Laboratory animals

VIB
science meets life

Animals in research: still essential

Despite technological and scientific progress and the protests of animal rights activists, research institutions and companies continue to use animals in scientific research. Why is this?

The short answer to this question is that we simply cannot answer certain research questions without using animals. Furthermore, it is unethical to use humans for the type of research we undertake on animals. And while animal research has its own ethical implications, it is necessary and unavoidable for many types of research.

That does not mean that the decision to do animal experiments is taken lightly. Scientists must treat animals in a careful, caring way. They must also be able to fully justify every animal experiment.

This justification is often based on the prospect of relieving suffering in humans, or in animals, caused by disease. And there are, in fact, strict standards for the housing, care and monitoring of animals. Moreover, researchers are not allowed to use animals if there is an animal-free alternative – such as cell cultures or computer models – and they must keep the number of animals they use to a minimum.

Critics sometimes claim that animal research is unnecessary, or even meaningless, and that mice for example, are a poor model for studying diseases in humans. Yet, these animals are highly valuable for research for several reasons: the mouse closely resembles humans in genetic terms, and there are many genetic tools available for mice that allow researchers to mimic certain aspects of diseases. They therefore do not simply randomly work with 'the mouse', but with hundreds of different modified mice or 'mouse models', which they specifically design to meet each research requirement.

In 2016, 24 both public and private research institutions in Belgium united in a pledge for openness on animal research. Yet misconceptions persist regarding experiments involving animals. Because people can't see what is happening in the labs, critics are quick to assume the worst. However, there is a lot of information to be shared on the subject, and that is exactly what we intend to do in this 'Facts Series'. We will provide transparent background information about the use of animals in biomedical research and we hope to enable a better understanding of the motivations of researchers – two aspects that are essential in forming a balanced opinion about animal research.

René Custers,
Regulatory & Responsible Research Manager at VIB

The pathway to animal research

Laboratory animal: what's in a name?

Much is written and said about laboratory animals: some condemn their use, others approve of it, but many are unsure what to think. To form an accurate picture, we first need to clearly define the term 'laboratory animal'.

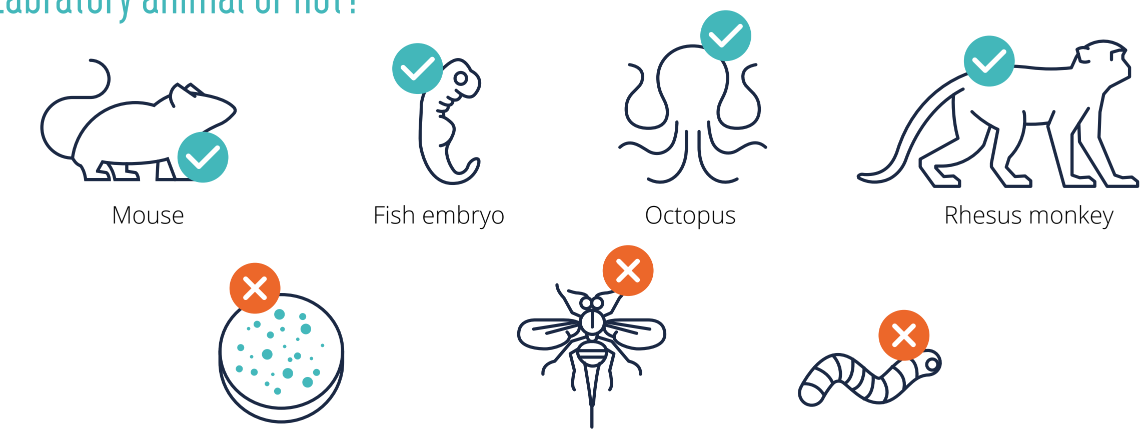
Determining whether an animal is labeled a *laboratory animal* is not up to the breeder, scientist or animal caretaker in question, but is established by law. In the past, the precise definition varied considerably between different European countries, but in 1986 for the first time, this was harmonized by a European Directive, which was slightly amended in 2010 (EU/2010/63).

Harmonized definition

Essentially, the law states that laboratory animals must be vertebrates (mammals, birds, fish, amphibians and reptiles) by definition. There is a total ban on experiments using great apes (bonobos, chimpanzees, gorillas and orangutans). Invertebrates – such as snails, insects and worms – are used in experiments, but strictly speaking they are not laboratory animals. Cephalopods, such as cuttlefish and octopuses, are an exception here.

According to this definition, rats and mice are therefore laboratory animals – at least if they are bred for use in an experiment – but fruit flies and worms are not. Nevertheless, those invertebrates make up most of the organisms that are used for biomedical research in Europe. The embryos of zebrafish, on the other hand – once they can feed themselves independently – fall within the scope of the law.

Labratory animal or not?



OFF-LIMITS TERRAIN

This definition of laboratory animals does not mean that vertebrates and cephalopods can be used for just any research. For example, tests for the development of cosmetics are strictly prohibited.

Why do we use animals in scientific experiments?

Many animal rights organizations oppose animal research: their concern is that they cause animals too much suffering and, moreover, are not strictly necessary. Although this reasoning is not entirely correct, the resistance is understandable. After all: what right does man have to decide on the fate of animals?

Despite criticism from various quarters, over 500,000 animals are used for scientific research in Belgium each year. They are badly needed: the knowledge that is thus acquired has already saved countless human and animal lives. Nevertheless, the decision to use animals is never easy.

An ethical debate

Biomedical researchers mainly use animals to gain insight into how the human body functions. Ultimately, they are trying to cure human diseases or defects. Reducing human suffering is weighed against the animal suffering. The key question: is a human life more valuable than an animal life?

To answer this question, we need to take the levels of consciousness of all living creatures into account. Because the greater the organism's consciousness, the more problematic the experience of discomfort, suffering and pain. All animals can be considered to have a lower level of consciousness than humans. That is why scientists opt to use animals for research and then, only later, humans. The next question is: which animals? The same principle applies here: researchers look for a species with the lowest possible level of consciousness to limit suffering as much as possible.

Scientists believe animal lives have intrinsic value. Every decision to test on animals is thoroughly considered. Each time, a balance is sought between society's need to combat disease and preventing animal suffering. An ethics committee carefully weighs all the pros and cons and decides whether animals may be used. If the societal need is not sufficiently great, the decision will be made to not run the experiment.

Replace, Reduce, Refine

In the context of animal research, scientists rely on the 3Rs that were introduced in 1959 by William Russel and Rex Burch, two British biologists, in their book *The Principles of Humane Exper* imental Technique. The 3Rs – replace, reduce and refine – have now been legally defined and provide robust guidelines for animal research throughout Europe.

Laboratory animals must be replaced as often as possible by alternatives, such as computer simulations *(in silico)*, cells in test tubes *(in vitro)* or tests on animals that are not considered laboratory animals, such as fruit flies. This is not always possible because the complex interaction between cells and tissues that is characteristic of humans and animals is difficult to reproduce. Certain studies also focus on specific characteristics that humans share with certain animals but not with others. An example: in research on the transfer of flu viruses between humans, ferrets are sometimes used because they transmit the flu virus the same way as we do.

If there are no alternatives, scientists must strive not to use more animals than strictly necessary to make statistically and scientifically meaningful statements. That is the principle of reducing. The number of animals required is calculated, because using too few animals would also be meaningless. The number of animals used must lead to a robust and statistically significant scientific result, because otherwise, the animals will have been used in vain.

Finally, researchers must refine their experiments (and the circumstances in which they are conducted) so that the animals experience as little discomfort as possible. For example, scientists can take blood samples in a low sensitivity area and use surgical techniques that leave smaller wounds. Whenever possible, treatments are given under anesthesia, and scientists always favor non-invasive methods, such as MRI scans, which do not penetrate the animal.

DID YOU KNOW...

- That not only people can benefit from animal research? They are also indispensable in researching diseases and developing therapies for animal diseases.
- That a quarter of all animal research in Belgium is conducted mandatorily in the context of safety tests? For example, before medicines are released on the market, companies are required to test them on animals. Pre-clinical research limits the risks for humans.

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A conversation with

GUY DE VROEY

From law to practical application

The law describes the conditions that laboratory animal research must meet in detail. How do scientists deal with this in practice? Guy De Vroey, chairman of the Flemish Committee on Laboratory Animals, explains various aspects.

Guy: "Although everyone who works with animals knows and applies the 3Rs, not everyone is aware of their entire scope. Especially the first R – replacement – is often interpreted too narrowly. In fact, this principle is much broader than strictly replacing an animal test with an alternative."

