



Non-human primates in research and safety testing

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SCHER (2009)

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Context - Every year, more than 100 000 monkeys and apes are used for biomedical research around the world. Their genetic similarities to humans make them particularly suitable candidates for testing the safety of new drugs and for studying infectious diseases or the brain. But those very similarities to humans also raise specific ethical questions about their use for scientific experiments.

Are there alternatives to the use of non-human primates in research and testing? Would it be feasible to stop using them altogether?

An assessment by the European Commission Scientific Committees on Health and Environmental Risks (SCHER).

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The answers to these questions are a faithful summary of the scientific opinion produced in 2009 by the Scientific Committee on Health and Environmental Risks (SCHER):
"The need for non-human primates in biomedical research, production and testing of products and devices"

The full publication is available at: <http://copublications.greenfacts.org/en/non-human-primates/>
and at: <http://ec.europa.eu/health/opinions/en/non-human-primates/>



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- Each question is answered in Level 1 with a short summary.
- These answers are developed in more detail in Level 2.
- Level 3 consists of the Source document, the internationally recognised scientific opinion which is faithfully summarised in Level 2 and further in Level 1.

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1. Introduction – Overview of the use of primates in research and testing in the EU

Around 12 million animals are used each year in scientific procedures in the EU, and among these, around 10 000 are non-human primates (NHPs), mainly monkeys and apes. Experiments on such primates have led to important findings in biology and medicine.



Currently, primates are only used in animal experiments when there are no suitable alternative methods or species. They are mainly used for safety testing of pharmaceutical products and devices, but also for fundamental research in biology and for research and development of medical products and devices.

Nearly all primates used in scientific experiments are born to animals that are themselves bred in captivity, sometimes for several generations. With some exceptions, research on animals that are bred rather than caught in the wild tends to deliver more accurate and reliable data. Primates caught in the wild are very rarely used in research but are still needed to avoid the adverse effects of inbreeding of stocks.

With regard to animal welfare, major investments have been made in recent years to improve housing conditions of captive primates, taking into consideration their physical and social needs.

2. Why are primates needed in research and safety testing?

2.1 Before **pharmaceuticals** reach the consumer, their **safety** has to be tested on humans during clinical trials. Preliminary experiments on animals – often rats and dogs – are intended to protect the health of people taking part in these trials. Only few candidate pharmaceuticals are actually tested on non-human primates (NHPs). Primates are needed to test certain drugs with potential effects on female genital organs, eyes, birth outcomes, blood coagulation, or the brain, as they are the only mammals with specific physiological traits similar to humans.



Only few candidate pharmaceuticals are actually tested on primates
Source: Understanding animal research

2.2 In **research on infectious diseases**, vaccines and drugs that are developed are typically first tested on cells grown in the laboratory, then on animals, and finally on humans to check their safety and effectiveness. Primates often remain the most suitable animal option because their immune system is very similar to that of humans. Primate species are the only ones that can be used to develop effective malaria, tuberculosis, hepatitis C, or HIV vaccines and drugs for humans. Primates may also be needed to quickly detect new diseases such as SARS that could spread across the world.

2.3 Primates play a unique role in **brain research** because they are the only animals with brains that approach the complexity of the human brain. Research on pain and experiments on primates which require entering their skull raise difficult ethical concerns. Some new, non-invasive research techniques are being developed that can be used on humans and primates, but important limitations remain.

2.4 Using pig organs for **transplantation** is a way to address the shortage of organ donors. However, the human immune system rejects pig organs strongly. Only certain primate species show a similar immune response so any animal-testing of drugs to prevent transplant rejection has to be done on these species.

3. Are there alternatives to the use of primates in research and safety testing?

Alternatives to the use of non-human primates (NHPs) in research and testing do exist and can complement but not yet completely replace testing on these primates. As far as possible, the number of animals used should be reduced, methodologies should be refined, and the use of animals should be replaced by alternative methods (3Rs principle).



