

Questions and answers on animal experiments at the German Federal Institute for Risk Assessment (BfR)

Updated BfR FAQ of 18 November 2021

The German Federal Institute for Risk Assessment (BfR) performs animal experiments as part of its statutory duty. For which scientific purposes are animals used at the Institute, which species are used and how is it guaranteed that the animals suffer as little as possible? The BfR has summarised and answered these and other questions below.

For what purpose does the BfR perform animal experiments?

Animal experiments are performed at the BfR as part of its statutory duty. Firstly, this involves research into the safety of food and animal feed. The goal of these experiments is to recognise and assess risks for humans and livestock. Secondly, animal experiments are performed at the German Centre for the Protection of Laboratory Animals (Bf3R). The centre is part of the BfR. Possible ways of reducing stress for animals in experiments (refinement) are investigated at the centre. The scientific goal is to establish better management and experimental conditions which can be used worldwide.

Which animal species are used in BfR animal experiments?

In the BfR's laboratory animal facility, mice, rats, guinea pigs, rabbits, chickens, turkeys, sheep, goats, cows, mussels, shrimps as well as farm fish and zebrafish are kept and used for scientific research.

Which types of animal experiments are carried out at the BfR?

Reference material: The statutory duties of the BfR include developing and refining detection methods for pathogens which are transmissible to humans via food as well as undesirable or prohibited substances in food. The National Reference Laboratories regularly inspect the methodical expertise of food safety laboratories. Animal reference material is required for this. The material either originates from untreated animals which have been proven to be free from the pathogens or substances in question, or animals which have specifically been infected with certain pathogens or treated with substances. Depending on the method, faeces, spontaneous urine, fur or feathers, eggs, milk, blood or meat can act as reference material.

Education and Training: The German Animal Welfare Act (Tierschutzgesetz) and the Regulation on the Protection of Animals Used for Experiments or Other Scientific Purposes (Tierschutz-Versuchstierverordnung) state that only persons with proven expertise in the care of laboratory animals and animal experiments may be involved in animal research. Expertise must be improved continually through regular further training. The BfR therefore educates animal keepers in the field of research and clinical practice, and trains employees in planned animal experiments in accordance with legal guidelines. Initially, many training methods are used that do not require the use of animals, such as instruction, instructional videos, working with artificial models and practical instruction in daily work. Only when these methods have been used and further experience is still essential then certain procedures are trained on living animals, so that they can be applied expertly in experiments and the laboratory animals suffer from as little stress as possible.

Refinement: In accordance with Article 4 of EU Directive 2010/63/EU on the protection of animals used for scientific purposes, there is a particular emphasis on 'refinement' (improvement, betterment) by the member states. This means that any possible pain, suffering, stress or long-term damage must be avoided or reduced as much as possible for animals. The unit

“Laboratory Animal Science” and the animal husbandry staff at the BfR are conducting research on how these parameters can be determined and reduced in an objective manner. The overall goal is to establish better management and experimental conditions.

Food and animal feed safety: As part of its legal duties, the BfR carries out animal experiments to assess the safety and possible contaminations of food of animal origin.

How many animals have been used in animal experiments at the BfR in recent years?

133 animals were used in experiments at the BfR in 2018. 180 animals were used in 2019. In 2020, the number of experimental animals comprised 269 animals.

How many animals have been approved for or reported by the BfR for animal experiments in 2021?

According to the old version of the Animal Welfare Act (TierSchG), animal experiments were divided into those requiring approval and those requiring notification (Section 8a in conjunction with Section 8 TierSchG o.v. (old version)). Animal experiments that were not subject to a licensing requirement, but only to a notification requirement, were, for example, those that are required by law, such as for the approval of pharmaceuticals and animal feed. The assessment procedure implemented by the competent authorities was simplified for animal experiments which required notification compared to the procedure for animal experiments that require a license. As of the revisions to TierSchG of June 18, 2021, the notification procedure does not exist in this form anymore, but animal experiments that were already in progress have not yet been affected by this change. Therefore, the animals used at the BfR this year (2021) are still divided into animals that are used in experiments requiring approval and animals that are used in experiments that are subject to notification.

Experiments requiring approval: In 2021 (as of July 15, 2021) the competent authority for Berlin approved the use of 28 fattening pigs, 17 dairy cows, 136 mice and 6 rats.

Experiments requiring notification: For the five-year period 2018-2023, the BfR gave notice of a maximum of 75 sheep, 15 goats, 25 cows and 60 turkeys as blood donors for the production of specific growing media in the laboratory. Of these, 23 sheep have been used in experiments so far in 2021. As part of the obligations of the National Reference Laboratories (NRL) for strain maintenance and the production of reference material for interlaboratory tests, three guinea pigs and two domestic pigs were reported, as well as 12 rabbits for immunization and the collection of diagnostic immune serum.