Replacement: a broad concept

Guy: "Right from the start of their research, scientists have to look for possible ways to answer their scientific questions without using animal research. Adapting an existing experiment so that no animals are needed is one way to deal with that. But it's better to think the other way around: what do I need to get valid results? Researchers are increasingly finding that animals are not necessary to answer their questions. For example, new insights and methods – such as human stem cells – offer possibilities that did not previously exist."

"In other words, replacement means not only exchanging existing animal tests for alternative methods, but also proactively searching for animal-free methods to answer new research questions. Although the number of animal experiments has only decreased slightly over the years, the impact of 'replacement' is greater: after all, more and more experiments are being conducted in which no animals are involved at all. Proportionately, there are therefore more scientific answers being found using animal-free methods than using animal research. It is unfortunate that there are no clear figures available on this, because it is precisely in this comparison that the important trends regarding alternative methods would be visible."

> "Researchers conclude more and more that animals are not necessary to answer their question. New insights and methods offer opportunities that weren't available in the past."
>
> **Guy De Vroey, chairman of the Flemish Committee on Laboratory Animals**

Reduction: *numbers matter*

Guy: "Scientists always look for the most appropriate species for their research and the right number of animals. Statisticians play a key role here: they calculate how many animals are needed to obtain statistically relevant results. It is therefore best to involve these mathematicians at an early stage in the experiment so that not one animal too many or too few is used."

"In choosing the animal species, researchers always consider the translational value of the animals: to what extent are biological mechanisms in the chosen species predictive of what would happen in humans? In other words, they do not simply choose the smallest or cheapest species, but rather the one that will provide the most valuable insights. Another factor, of course, is the animal's level of consciousness: the most relevant species with the lowest possible consciousness level will always be chosen. Very frequently, genetically modified mice, rats or even zebrafish are used, in which the genes have been adapted to make the mechanism to be studied in those animals resemble that of humans as closely as possible."

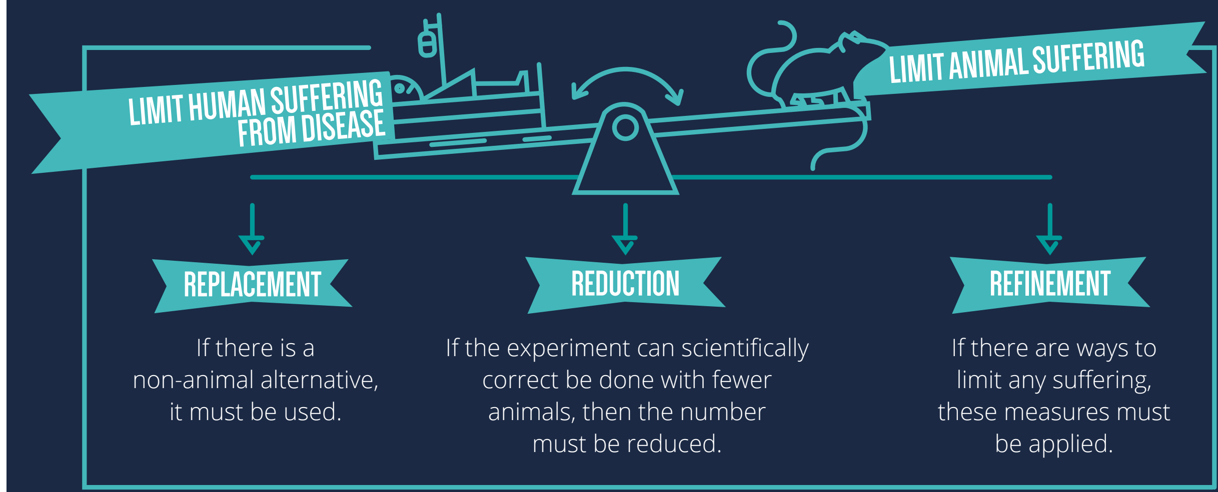
Refinement: innovative techniques

Guy: "The third R has many practical implications. The housing, feeding and living environment of the animals must be appropriate to the species to minimize their stress levels. For example, the size of the cages and the ambient temperature is legally determined. The day and night rhythms of the animals are also strictly controlled."

"But the techniques used during research also play a role. If you can choose between drawing blood from the cluster of veins at the back of the eye or from a vein in the tail, the choice is clear. Moreover, the techniques are evolving at lightning speed, and that, too, is contributing to the refinement of laboratory animal research. An example: currently, researchers can derive the same amount of information from a single drop of blood whereas in the past they would have needed several milliliters for the same result. The latest imaging techniques also have a major effect. Whereas scientists of the past would have to kill an animal in order to examine its internal organs or processes, there are now methods of non-invasively monitoring the same animal and for a longer period of time without having to euthanize the animal."

"That is why it is so important for lab technicians, experiment directors and animal handlers to continue to educate themselves on new developments and innovative techniques. And they certainly do so. Because the need for continuous learning – in addition to the certified basic training that all involved are required to follow in any case – is not only necessary to be able to continue doing top-level research, but it is also included in the European Directive (EU/2010/63) and supported by the Flemish Committee on Laboratory Animals and local ethics committees as well. Many institutions already provide this type of training in various educational plans."

A BALANCED CHOICE



A FOURTH R: RESPONSIBILITY

In addition to the familiar 3Rs, in recent years, a fourth R, responsibility, has become increasingly important. This means that all parties involved are made aware of their responsibilities. Not only the project manager, but the animal handlers, statisticians, lab technicians and managers also share the responsibility of ensuring that everything is done correctly. Thus, the director of an institute must provide sufficient resources to optimally organize animal research, the scientists who work with animals are thoroughly trained to do so, and the statisticians calculate as precisely as possible how many animals are required to obtain significant results.

This so-called fourth R is the spearhead for the Culture of Care, an attitude that is becoming increasingly prevalent in labs all over Europe. According to this idea, researchers do more than is strictly necessary: they commit to working in a self-regulating, ethical and fair way, and to always strive for minimal animal suffering and maximum scientific progress.

WHO DOES WHAT?

Many organizations, committees and boards oversee laboratory animal research. An overview:

1. *European Commission: provides the legal framework that each member state must implement.*
2. *National contact points: each member state must establish a central contact point that serves as a link with other member states and the European Commission. In Belgium, the three regional Animal Welfare Departments play this role on a rotating basis.*
3. *Belgian Council for Laboratory Animal Science (BCLAS): this body unites all who work in laboratory animal research and also strives to promote respectful handling of laboratory animals.*
4. *Animal Welfare Department: regional government body that grants certification to labs and breeders, implements the policy on laboratory animal research and monitors labs.*
5. *The Flemish Committee on Laboratory Animals: a council of 18 experts that provides recommendations to the Minister for Animal Welfare and the Animal Welfare Department and stimulates mutual dialogue and cooperation between all researchers and the government.*
6. *Local ethics committees with internal and external experts: responsible for evaluating and approving applications for animal research. Every animal research laboratory is required to work with a government-certified ethics committee, a committee of its own or one set up by a different lab.*
7. *Local animal welfare units: teams of employees within the institutions that are involved in animal research on a day-to-day basis, responsible for keeping an eye on things and advising researchers and animal handlers on optimal treatment of the animals. The animal welfare units are a mandatory European requirement. In 2017, the BCLAS launched a platform for animal welfare units to encourage dialogue between all animal welfare units and to share best practices and expertise.*

THE RULES IN BRIEF

- *Application for an animal experiment: every project application is evaluated by an ethics committee, adjusted in consultation with the scientist, and then approved or not.*
- *Housing: there are strict guidelines for the size of cages, ambient temperature, day and night rhythm, environmental enrichment and appropriate diet.*
- *Administration: separate registration of each animal, including the purpose of its use and the estimated discomfort.*
- *Reporting: mandatory retrospective analysis of each animal test, including the number of animals used, the severity of discomfort, efforts to limit this discomfort and insights on refining the tests.*

What are the alternatives to animal research?

Animals are never the first choice. At the start of each experiment, alternative methods are always sought first. Only if all other options have been exhausted will animal research be considered.

If scientists can avoid the use of animals, they will. After all, nobody likes to cause discomfort or suffering. For scientists this goes even further: they are legally required to explore other options wherever possible. That is determined by the first of the 3Rs in the European directive: replacement.