Tests are first carried out on cells grown in the laboratory
Source: Jean Scheijen

3.1 Because of scientific reasons, testing **pharmaceuticals** on non-human primates is in certain cases a very small but almost compulsory part of the global testing procedure, especially for drugs and vaccines that involve the immune system.

In certain cases, genetically modified rodents could potentially replace primates. Experiments on humans using extremely low doses of the new pharmaceutical being tested (microdosing) have also been proposed as an alternative to animal experimentation, but since prior tests on animals would still be needed to make sure that the small dose given is safe, it is not clear whether this would reduce the number of animals used.

3.2 In the search for new **drugs and vaccines** against HIV, hepatitis C, or malaria, tests are first carried out on cells grown in the laboratory, on mice, or on both. Such tests provide insight into the cell mechanisms, but cannot explain how a whole body would react to the infection. Experiments on non-human primates are therefore still needed.

3.3 Non-invasive techniques that study the brain without entering the skull are very useful and promising to understand healthy and diseased **brains**. However, such techniques are not yet as informative as invasive methods and still need to be further developed.

Computer modelling is rapidly improving but the human brain is so complex that a realistic model is unlikely in the foreseeable future.

3.4 Cells grown in the laboratory and rodents can be used to carry out preliminary research into the use of animal organs for **transplantation**, but transplants still need to be tested on animals, including primates.

4. Could alternatives completely replace the use of primates in the future?

In the foreseeable future, experimentation on non-human primates (NHPs) is unlikely to be completely replaced by laboratory methods or by test on other animal species.

For the **safety testing of new pharmaceuticals**, primates are also likely to remain the most suitable mammals.

To study **HIV infection**, genetically-modified mice will probably be available in the future. However, for scientific reasons, studies using mice cannot completely replace those using primates.

In research on the **brains' structure and function**, non-invasive techniques which do not require entering the skull and computer modelling can be used alongside invasive methods

but cannot replace them completely. However, new techniques and technologies are developing quickly and advances must be assessed frequently.

The development of artificial organs and tissues may reduce the need to use primates to test drugs that prevent rejection of animal organs (mostly pig organs) by humans. However, these artificial body parts are mainly used in life-support machines and do not represent an alternative to **animal-to-human organ transplantation**.

5. When primates cannot be replaced, how could their use be reduced?

There are several ways to reduce the use of non-human primates (NHPs) in research areas where it cannot be avoided altogether:

- By analysing more carefully the results of drug safety experiments carried out first on rodents such as rats and mice, then on dogs and other non-primate mammals. This could reduce the numbers of primates needed, although it might increase testing on other mammalian species.
- By reusing the same non-human primates in different experiments. There are regulations to avoid the same animals being continually re-used for experimentation, but overly restricting the re-use of primates could increase the overall number needed.
- By making current animal tests for reproductive toxicity more effective so that fewer primates are needed.
- By improving communication between facilities that carry out experiments on animals so that they share information, ideas and expertise and avoid duplicating experiments.
- By encouraging the development of new techniques that may reduce and partly replace the use of non-human primates in testing of medicines, vaccines, and drugs used in animal-to-human organ transplantation.



Careful analysis of the results of tests on rodents could reduce the number of primates needed
Source: Understanding animal research

In addition, clear information on the species and number of animals used for experimentation as well as on the types of tests involved should be publicly available.

6. How could the welfare of primates used in laboratories be improved?

There are several ways to enhance the welfare of non-human primates (NHPs) in scientific research.

- The importance of the physical and mental well-being of primates should be acknowledged. New standards of care, treatment and living conditions for primates used in research and testing should be adopted as soon as possible.
- More research is needed to understand the impact of pain and distress on animals and to recognise the signs of suffering.
- Experiments should be designed so as to minimise pain and discomfort. Testing should not last longer than absolutely necessary and should be stopped early if there is significant pain and distress.
- The use of 'non-invasive' technologies which do not require entering the body or puncturing the skin, such as magnetic resonance imaging (MRI), should be improved and increasingly used.