Are animals that are not used in animal experiments kept at the BfR?

In addition to the animals mentioned above, animals are also kept at the BfR that are currently not used in animal experiments and may, for example, be kept for breeding or to be used in notified experimental projects when required. Currently (as of July 15, 2021), this comprises 13 goats, 21 cows, 6 turkeys and 600 fish. The latter are used for scientific research on refinement that does not require approval or notification.

What is the 3Rs principle?

The 3Rs principle was published in 1959 by the British scientists William Russell and Rex Burch and is anchored in the European Directive 2010/63/EU for the protection of animals used for scientific purposes, which was passed in 2010. The aim of the **3R** principle is to avoid animal experiments completely (**R**eplacement) and to limit the number of animals (**R**eduction) and their suffering (**R**efinement) in experiments to the absolute minimum. All persons and institutions that conduct animal experiments are legally obliged to act according to this principle.

Further information on the 3Rs principle can be found on the website of the German Centre for the Protection of Laboratory Animals at the BfR (Bf3R).

➤ <http://www.bf3r.de/>

What research is the BfR conducting to replace animal experiments?

Various research projects are continuously being planned and carried out at the BfR to replace animal experiments. Some examples are shown below. The list does not claim to be complete.

Cell and tissue culture methods are being developed at the BfR in order to completely replace an experimental method in which animals are used with an alternative method. They are intended to lay the foundation for the creation of new, animal-free alternative methods for basic research and toxicological assessment.

Research projects for basic biomedical research include, e.g.

- Bone-on-a-chip / organ-on-a-chip systems
- Development of an *in vitro* implantation model (MIVI)
- A search engine for alternatives to animal testing (SMAFIRA)

Research projects for toxicological risk assessment

- Development of an alternative method for testing the cancer-causing potential of hormone-active substances
- Alternative methods to animal experiments for detecting hormone-active effects *in vitro*
- Influence of circadian regulatory systems on *in vitro* test methods
- Toxicological *in vitro* studies on the combined effect of fungicides
- Computational toxicology: Role and importance of novel methodological approaches in health risk assessment
- Establishing Integrated Approaches to Testing and Assessment (IATAs) to support nanomaterial groups
- Prediction of the sensitising potential of chemicals and products *in vitro* in the human system as a substitute for animal experiments
- Development of “tattooed” 3D skin models
- *In silico* methods for predicting adverse health properties of pesticides

Further information on the 3Rs principle can be found on the website of the German Centre for the Protection of Laboratory Animals at the BfR (Bf3R).

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What research is the BfR conducting to reduce the use of laboratory animals?

Various research projects are continuously being planned and carried out at the BfR to reduce the use of animals in experiments. Some examples are given below. The list does not claim to be complete.

In order to identify the extent to which the number of laboratory animals used in research can be reduced, the BfR's research includes, for example, new statistical and bioinformatic analysis models. They are intended to be used to draw conclusions as to which methodological and institutional changes in research and the publication process might contribute to a reduction in animal experiments. At the same time, the BfR applies novel biometric approaches to make the statistical planning of experiments more efficient, both with and without the use of laboratory animals. In the case of planned research projects featuring laboratory animals, the number of animals required should be reduced to the basic minimum.

Further information on the projects can be found on the website of the German Centre for the Protection of Laboratory Animals at the BfR (Bf3R).

➤ <http://www.bf3r.de/>

What research is the BfR conducting to reduce the pain and suffering of laboratory animals?

Various research projects are continuously being planned and carried out at the BfR to reduce the pain and suffering of laboratory animals. Some examples are shown below. The list does not claim to be complete.

Measures to reduce stress and improve well-being are being investigated in order to reduce pain, suffering or stress in laboratory animals and thereby, simultaneously, increasing the quality of experimental results. In addition, assessment criteria for determining the degree of pain or suffering are being developed. Examples of previous research projects include:

- Improvement of the housing conditions for laboratory animals
- Development of choice experiments to determine the needs of the laboratory animals from their point of view
- Influence of chronic monotony and boredom on psycho-emotional behaviour and cognition in laboratory animals
- Automated detection of stress based on facial features
- "Animal personality" - personality traits and their influence on experimental results and their reproducibility
- Pain perception in fish (using the zebrafish model organism)
- Methodology and effectiveness of training measures for laboratory animals

Further information on the 3Rs principle can be found on the website of the German Centre for the Protection of Laboratory Animals at the BfR (Bf3R).

➤ <http://www.bf3r.de>

Who authorises animal experiments at the BfR?