In vitro: cell and tissue cultures

In a lot of biomedical research, tests are performed on cells in a test tube. This type of *in vitro* test mainly helps scientists learn about the interactions between cells and the molecules they contain. Cell cultures are simple and inexpensive to grow and have become the standard for a significant amount of research in labs all over the world. To develop certain types of cell cultures, animal or human donors remain necessary.

Moreover, *in vitro* tests are evolving at incredible speed: research into stem cells and innovative 3D cell cultures have been available for some time now. These more complex models form a new intermediary step between cell cultures and living animals. But no matter how innovative technology is, modeled cells do not always behave in the same way as cells in the human body, where the interactions are considerably more complicated. For example, in the case of Parkinson's disease, it would be impossible to determine the effect *in vitro* of the influence of a genetic defect or a change in a cell on motor skills. It is also impossible to study every aspect of inflammation *in vitro*: different cells from various places in the body travel to the place of infection. However, *in vitro* tests are invaluable in organizing animal research more efficiently at a later stage.

In silico: computer models

In silico research simulates the body's systems using computer models. Thanks to the ever-growing computing power readily available to researchers, it is possible to study the effects of a medicine on a system or communication between cells. In this way, *in silico* models offer a very useful complement to animal research.

But even this technology cannot yet replace animals. To construct *in silico* models, scientists need data derived from animal research. For example, a model that needs to predict the interaction between certain brain cells will have to be optimized based on research into those cells in a living animal. Laboratory animals are also indispensable in confirming the results of *in silico* research.

Imaging techniques

Modern techniques such as CT scans (computed tomography) and MRI scans (magnetic resonance imaging) are excellent complements to animal research. They provide researchers with insights into the anatomy and physiology of humans and animals. An example: with fMRI (functional magnetic resonance imaging), brain activity can be measured during the execution of a specific task. According to the letter of the law these are also animal experiments, although the degree of suffering in animals is very low. In practice, these scans are alternatives to more invasive tests. In fact, they thus constitute a type of refinement: another research method that causes less stress, discomfort or suffering.

Modern imaging techniques: studying organs and tissues without killing animals

Another advantage of imaging techniques is that they can offer a wealth of information based on one animal. Each mouse can be scanned in different ways and at different times. In other words, imaging techniques are also a form of reduction: gathering many results using just a handful of laboratory animals.

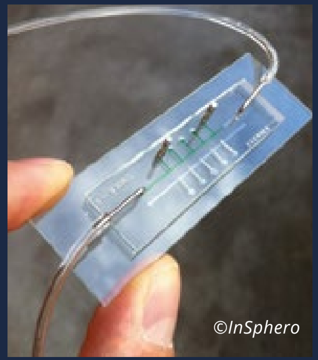
Just like *in vitro* and *in silico* methods, these techniques do not provide enough information to gain a complete picture of diseases and defects. Complex diseases, such as epilepsy, are difficult to study with non-invasive scans. Moreover, animal research is still needed to refine these techniques.

Using animals after all?

These alternatives clearly have their limitations. Nevertheless, they are currently resulting in fewer and fewer animals being required to give their lives for science. By intelligently combining different methods, researchers make many laboratory animals unnecessary.

IN VITRO INNOVATION: BODY-ON-A-CHIP

In the latest in vitro developments, miniature human organs are grown on a chip. This type of chip with, for example, a miniature liver, can be used to test the effect of a new medicine on the liver. Various artificial tissues are connected to one another via tiny ducts. By allowing a liquid – comparable to blood – to flow through this system, an important step is being taken toward simulating a mini organism. This is still far from a real organism in which the immune system and hormones also have important influences on the whole.



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It will take at least another 10 years before this high-tech system is fully developed. It is expected that this will enable us to replace toxicological tests on mice – possibly up to a third of them. But in basic research, this technology is not expected to offer a complete replacement. It is primarily an extra alternative in the spectrum ranging from simple in vitro cell cultures on one hand, to the animal at the opposite extreme.

The right species for each study

Rats, mice, rabbits, hamsters, pigs, frogs and fish: you can find them all in labs. But how do scientists determine which species is best suited for their research?

The higher an animal's level of consciousness, the more difficult it is to ethically justify its suffering in experiments. That is why scientists are legally required to choose animals with the lowest possible consciousness level. Zebrafish are, for example, ranked lower in these terms than rats, which in turn are subordinate to monkeys.

In selecting an animal, scientists therefore always need to consider precisely what they exactly need to be able to answer their research question, and in doing so, they must strive to use laboratory animals with the lowest possible consciousness level.

Depending on the need

Still, not all laboratory animal research is conducted on fish, frogs or mice. After all, for many research questions, these species are too far removed from humans. There are also limitations in terms of structure: for studies on visual perception, mice are inappropriate, because unlike us, their eyes are positioned on the sides of their heads.

The lower the level, the simpler the organism

Choosing a species with a lower level of consciousness does not only benefit animals. These organisms are often easier to study. The brains of zebrafish, for example, are considerably less complex to examine than those of rats. Even more, they reproduce faster than their counterparts with higher consciousness levels, which usually enables studies using these species to go faster. It is precisely for this reason that fruit flies are popular for use in labs: they have no consciousness, feel no pain and reproduce exceptionally quickly. Conducting experiments on fruit flies does not constitute animal research, in legal terms, but they do contribute tremendously to research on brain diseases. After all, the way that the nerves of fruit flies communicate is similar to how this occurs in humans. Problems with this signal transmission are thus similar and give rise to a variety of diseases. Animals that may not look anything like humans at first sight can therefore still be relevant models for human diseases.

Animal research in Belgium

In Belgium, a total of 535,829 animals were used in experiments in 2016. The great majority of these were mice. Rats and fish were also frequently used. Dogs, cats and monkeys are used only in very rare cases.

The reason that mice account for such a large share is – besides their small size and rapid reproduction rate – their strong genetic similarity to humans. They are the ideal animals for studying specific genes and defects in those genes. Moreover, they can easily be genetically modified to be even better-suited for research into human diseases.

Zebrafish are regularly used for genetic research. Like mice, they reproduce rapidly and housing them is inexpensive. The zebrafish genome – its entire DNA collection – is well-understood, and scientists can easily make changes to it. Rabbits are good models for studying arteriosclerosis. Their cardiovascular systems are very similar to those of humans. And the organs of pigs are ideal for transplantation studies and research into eating habits.

In Belgium, a small number of llamas are also used for the culture of antibodies produced by white blood cells. Camelids, including llamas, produce antibodies that are smaller than those of other vertebrates. And the even smaller 'nanobodies®' derived from them also retain their functionality. That small size has many advantages for applications: they can reach places that larger antibodies cannot, they are more stable and easier to produce. Such nanobodies have by now found various valuable applications in scientific research, and their uses include the development of medicines for inflammatory and infectious diseases and cancer.

Dogs and cats are used only very occasionally in biomedical research. However, in exceptional cases, they can prove invaluable, for example, in studies on cancer or diabetes. Moreover, they contribute to veterinary medicine, as they are often used to study diseases in the animals themselves and to develop medicines for them.

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A conversation with

TINO HOCHEPIED

Where do animals for biomedical research come from?

Where do scientists get their mice, rats or fish? Are these animals bred for a single purpose? And what if researchers need animals with a specific disease? Dr. Tino Hochepied, head of the VIB-UGent Transgenic Mouse Core Facility, explains.

Tino: “Almost all animals used in experiments are bred in specialized centers. Breeders need to be certified by the Minister for Animal Welfare. Each center maintains a register, by species, of how many animals are bred, and adheres to strict rules for the care and housing of the animals. Moreover, breeders are also required to individually monitor larger species such as cats and dogs. Labs that perform experiments using genetically modified animals (see box) often breed them themselves. They need a permit for that, too.”

Are animals caught in the wild for research?

“In highly exceptional cases, this may be allowed, but the researcher must in this case submit a separate application to the Animal Welfare Department explaining the justification for the request. Only after approval from the Flemish Committee on Laboratory Animals can the government grant permission.”

Why is it better to use bred rather than wild animals?

“The major advantage is standardization. Bred animals live under the same conditions: they all receive the same food, their cages are the same size, the temperature and air quality are consistently identical, and so forth. This results in minimal variation between the animals, which is important in making reliable scientific statements. Moreover, it is crucial for laboratory animals to be healthy. After all, undesirable infections can significantly distort the results of experiments. Scientists and breeders therefore have every interest in taking good care of their animals.”

