public will draw from these figures and whether these new figures will show the same upward trend as the already transparent ALURES figures.

Safety comes at a cost. Let us find a way to reduce (refine, replace) and reuse our investments for better animal welfare and more sustainability.

REFERENCES

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2. REACH – Registration, Evaluation, Authorisation and Restriction of Chemicals

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