Non-human primates

in research and safety testing

Source document:
SCHER (2009)

Summary & Details:
GreenFacts (2009)

Level 2 - Details on Non-human primates

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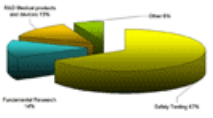
1. Introduction – Overview of the use of primates in research and testing in the EU



Use of primates in EU research and safety testing
[see Annex 1, p. 13]

Experiments on non-human primates (NHPs) have brought about important advances in biology and medicine. Primates often play a crucial role in the safety testing of new drugs and in research aimed at understanding how the brain works and how to prevent infectious diseases in humans.

Worldwide, more than 100 000 primates are used each year for biomedical animal experimentation: over half in the USA, one tenth in Europe and the rest in Japan and other countries. Primates represent a tiny proportion of the total number of animals used in experiments (less than 1 out of thousand animals in the EU and approximately 3 out of thousand in the US). According to the pharmaceutical industry, of all the primates used, less than 0.1% are involved in experiments where their level of suffering is categorised as "substantial".

Non-human primates are a group of mammals composed of simians – monkeys and apes – and prosimians, such as lemurs. Monkeys are further divided into two subgroups: Old World monkeys, which are native of Africa and Asia, and New World monkeys, which originate from Central and South America.

The most frequently used primate species are the long-tailed macaque and the rhesus monkey (both Old World monkeys). In Europe, there is a shift towards using more new-world primates and fewer prosimians. Great Apes were not used in the EU in 2005.

In the EU, animal experimentation is regulated and is only allowed in specific research areas.

Safety testing of new drugs, substances and devices, especially those aimed for human medicine and dentistry, accounts for about 67% of the total number of NHPs used. Almost all these tests on primates are mandatory and requested by safety testing regulations. Of all primates used in safety testing, approximately half are involved in mid- to long-term toxicity studies, which entail repeated administration of the substance; one third are involved in single-administration studies; and the rest are used to study the effects on reproduction and development or for other tests.

Primates are also used in **fundamental biological research** (about 14% of all NHPs used) as well as in **research and development** of medical and dental products and devices for humans (about 13% of all NHPs used).

Nearly all primates used in scientific experiments are born to animals that are themselves bred in captivity, sometimes for several generations. Wild-caught animals are very rarely used but are nonetheless still needed to avoid the adverse effects of inbreeding of stocks. Captive-bred animals give more accurate, reliable and reproducible data. However, research on aging and on pregnancy is more reliable if conducted on wild-caught animals.

One way to avoid inbreeding while reducing the use of wild primates is to exchange wild-caught males between facilities, as zoos do. Another option is to use the captive offspring of wild-caught parents for breeding only and not for research. However, this would create a shortage of animals for experimentation that, in the short term, would result in more wild primates being captured to increase the breeding stock. Another complication relates to the difficulty to breed successive generations from captive-born parents because such animals often show reduced birth rates and poor mothering, and their offspring can have health problems.

It is important to note that in recent years there have been major investments to improve housing conditions for primates.

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

2.1 Why are primates needed in the safety testing of pharmaceuticals?


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

Before a new pharmaceutical can be introduced on the market, it has to be tested on humans during clinical trials. The purpose of animal testing is to safeguard the health of the people taking part in these trials. The vast majority of drugs initially selected for development are rejected during this process, either because they are not effective or because they cause unwanted side-effects.

First, newly designed drugs go through a series of preliminary laboratory tests that do not involve animals. Based on the results, the best 'candidate' drugs are then tested on animals to see if they work, and to identify any possible health risks. Drugs are often tested on rats but the results are difficult to extrapolate to humans because of some fundamental differences between the two species. Therefore, pharmaceuticals must also be tested on a second species other than rodents, often dogs. Normally, there is no routine requirement for the use of non-human primates as a second species. While safety testing of new pharmaceuticals and other medical products represents one of the major uses of these primates, only few candidate pharmaceuticals are actually tested on them.

Primates should only be used when it is scientifically demonstrated that none of the other non-rodent species commonly used in safety testing is appropriate for the purpose of the study.