“Moreover, certain animals, such as mice, are also genetically standardized. Many strains known as 'inbred lines' have thus been created. All descendants of such a line are genetically identical. This makes the results of tests with these mice even more reproducible and ensures that fewer animals are needed per experiment to produce statistically significant results.”

Why are animals sometimes genetically modified?

“Genes play an important role in the development of certain diseases. To answer a specific research question about such a disease, you need animals with the precise genetic composition that plays a role in the disease pathology. That animal may be out there somewhere, but the chances of finding it are virtually nil. The DNA of animals in nature varies enormously. That is why scientists work with bred animals, adding pieces of DNA or modifying them slightly through breeding techniques. If there is a risk that the animal will suffer because of the genetic modification, for example in developing a disease, this must be submitted to the ethics committee in advance.”

DESIGNER MICE

In reference to animal research, people sometimes argue ‘that a mouse is not a human being’ or that certain human diseases do not occur in these animals. That is true, and effectively demonstrates the limitations of animal research. To get around this problem, genetic modifications are often applied to animals, especially when mice or zebrafish are used. This way, scientists can specifically modify genes that are associated with specific diseases or even completely disable them. Such modifications still do not turn a mouse into a human being, but researchers can thus increasingly replicate molecular mechanisms that function in the same way as they do in humans.

These modifications have grown increasingly complex over the years. For example, researchers can now modify or disable specific genes in one or more cell types. In addition, they can also cause genes to be activated at a certain moment (referred to as ‘knock-in’ mice) or conversely, switch off at that moment (‘knock-out’ mice). And by cross-breeding animals that carry different modifications, mice can be created in which different molecular mechanisms associated with a disease are expressed simultaneously.

Moreover, linking so-called 'reporter genes' to the genes associated with specific pathologies through genetic modification enables researchers to learn a great deal about the behavior of these genes. After all, these reporter genes emit a signal when a gene is expressed. In combination with advanced microscopes, this approach yields extremely valuable data.

“Unhealthy animals can seriously distort the results of an experiment. Scientists and breeders therefore have every interest in taking good care of their animals.”

**Dr. Tino Hochepied,
head of the VIB-UGent Transgenic Mouse Core Facility**

Animal research: what's in a name?

We presented the definition of what laboratory animals are at the very beginning of this Facts Series: vertebrate or cephalopodic animals used in experiments. But what exactly does such an animal experiment involve?

Just like the definition of the animal, the definition of a test is also described in the European Directive of 2010. It harmonizes all national legislation in the EU.

The law in layman's terms

The directive applies the suffering of the organism as the central criterion. Both invasive (such as injections or surgical procedures) and non-invasive techniques (such as MRI scans) are covered by the law. In addition to physical pain, this suffering – referred to as discomfort in the directive – also includes stress, loneliness, fear and lasting injuries. There are different categories of discomfort, whereby even the mildest form is sufficient to qualify an experiment as an animal test.

The severity of the discomfort depends on many factors, including the type and duration of the experiment, the degree of pain, and whether the animal can express natural behavior. For example, mice are very social animals, but experiments sometimes require them to live in isolation.

Some examples:

- Mild discomfort: an x-ray is taken of a rat under anesthesia.
- Moderate discomfort: a non-life-threatening disease is initially cultivated in a mouse, temporarily causing fever and weight loss, followed by the collection of several blood samples over a longer period.
- Severe discomfort: a mouse undergoes treatment for cancer with metastases.

EUROPEAN DIRECTIVE 2010/63/EU

Animal test: any use, invasive or non-invasive, of an animal for experimental or other scientific purposes, with known or unknown outcome, or educational purposes, which may cause the animal a level of pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice.

DISCOMFORT WITHOUT EXPERIMENT

Since the introduction of the European Directive 2010/63/EU, the breeding or maintenance of genetically modified animals that suffer without being included in an experiment also falls under the definition of an animal experiment. An example: breeding mice with Parkinson's disease.

For what purposes are experiments with animals carried out?

Animal experiments have proven their worth for many years in basic biomedical research (some 53% of the tests undertaken in Belgium). They help scientists understand the structure and functioning of the human body and reveal the underlying mechanisms of various diseases. In more applied research (43%), involving, for example, translating basic insights into treatments for various diseases and disorders, animal experiments are highly important as well. They are often required before proceeding with the development of clinical treatments for people.

Animal experiments are done in highly diverse fields of research. Cancer studies, cell therapy and research on organ transplantation, as well as experiments aimed at the conservation of certain species or the improvement of nutrition for farm animals, are utterly dependent on the use of animals. A small part of the animal research in Belgium is done to train scientists (<2%), so that they can learn to treat the animals correctly and with care.

Ethical justification

The fact that animal research takes place in labs all over the world does not mean that it is allowed for all types of research or purposes. Using mice, hamsters or other organisms to test cosmetics has been banned in Belgium since 2003, and in the EU since 2009. The Belgian ban on animal research for tobacco products followed in 2010. This is only logical, because making animals sick to make non-vital – or, in the case of tobacco, even life-threatening – products is ethically difficult to justify.

Although not all countries take equally strong measures against such unethical practices, Europe also contributes. For example, the EU Environment Committee is committed to stopping cosmetic research on animals worldwide by 2023. Of course, this is vastly different from well-considered, useful and necessary biomedical research.

A TYPICAL ANIMAL EXPERIMENT: ALZHEIMER'S IN MICE

To better understand the breakdown of the brain in Alzheimer's patients, mice that have a form of Alzheimer's disease are used. But how exactly can the memory of a mouse be tested?

First the mouse is trained: the animal is placed in a bath filled with an opaque lukewarm liquid. This contains a platform just below the water's surface (so it is invisible to the mouse). The mouse is allowed to swim around for a while in that bath. In the meantime, it gradually learns to orientate itself using the visual reference points that have been installed in the room. As a result, after a while it knows how to perfectly locate the platform where it can rest.

A few weeks later, the mouse is placed in the bath again. It soon becomes clear whether the animal has remembered the position of the platform. In this way, scientists can see to what extent the memory of the laboratory animal has been affected by the disease, and better understand Alzheimer's.

From idea to implementation: the procedures in brief

Imagine: a scientist wants to investigate the effect of a certain substance on the growth of a cancerous tumor. To do this, an animal experiment is indispensable. What are the steps that the scientist must take before the study can begin?

Apart from the specific subject or animal, animal research may only take place in authorized laboratories. Before a study can even begin, the research institution must therefore receive general permission.

Authorized labs

To obtain this authorization, the laboratory director must submit an application to the Minister of Animal Welfare. The application file describes the nature of the experiments, the species and housing facilities used, and contains a list of the personnel involved and their level of education.

Each lab is also required to appoint an expert for animal welfare. This expert supervises the welfare of the animals, and regularly checks on them. The lab keeps records of the origin, identification and destination of animals. Moreover, labs must establish an ethics committee, or be affiliated with an existing committee. In addition, they must provide an animal welfare unit, which ensures that the recommendations of the ethics committee are followed up on. This unit evaluates the welfare and health of the animals and makes practical improvements.

The state Animal Welfare Department evaluates whether all conditions have been met, and whether the lab may be granted authorization. Since every application is different and the decision is not always simple, the Animal Welfare Department can count on support from the Flemish Committee on Laboratory Animals. This regional body issues recommendations on animal research policy in general, and on the development of methods to reduce, refine or replace animal research.

WHERE IS ANIMAL RESEARCH DONE IN BELGIUM?

Belgium had a total of 284 approved animal research labs in 2016. However, this does not mean that 284 organizations perform experiments on animals. After all, large institutions such as universities are often home to multiple authorized facilities, sometimes up to 20 per university. In addition to research institutes – which account for the bulk of the authorizations – many companies also have authorized labs.

AUTHORIZED BREEDERS

In addition to the research institutes, animal breeders are also required to undergo several procedures to receive approval.

Authorization for each experiment

The authorization of a laboratory does not grant its researchers carte blanche to simply launch any experiment at will: a separate approval is required for each study.

Before starting the procedure, the researcher must carefully consider whether the use of animals is strictly necessary. If there are alternatives available, the researcher must use them. If the use of an animal is necessary, then the scientist must identify the least complex possible organism - the species with the lowest level of consciousness, in other words.

The laboratory director writes a project application or research plan and presents it to the ethics committee. The project's purpose and the animal species to be used are stated in this file. The plan also contains a detailed description of the experiment: what happens to the animals, how the 3Rs will be upheld, how the number of animals will be statistically substantiated, etc. The application also provides a list of the personnel that will participate in the experiment, with their levels of education.