The State Office for Health and Social Affairs (LAGeSo) is responsible for assessing and authorising animal experiments in the German federal state ("Land") of Berlin. Each animal experiment planned at the BfR contains a written application which is submitted to the LAGeSo. Each experimental project is extensively discussed and planned internally within the BfR with animal welfare officers and other experts beforehand. We strictly adhere to the 3Rs principle in this regard: First, checks are performed to see whether the goal of the experiment can also be achieved with methods not involving animal experiments ('replace'). If this is not the case, the number of animals to be used is selected in order to ensure that as few animals as possi-

ble are used ('reduce'). This is achieved by means of careful statistical calculation while planning animal experiments. Care is also taken to ensure that the experimental conditions are designed in a way that reduces pain, suffering and harm to the lowest possible level ('refine'). Examples of this include the continued improvement of animal housing conditions, the organisation of their surroundings and the handling of the animals. Training laboratory animals for certain measures reduces stress and burden. If painful procedures are performed, the appropriate painkillers are administered.

Experiments may only be performed by people with the appropriate training who are named in the application. The LAGeSo checks that the application documents are complete and comprehensible, advised by an independent animal experimentation committee. All questions arising about the experimental procedure are answered in a written form and revised by the LAGeSo. When all questions have been sufficiently answered, an authorisation can be issued for this proposed experiment for a maximum of five years.

Who is responsible for ensuring that animal experiments at the BfR are performed appropriately?

The competent authorities are responsible for monitoring animal experiments; in the case of Berlin, it is the State Office for Health and Social Affairs (LAGeSo). The LAGeSo monitors experiments with announced or unheralded visits. All animal experiments are accompanied internally by the BfR animal welfare officers. In addition to being veterinarians, they also possess a specific qualification in the field of laboratory animal science. Performing experiments properly is in the interest of all parties involved in the experiment and is documented accordingly.

Where do the animals in the BfR animal experiments come from?

Some animal species are specifically bred at the BfR for in-house experiments. Other animals are purchased from specialist laboratory animal breeders or selected agricultural enterprises, in accordance with legal guidelines.

How does the BfR ensure that the suffering of animals is kept as low as possible?

Applications for animal experiments define the unavoidable maximum degree of distress for the animals. This specifies all measures for keeping pain and stress as low as possible. These include suitable painkillers, as well as sufficient rest periods and an environment designed to be animal-friendly (including factors such as suitable toys or lighting conditions). The German Animal Welfare Act stipulates that animals must be constantly monitored during animal experiments. The animals are therefore systematically and regularly monitored for signs of distress. If a defined stress limit is reached, the experiment is stopped for the affected animal. Monitoring of the signs and the limit above which the animal must be excluded from the experiment is authorised beforehand by the competent authority who also checks for compliance. All parties involved in animal experiments are obliged to frequently make use of veterinary medicine and care measures for improving the welfare of the animals and reducing stress wherever possible.

What happens to the animals after the experiment?

What happens to the animals after the experiment essentially depends on the type of experiment. For some experimental purposes, the animal must be slaughtered or killed in accordance with the Animal Welfare Act, so that further investigations can be performed on its organs. If it is possible for the animals to survive without impairment of their well-being and any hazard to humans, other animals and the environment, they either remain at the BfR or attempts are made to place them in experienced private homes.

Which other statutory duties and initiatives does the BfR follow with regards to animal welfare?

The German Centre for the Protection of Laboratory Animals (Bf3R) was founded at the BfR in 2015 as part of the animal welfare initiative of the German Federal Ministry of Food and Agriculture (BMEL). The centre coordinates all activities nationwide with the goals of restricting animal experiments to only those which are considered essential, and of guaranteeing the best possible protection for laboratory animals.

Selected questions and answers are available here:

➤ <http://www.bf3r.de/>

On 7 January 2019, the German Centre for the Protection of Laboratory Animals at the BfR started the digital animal experiment register www.animalstudyregistry.org. The register was set up as a reaction to the reproducibility crisis and offers scientists a platform to register a detailed study plan before beginning their experiments, thereby preventing selective reporting.

The legislator has also assigned the BfR the task of publishing anonymised summaries of authorised animal experimentation projects in Germany. The database www.animal-testinfo.de is for this purpose.

Does the BfR support the “Transparency Agreement for Animal Research”?

The “Transparency Agreement for Animal Research” is a joint project of the Permanent Senate Commission on Animal Protection and Experimentation of the German Research Foundation (DFG) and the information platform “Understanding Animal Research” of the Alliance of Science Organisations, which began on July 1, 2021.

The BfR not only supports this initiative, but is also one of its very first signatories. The project’s declared aims include promoting transparency and openness in communicating information about the use of animal experiments in research. The BfR has been active in this field for many years with its German Centre for the Protection of Laboratory Animals (Bf3R). The BfR is committed to ensuring that animal experiments maintain transparency vis-à-vis the public. The BfR’s AnimalTestInfo and AnimalStudyRegistry databases are intended to help to make studies more comprehensible and to avoid unnecessary animal experiments.