For instance, because no other animal species is as close to humans in their anatomy or in the way they respond to drugs, primates may be preferred over other mammals to test the safety of the following drugs:

- drugs with possible effects on female genital organs
- drugs with possible effects on the eyes
- drugs that may cause vomiting
- drugs that affect how the blood coagulates
- certain antibodies
- drugs with psychoactive properties
- drugs capable of causing birth defects

Primates have been used effectively to test the safety of major new treatments for diseases such as severe asthma and certain eye diseases.

Regarding the potential effects of a drug on reproduction, rabbits and rodents such as mice and rats are often used, but the results are not accurate. Studies on primates are more likely to identify possible hazards to humans. For instance, a new drug developed to treat multiple myeloma, a type of cancer affecting immunity cells in the bone marrow, was safe for rats but produced limb abnormalities in the offspring of pregnant primates so we now know that it cannot be given to pregnant women.

Because humans and primates develop in a similar way in the early years, young primates may also be the preferred option for specific safety testing of drugs aimed at infants and children.

In some cases primates are not the best animal choice, for instance dogs are more suitable for testing toxicity to the liver. It is also important to note that animal testing on primates does not always predict all harmful effects on humans. Therefore, safety assessments of new products require information from both animal and non-animal testing.

2.2 Why are primates needed in research on infectious diseases?

There is an urgent need to develop vaccines, antibiotics, antivirals and other medicines that are effective against current and emerging health threats such as HIV, malaria, tuberculosis, severe acute respiratory syndrome (SARS), and avian influenza.

Before they are used on humans, vaccines must be tested on animals to see if they are safe and effective. The choice of a particular animal species depends on the disease but, often, non-human primates (NHPs) remain the most suitable option because their immune systems are very similar to that of humans. Sometimes, primates are even the only choice because they are the only mammals besides humans, which can catch certain diseases (e.g. smallpox).

Primates may be needed to quickly detect new diseases that could affect a large number of people across the world and spread over a wide geographical area. For instance, studies on primates were used effectively to prevent a pandemic spread of SARS in 2003.

2.2.1 **HIV**

Non-human primates (NHPs) are the only mammals that mimic important aspects of HIV infection in humans. They are used to understand how the immune system works and how AIDS develops. This work is important because the spread of HIV/AIDS can probably not be stopped without the use of an easily accessible vaccine.

Even though the HIV-vaccines tested to date have failed to provide the desired immune protection to patients in clinical trials, results of studies on primates are coherent with effects seen subsequently in humans and there is a growing consensus that any candidate vaccines should be studied even more thoroughly on primates before moving into large and expensive trials on human patients.

2.2.2 **Tuberculosis**

The current tuberculosis vaccine was developed at the beginning of the 20th century and, although it is still widely used worldwide, its effectiveness varies. As for many infectious diseases, there is no animal species that is perfectly suited to study tuberculosis and to draw conclusions applying to humans. Therefore, information needs to be gathered from different animal species. New vaccines are tested first on mice and guinea pigs. Only the most promising vaccines are then tested on non-human primates (NHPs) before proceeding to clinical trials in humans.

2.2.3 **Malaria**

It is very difficult to develop a vaccine against malaria because there are four different parasites that cause the disease and because each parasite goes through four different stages during the course of its infection of a human host, each time presenting different

substances that the human immune system has to fight (antigens). In addition, any vaccine has to account for human genetic differences that also influence the level to which the human body can defend itself against the disease.

The owl monkey and the squirrel monkey are the only species (besides the chimpanzee) that are susceptible to the human malaria parasite, and they are used in very limited numbers for preliminary testing of vaccines.

2.2.4 **Other infectious diseases**

Currently about 170 million people worldwide are infected with the Hepatitis C virus and the only species besides humans that is susceptible to Hepatitis C is the chimpanzee. Vaccines are first tested on cells grown in the laboratory and on other species such as baboons and genetically modified mice. Chimpanzees are only used for testing the effectiveness of very promising candidate vaccines.

Currently, in Europe, no research is conducted on chimpanzees, and research groups that are studying this virus use laboratories in the USA and other parts of the world to carry out the necessary experiments.

2.3 Why are primates needed in research on the human brain?

Brain injuries and diseases such as epilepsy, damage to blood vessels in the brain, depression, drug addiction, Alzheimer's disease, Parkinson's disease, and multiple sclerosis have a large impact on society. Therefore, brain research is urgently needed and likely to grow.