The ethics committee then weighs the social and scientific relevance of the research against the suffering of the animals. This assessment determines whether permission is given to carry out the experiment. In practice, the ethics committees usually ask extra questions about the experiments, and if necessary, they encourage the researchers to adjust their design so that fewer animals are needed and they suffer less.

Inspection and reporting

Laboratories where animal research takes place may be visited at any time by an inspector from the Animal Welfare Department. This inspector monitors the quality of the accommodation, the care of the animals and compliance with the procedures during tests and checks whether administrative records are being properly kept.

After an animal experiment has been completed, the researcher must perform a retrospective analysis that is submitted to the ethics committee. On this basis, the committee examines whether the goals of the experiment have been achieved and estimates the severity of the suffering of the animals. The analysis provides insights that can serve to improve alternative methods, thus requiring the use of fewer laboratory animals in the future. Since ethics committees decide whether animal research should continue, it is naturally in the best interests of researchers to evaluate each project with diligence and integrity. In this way, they create a continuous cycle of refinement and improvement.

The labs are required to pass on statistical data – for example, regarding the origin of the laboratory animals and the purpose of the experiment – to the Animal Welfare Department, enabling it to monitor the evolution of laboratory animal use and report to the European Commission.

KL

A conversation with

KIRK LEECH

A Kafkaesque situation… or is it?

The European legislation 2010/63/EU is the result of years of consultation between all parties involved and was favorably reviewed across the board by the European Commission in 2017. It ensures controlled, standardized animal research and guarantees the well-being of laboratory animals. Nevertheless, some scientists consider the paperwork and the often lengthy application procedures to be cumbersome. They don't have a problem with strict administrative requirements, but they do object to pointless regulations that don't give extra protection to the animal. Keeping up with this administration requires large budgets and extra staff. Some see the many rules as an obstacle to scientific research. What exactly is the problem?

Kirk Leech, executive director of the European Animal Research Association (EARA): "The frustration among researchers is certainly understandable: it is true that they sometimes have to wait a long time for approval for an experiment or an authorization for their lab. These waiting times vary considerably between different countries. This is not surprising: each member state implements the European Directive in a slightly different way, and there can be occasional hiccups.

A crucial role is played by the national or regional animal welfare committees: they advise the authorities on transposing European law into national regulations. These committees are often made up of highly diverse members: NGOs, scientists, activists…

Some see this as a problem: opponents of animal experiments could inhibit animal research through the committees. Politics certainly also plays a role: in Italy, for example, dogs cannot be bred for scientific research – a rule that was introduced under Berlusconi.

> "The resistance of opponents shoud stimulate scientists to continuously highlight the value of their animal research."
>
> **Kirk Leech, executive director of the European Animal Research Association**

But isn't balancing different opinions and seeking a compromise between them the very essence of our democratic society? If we are not open to the opinions of others, then something is wrong. The resistance of opponents within the animal welfare committees should offer an extra stimulus for scientists to constantly highlight the value of their research.

It is precisely by communicating clearly and proactively about research that scientists can build societal support. If people understand the importance of animal research, this will increase the pressure on policymakers to organize these tests more efficiently, for example, by allocating extra staff or updating technical systems. If the public is behind you, the policy is bound to follow."

FACTS AND FIGURES

EVOLUTION OF USING LABORATORY ANIMALS IN BELGIUM

1997: 859,620	2002: 695,091	2007: 779,860	2012: 600,986
1998: 837,560	2003: 676,564	2008: 725,370	2013: 626,742
1999: 790,089	2004: 708,746	2009: 741,989	2014: 664,472
2000: 651,504	2005: 718,976	2010: 700,708	2015: 566,603
2001: 655,217	2006: 759,715	2011: 665,079	2016: 535,829

CURRENT USE OF LABORATORY ANIMALS IN DETAIL

WHICH ANIMALS

MICE: 62.9%
FISH: 11.6%
RABBITS: 9%
BIRDS: 5.7%
RATS: 5.7%
GUINEA PIGS: 3%
DOGS: 0.29%
REPTILES AND AMPHIBIANS: 0.26%
CATS: 0.023%
PRIMATES: 0.007%
OTHER MAMMALS: 1.5%

Exact figures on the use of fruit flies and worms are unknown because they do not fall within the scope of the animal research law and are therefore not counted.

GENETICALLY MODIFIED ANIMALS

76.6% NON-MODIFIED ANIMALS
20.2% GENETICALLY MODIFIED, WITHOUT HARMFUL CHARACTERISTICS*
3.2% GENETICALLY MODIFIED, WITH HARMFUL CHARACTERISTICS*

* By harmful characteristics, we mean that the animal suffers from the modification itself without being subjected to an experiment.

PROVENANCE OF THE ANIMALS

99.03% EU
0.96% NIET-EU

RE-USE OF ANIMALS

1.52%

TYPE OF RESEARCH

53.07% FUNDAMENTAL RESEARCH
19.75% APPLIED RESEARCH
24.81% LEGALLY REQUIRED RESEARCH AND ROUTINE PRODUCTION
1.66% EDUCATION
0.19% PROTECTION OF THE ENVIRONMENT FOR HUMANS OR ANIMALS
0.05% SPECIES CONSERVATION
0.49% MAINTENANCE OF GENETICALLY MODIFIED COLONIES

DISCOMFORT OR SUFFERING

LIGHT: 55.56%
MODERATE: 22.26%
SEVERE: 18.06%*
DEATH: 4.02%

*In reality, this proportion is lower, due to the fact that when even one animal experiences severe discomfort, many researchers will categorize all animals in a given experiment according to this one baseline.

KC

A conversation with

KIMBERLY CREVITS

A day in the life: the lab

Researchers take great care to ensure that the animals suffer as little as possible for scientific tests, not only during the experiments themselves – for example, by using advanced techniques – but also before and after experiments. What is life like for an animal in a lab?

Kimberly Crevits works as a laboratory technician in the Department of Oncology at KU Leuven. Together with the animal handlers, she ensures that mice for laboratory animal research live as healthily and happily as possible.

Safe, clean housing

Kimberly: "Our mice are kept in individually ventilated cages (IVCs), which have been specifically designed for this purpose. These protect the animals against diseases by purifying the outside air of bacteria and harmful substances."

"Water and food are available in abundance," says Kimberly. "We keep the temperature perfectly controlled, and the cages are cleaned twice a week. Using timed lighting, a perfect day and night rhythm is maintained. We also provide cage enrichment materials, such as shredded cardboard, with which the mice can build nests."

In recent decades, increasing attention has been paid to cage enrichment, not only because it can reduce stress in the animals. For example, larger animals, such as monkeys, get toys to prevent boredom, and sheep may occasionally graze outside. Kimberly: "Mice love to build nests. Every time the cage is refreshed, they get busy with the shredded cardboard all over again."

> "In our facility, every individual mouse used in animal research is followed up. In this way, the caretakers know which animal needs special care."
>
> **Kimberly Crevits, laboratory technician in the Department of Oncology at KU Leuven**

Social contact reduces stress

Most species used in biomedical research are social animals. Putting them alone in cages causes them stress and discomfort. This is not only detrimental to the animals, but it also influences the results of the experiments. Kimberly: "In each of our cages, there is room for five mice, although we usually keep it to four. If a solitary animal is left over for any reason, we will put it in a different cage with other mice."

Every mouse matters

Kimberly: "Each mouse has a chip, ear clip or identification number, and is individually monitored. All information about the animals is displayed on the cage. This way the handlers know which animals need special care. We check all the mice up to twice a day and extra thoroughly after the weekend. On very rare occassions, several mice will lose their ear clips at the same time. But because we spend so much time with them, we can quickly recognize who's who according to their behavior."

When a mouse becomes ill, researchers will place it in quarantine. Its accommodation and food will then be adjusted to its situation, and a veterinarian will be called in as necessary.

A SOCIAL LIFE FOR EVERY ANIMAL

The facility where Kimberly works houses female mice only. You can easily house them together. "It is more difficult with males," says Guy De Vroey, chairman of the Flemish Committee on Laboratory Animals. "Male mice that share a cage soon become aggressive, but they, too, deserve a social life. That is why scientists provide them with places to hide and keep the cage free from scents of female animals. That alone makes them a lot calmer."

Myths versus the facts

Myth 1. Animal research is unnecessary

Despite alternative methods, animal research remains necessary to answer certain research questions. The complex interaction between cells, organs and molecules that is so typical of organisms such as humans, is not found in *in vitro* and *in silico* models. We owe many scientific and medical breakthroughs – aspirin, for example – to experiments on animals (also see p.30).