New standards of care, treatment and living conditions are needed
Source: Jorge Vicente

- In the case of vaccine research, tests should be stopped at humane limits (endpoints) set beforehand, for instance as soon as early symptoms are detected.

7. Conclusions and recommendations

The Scientific Committee on Health and Environmental Risks (SCHER) concludes that, because non-human primates (NHPs) have close and sometimes unique similarities to humans, their use remains necessary in the safety testing of new pharmaceuticals and in several areas of biomedical research, such as research on infectious diseases and on the brain.

The SCHER considered only scientific aspects, specifically excluding ethical, economic, cultural and social considerations which will be addressed by other groups.

At present, the SCHER sees no valid scientific arguments to stop using non-human primates for scientific research and drug safety testing, but this position should be frequently reviewed as new alternatives are constantly being developed.

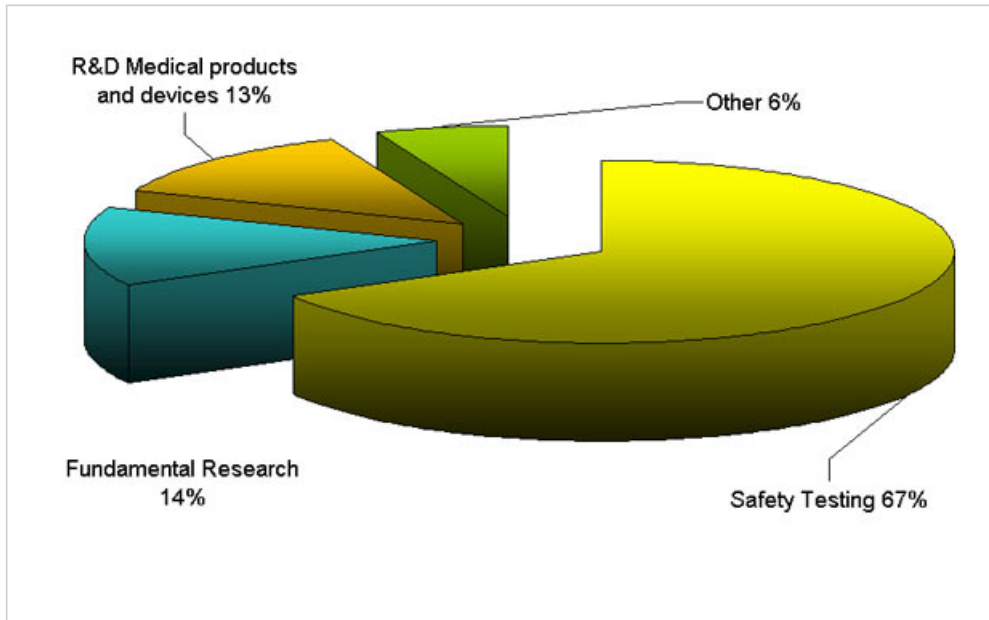
The SCHER supports the “three Rs” principle of reducing, refining and replacing the use of non-human primates in scientific testing and makes a series of recommendations:

- Non-human primates should be used only when this is scientifically justified.
- Tests on cells grown in the laboratory, computer modelling, and improved techniques which do not require entering the skull should be encouraged.
- The replacement of primates by other animal species should be further investigated.
- Coordination and communication between facilities doing animal testing should be improved to avoid duplication of tests, to optimise procedures, and to minimize the numbers of primates used.
- Any tests on primates should cause as little pain and distress as possible, and not last any longer than necessary.
- Housing and breeding of primates should follow high standards of care, consider their welfare as well as their physical and mental needs.
- The use of primates caught in the wild should be discouraged for both scientific and animal welfare reasons.
- Research that leads to further replacement, reduction and refinement of the use of primates should be promoted.

Annex

Annex 1:

Use of primates in EU research and safety testing



Source: SCHER, *The need for non-human primates in biomedical research, production and testing of products and devices (2009)*
[see http://ec.europa.eu/health/ph_risk/committees/04_scher/docs/scher_o_110.pdf]

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