Myth 2. Animals are used for research because it is cheap

Housing laboratory animals costs research centers plenty of money. For example, the housing is a complex matter that must meet high standards, as do other design elements that protect the animals against illnesses from outside. The care of the animals is also expensive. Plus, the many rules and procedures that guarantee the welfare of the animals make animal research very expensive – yet another reason to use alternative methods. *In vitro* and *in silico* trials are a lot cheaper, so if saving money was the goal, animals would be the last option scientists would choose.

Myth 3. Cats, dogs and monkeys are frequently used as laboratory animals

Opponents of animal experiments often use images of scientific experiments involving cats, dogs and monkeys, thus implying that these animals are widely used. However, the vast majority of experiments in biomedical research are done on fruit flies and worms. Strictly speaking, however, these organisms are not covered by the definition of laboratory animals. Around 63% of animal experiments are done on mice. Cats, dogs and certain monkeys are used very rarely: solely if other species cannot answer the research question.

Myth 4. Animals are caught in the wild for use in research

The animals used in Europe for biomedical research have been specially bred for this purpose by accredited breeders. Catching wild animals for use in scientific experiments is prohibited, except in very exceptional cases where the scientist must thoroughly demonstrate why bred animals are not an option. The catching process is also subject to strict rules and may not cause animal suffering in itself.

Myth 5. Animals have short, painful lives in laboratories

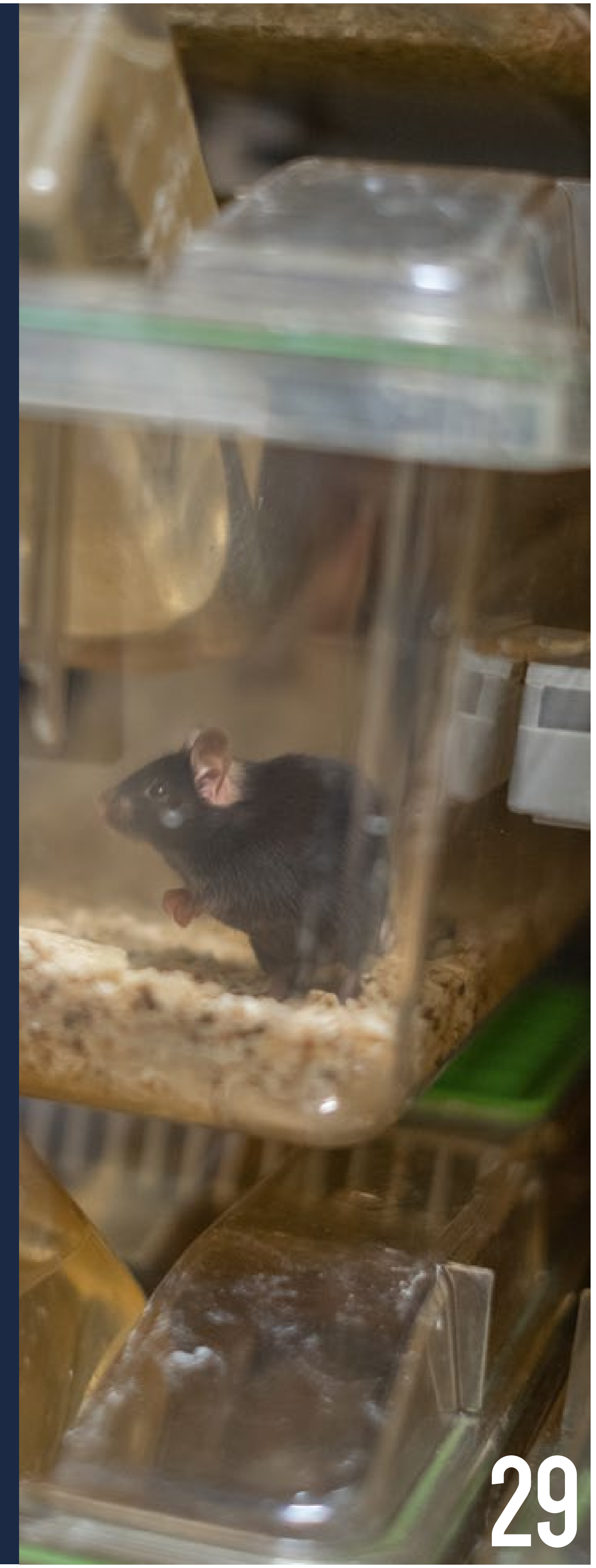
Animal experiments usually involve some level of discomfort, pain or suffering for the animal. The severity of that discomfort differs from one experiment to the next. The question of whether the animals have long lives also depends on the experiment. But animals are entitled to live in dignity with as little suffering as possible. That is why their living conditions are subject to very strict rules. All laboratory animals receive appropriate food and sufficient room to move. Social animals, such as mice, are housed together. And leisure activities are even considered: sheep and llamas graze from time to time and mice are given shredded cardboard for building nests.

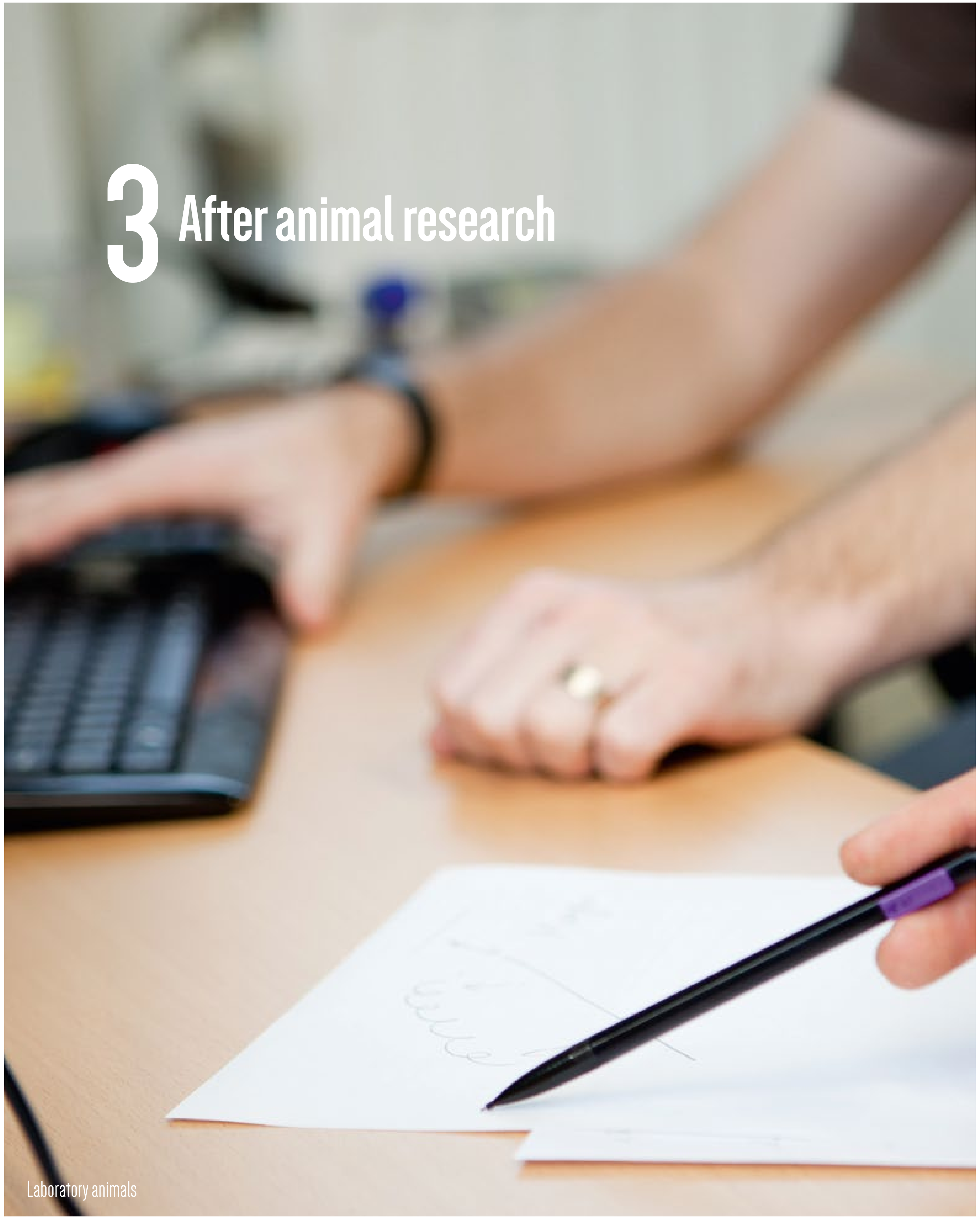
Myth 6: Medication that works in animals does not work – or is even harmful – in humans

By far, the most famous example of this is thalidomide. This medicine was tested and found safe in rats and mice, but turned out to be extremely damaging to the development of human embryos. Afterwards people realized that the medicine used in humans wasn't the same as the one used in the animals. The medicine tested in animals only contained one form of the component: the so called S-enantiomer. The medicine given to humans contained both the S-enantiomer, and its mirror image: the R-enantiomer, which caused birth defects. These negative results had nothing to do with the difference between animals and humans, but were the result of a difference between what was given to the animals and what was given to humans. Since this scandal, the procedures for testing medicines have been made stricter and more extensive.

Myth 7: Animal research will soon be a thing of the past

Although alternative methods are making great strides, the end of animal research is by no means at hand, certainly not for basic biomedical research. In more applied research, such as in toxicology, the use of animals is declining more sharply. But even the most innovative techniques cannot mimic the complex interactions in the human body as well as an animal can.





3 After animal research

Working with data from animal research

The immediate result of an animal test is quite abstract: a data set. From this, researchers distil statistically relevant information. This yield continues to grow in both quantity and quality. To give an analogy, scientists from 100 years ago had to use a 'bazooka', so to speak, to measure an effect, which has become an ultra-fine laser beam today.

It usually takes many years to get from scientific experiments for medicines to a treatment method available on the market. There are several reasons for this. To start with, several studies are often needed to clarify a disease process and to identify possible approaches to treatment. But also, the development of the drug and clinical studies in humans takes a lot of time. Consequently, the major results of animal experiments are not always immediately clear.

Measuring and comparing

In an experiment, researchers will first and foremost compare two groups of data: that of the animals that underwent treatment, and that of the control group of animals not subject to the treatment. This standard scientific practice enables them to rule out any coincidences or spontaneous changes.

More data with greater accuracy

Nevertheless, we have already come a long way. Genetic technologies offer us the possibility to simulate human diseases with great precision, and thus to obtain the right data with much greater accuracy. Think of the 'knock-in' or 'knock-out' mice, where genes are added or omitted, respectively, or more recent techniques, such as linking time and place-related changes to genes or creating combinations of different genetic modifications. In this way, tests can provide reliable and, in many cases, even predictable results more consistently than ever.

In addition, thanks to recent technologies, we can derive increasing amounts of data from a single piece of tissue. An example is 'high-throughput screening', a method that allows researchers to quickly carry out a huge number of automated tests or measurements. In this way, we are slowly but surely making progress towards mapping the thousands of mechanisms within a biological system. We have also just recently been able to collect masses of data from individual cells. This allows us, for example, to map the individual differences between cells in the tissue of a tumor, even when we are studying a tumor in a laboratory animal. Tumors are not homogeneous, which has an impact on treatment approaches.

More useful deployment of animals

What is the result of these two recent developments? Per animal, we can now generate much more information than we did a decade ago. Or, to look at it in another way: each animal is making an increasingly large contribution to solving our major medical challenges.

HUMAN-MOUSE HYBRID FOR ALZHEIMER'S

Basic biomedical research, including that performed using animals, often reveals subtle but essential differences between humans and animals. For example, recent insights show that human brain cells are much more susceptible to Alzheimer's disease than the brain cells of mice. However, this is not an obstacle to research: after all, scientists are able to let human stem cells grow into brain cells, and then transplant them into mouse brains. In this way, the typical human aspects of a disease can still be studied within the context of the entire organ.

From animals to humans… or back to the alternative

An animal experiment never stands alone. According to the standard process, you would expect such an experiment to be conducted following an alternative test method, and before clinical research in people. In practice, however, it is rarely that straightforward.

In basic research, scientists often try to understand a single but essential molecular mechanism. They start with an alternative research solution and exhaust it completely before considering an animal experiment. This test itself can then provide insights that are further investigated by alternative means. So, animal experiments and alternatives are thus used in tandem with each other.

But before we test substances on people, animal research is a well-established step – not so much as a 'confirmation' that a drug will work, but mainly to reduce risks before humans are involved.

> "Without animal research, the development of new drugs would be a toxic roulette for patients."
>
> **Adrian Liston, VIB-KU Leuven Center for Brain Research**

The further along in this process, the more potential medicines will end up being excluded. This means that researchers are sometimes forced to go back a step, often even going from clinical trials (if they have shown insufficient potential) all the way back to the beginning. That is why it often takes several years before a scientific breakthrough leads to an effective medicine. The process therefore only rarely proceeds according to the neatly defined phases in the example below.

1. Basic research *Alternatives* → **2. Basic research** *Animals* → **3. Applied research** *Alternatives* → **4. Pre-clinical phase** *Animals* → **5. Clinical tests** *Humans*

EXAMPLE: A PROTEIN AS A TARGET IN CANCER DEVELOPMENT

A project team studies the role of a single specific protein in the development of cancer. After numerous in silico and in vitro tests (phase 1), the team then sets up an animal test with mouse models (phase 2). They have disabled the effect of the protein in these animals. The animal research confirms the hypothesis: elimination of the protein has an inhibiting effect on the cancer growth. The protein has now been identified as a 'target'.

In practice, another lab specialized in the development of new drugs usually continues the work based on these findings. To find substances that can interact with the target, they switch from using animals back to alternatives (phase 3). After this preselection, they are left with certain promising molecules. These can then be tested on animals (phase 4). In doing so, they check whether the substances also have a relevant inhibitory effect on tumor growth in the complex cancer environment. Moreover, at this stage, the researchers also look at the toxicity and the (side) effects of the dose.

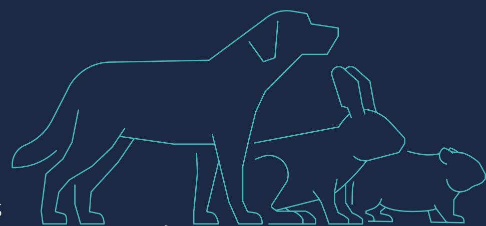
Only when they are convinced that the efficacy and safety of the substances have been sufficiently proven can clinical trials (phase 5) begin on humans. These, in turn, will be conducted in 3 phases on volunteers. Every step is strictly regulated and closely monitored. Once on the market, there is a fourth phase designed to detect unexpected long-term effects.

Revolutionary discoveries thanks to animal research

There can be no doubt: animal research has played a key role in numerous important medical breakthroughs in the past century. The examples shown below are just a small selection of countless discoveries.

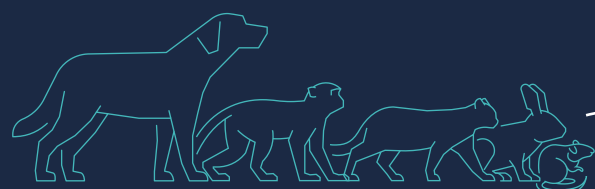
1898
Malaria parasite discovered in mosquitoes *- birds*

1912
Discovery of vitamin C *- guinea pigs*



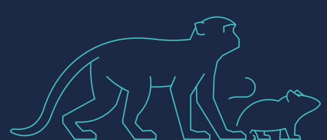
1914
First successful blood transfusions *- dogs, rabbits, guinea pigs*

1922
Insulin isolated and used as treatment *- dogs, rabbits, mice*

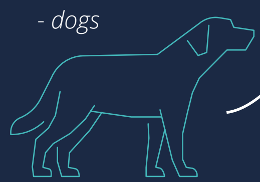


1934
First synthetic anesthetic is developed - *dogs, rabbits, rats, cats, dogs, monkeys*

1940
NOBEL PRIZE
Discovery of penicillin - *mice*

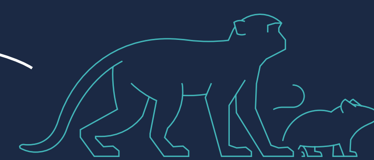


1955
NOBEL PRIZE
Polio vaccine is developed - *mice, monkeys*

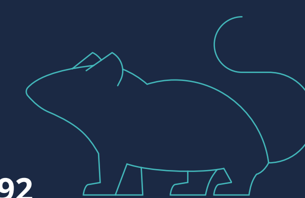


1958
The first pacemaker *- dogs*

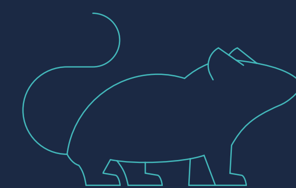
1970
Chemotherapy as treatment for leukemia - *mice*



1987
AZT, the first treatment for HIV *- mice, monkeys*

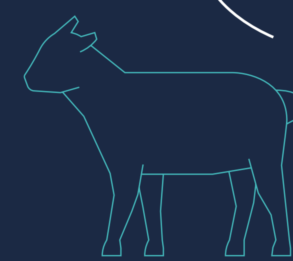


1992
Meningitis vaccine - *mice*

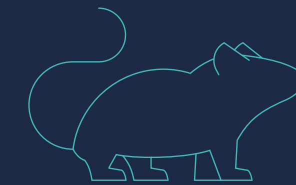


1994
Successful aromatase inhibitors for breast cancer treatment become available on the market - *mice*

2000
Development of nanobodies® - *llamas*

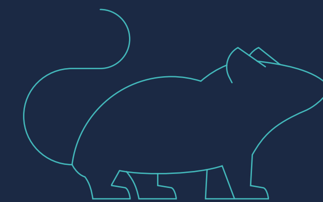


2000
Anticoagulants made from animal proteins *- goats*

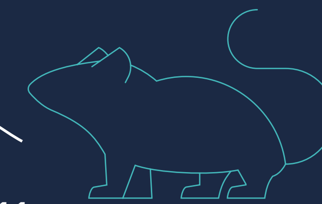


2002
Humira, monoclonal antibody against rheumatoid arthritis. It was later also approved for the treatment of other diseases such as psoriasis and Crohn's disease *- mice*

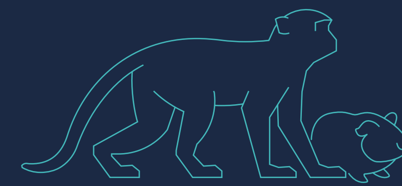
2006
Rapid advances in stem cell research - *mice, rats*



2008
First preventive vaccine for cancer (cervical cancer) - *mice*



2011
Immunotherapy for cancer treatment - *mice*



2016
Ebola vaccine - *hamsters, macaques, rhesus monkey*

ALSO WORTH NOTING: RESEARCH CAN BENEFIT ANIMALS TOO

The veterinary medicine and veterinary products we know today are rooted in animal experiments. It has only been possible to develop many of the veterinary vaccines through animal research. Just as human vaccines are tested on humans in clinical trials before they are put on the market, the same applies to veterinary medicines.

But wild animals, too, can benefit from laboratory animal research. For example, tests on fish or birds can provide relevant information about the impact of certain ecological factors on their growth or reproduction, and we can develop measures based on the knowledge gained in this way to better protect these animals in the wild.

Furthering our knowledge of humans and animals

Thanks to animal experiments, scientists have succeeded in unraveling the fundamental principles of biology and medicine. Or, to put it another way: without animal research, we might still be conducting bloodlettings today.

We have gradually combined this steady accumulation of knowledge with new technologies and research methods. The result: nowadays, we need proportionately fewer animals to obtain the same results. The amount of information we can extract from experiments has increased tremendously over the past few decades. This enables us to offer ever better answers to what were, until recently, complex and even unfathomable medical mysteries.

Is there life after the test?

Most animals in biomedical research give their lives for science. Particularly small animals, such as mice and rats, usually only survive one experiment. Larger species can, however, be useful in multiple trials, and sometimes they retire after that.

After the end of each test, the head of the research team, together with or on the advice of the animal research expert and ethics committee, decides on the future of the laboratory animal. Certain rules apply here. If it is found that the animal will experience permanent pain or injury, they cannot legally allow it to live. Animals that can no longer be used in a new trial are painlessly euthanized. Usually they are put to sleep through an overdose of sedatives or CO_2 gas.

Varying ends of life

Most laboratory animals in Belgium are small rodents (mice, rats and rabbits). For them, there are often few alternatives to death after an experiment. Some treatments do not offer the prospect of a high-quality end of life. Moreover, these animals can often undergo only one test, because a previous treatment could possibly influence the results of a subsequent test. Often, the collection of tissues is also necessary for further research. Finally, environmental legislation also plays a role: releasing genetically modified animals into the wild is not allowed.

Larger animals (cats, dogs, monkeys, etc.) have more options. After a trial, they usually do not have to be killed and can therefore be used more than once. The nature of the tests plays a role, of course. For example, in the case of short-term safety studies with experimental drugs that had already been extensively screened in the lab, dogs that have been used for tests that cause them relatively little discomfort, can enjoy a well-deserved life as a pet after a few years of service. They are assigned to adoptive families through a non-profit organization.

A lot depends on organizations, or people, who take an interest in the fate of ex-lab animals. At some universities, veterinary medicine students can adopt former 'guinea pigs' that are in good health. Retired monkeys are given a second home in, for example, animal parks. Unfortunately, this is not always possible: not every animal can easily be resocialized into a group and scientists do not allow animals that are old and sick to suffer needlessly.

AL

A conversation with

ADRIAN LISTON

Better understanding of immunology in humans and animals

Professor Adrian Liston (VIB-KU Leuven Center for Brain Research) specializes in translating immunology insights in mice to patients. At the same time, throughout his life, he has been an animal rights advocate and is a vegetarian on ethical grounds.

"Even as an animal lover, you cannot deny that animal research is a necessary evil, especially when you put it in concrete terms. For example, our team has been searching for about five years for an answer to the 'leaky SCID' disease, a really severe immune disorder found in a rare group of kids, often fatal. Because you can't just randomly start giving drugs to sick kids, we generated a new mouse model. After spending five years working out exactly what is going wrong with the immune system of these mice, we rationally selected a drug (Abatacept) that we predicted would correct the defect. Treating the mice with it worked like a charm: they got better, and lived much longer and healthier lives. Clinical tests with leaky SCID patients can now take place. Who would be willing to deny the prospect of a better life to thousands of children because the work is based on animal research?"

Animal research will remain an inevitable step in the future as well. Here's a thought experiment: imagine a perfect computer simulation that incorporates every bit of data ever known. You could treat that simulation with a new drug and it could come up with an accurate prediction. But until you follow that prediction up with an actual animal experiment, it remains a prediction. Ultimately, for medical testing we will always need to go into an animal model."

"Due to new technologies and more sophisticated research methods, the number of animals per research question has been declining for some time now," says Kris Meurrens, director of the Experimental Animal Center at KU Leuven. "Scientific progress will further improve the fate of laboratory animals. For example, future imaging technology will enable us to better study the influence of a treatment on organs, tissues and cells without having to kill the animals. As a result, we will be able to use more animals multiple times, which means that hopefully, over time, we will need to breed fewer animals."

Kris Meurrens, chairman of the Laboratory Animal Center at KU Leuven

A more balanced picture of animal research

With this issue of Facts Series, our primary aim has been to provide information for anyone interested in a more balanced picture of animal research.

According to the letter of the law, animal research concerns experiments with vertebrates and animals, such as octopuses, that entail some form of discomfort or suffering that is equal to or greater than the introduction of a needle. The mouse is the most commonly used vertebrate animal. In practice, insects and worms are used more often, but experiments using these animals do not legally count as animal research.

Researchers use animals because they want to understand diseases and develop new treatments for both humans and animals. These are important motives that are carefully considered by ethics committees when ruling on whether to authorize an animal experiment.

Not just anyone is allowed to use animals for research, and once approved, the animal experiment must comply with numerous rules and procedures. These are intended to maximize the welfare of the animals and to limit their discomfort as much as possible. There are also numerous administrative requirements which, for example, entail that every animal must be monitored individually.

Animals are not people, but there are enough similarities that animals can be used as relevant models. Using modern genetic techniques, the relevance of these models can be further increased. Alternative models have been discussed in detail in this document, but alternatives also have their limitations. Computer simulations and test tube research are currently already used for virtually every study conducted today, and scientists are hard at work developing high-tech methods that will allow the replacement of even more animal experiments. Nevertheless, the world is not about to be free of animal research anytime soon.

Animal experiments have undeniably improved lives and the animal research that is being carried out today will certainly improve the lives of people within a few years. However, these experiments continue to be the subject of debate – a debate for which we hope this Facts Series will provide a more balanced basis.

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