Research in neuroscience aims to understand how the brain works when it is healthy and when it is affected by a disease or an injury. Despite great progress over the last 50 years, our knowledge of the brain is still limited. Much of what we know is based on studies on cats, rats and even invertebrates. However, information from these relatively simple brains is of limited use when trying to understand and treat brain injuries and disorders that involve complex interactions between different parts of the human brain. As non-human primates (NHPs) and humans have very similar brains, experiments on primates remain crucial. At present, primates are the only animals available to study how the activity of a single nerve cell is related to more complicated brain functions.

Experiments on primates have been particularly valuable in a number of cases:

- to understand how humans see, hear, feel, control movement, think and reason.
- to establish a method with a type of pacemaker in the brain to control the symptoms of Parkinson's disease. This method seems promising to treat other brain diseases.
- to develop techniques where patients can use their brain to control the movement of paralysed limbs or command computers.
- to gain unique insights into brain diseases in newborn and premature babies.
- to study mental health and to do research on conditions such as depression as large primate colonies have complex social structures and some individuals behave in the same way as human psychiatric patients.

The use of animals in pain research is very controversial. Research in this area is nevertheless vital because 19% of adult Europeans live with moderate to severe long-term pain, seriously affecting the quality of their social and working lives. Animal experiments mainly involve rodents and only very rarely primates. In some areas of pain research it might be possible to replace animals with human volunteers and patients.

Stem cell technology uses undifferentiated cells that can multiply and become any sort of cell in the body. This technology opens the possibility to use cells from patients to repair their own tissue and would eliminate the problem of rejection of transplanted tissues or organs and ethical issues concerning embryos. Such techniques are being developed for the treatment of Parkinson's disease, Huntington's disease, strokes and spinal cord and brain injuries, but will likely need to be tested on primates first.

Experiments on primates are useful not only to understand diseases and find ways to cure them but also to develop alternative laboratory, non-animal testing methods and computer models.

Experiments which require entering the skull of non-human primates, raise difficult ethical concerns. New, non-invasive techniques to assess brain structure and function are developing rapidly and are increasingly used in clinical studies and in research. Although powerful, they can only study brain activity close to the surface. Studying regions deeper in the brain still requires invasive techniques and non-human primates.

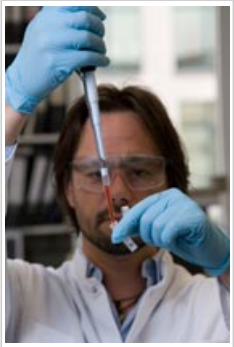
2.4 Why are primates needed in research on organ transplants?

Transplantation is a surgical procedure in which tissue or whole organs are transferred from one organism to another. It is used to replace irreparable damaged or non-functioning vital organs such as kidneys, lungs, liver and heart. Transplanted cells are also used to treat diseases such as cystic fibrosis, diabetes and Parkinson's disease. However, there is a serious shortage of donors and 10-20% of patients on the waiting list for organ transplants die before a donor organ becomes available.

To alleviate this problem, animals have been considered as a source of organs for transplantation and the most suitable species is likely to be the pig, since its organs are similar in size to human organs. However, before pig organs are transplanted into humans, they need to be tested on non-human primates to see if such transplants are feasible and effective. Tests on rodents would not be credible because their immune system is quite different to that of humans. Humans, Old-World primates and great apes are the only species with a particular type of antibodies that make them reject pig organs and therefore tests need to be done on these species.

Transplanted patients need to take medication to suppress their immune systems considerably so that they do not reject the foreign organ, and this can have long-term side effects. There are also concerns about potential infections that might be transmitted from source animals to transplanted humans and about how well the transplanted organ would work. Despite these difficulties, some primates transplanted with pig organs have survived for 2 to 3 years which proves that transplants with animal organs are viable.

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


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

To protect human health and the environment, it is essential to have accurate information on the effects of exposure to chemical, physical and biological agents. It is also important to do basic research to understand the human body and the diseases that can affect it, and to test any medicines or vaccines before they are given to humans. The Scientific Committee on Health and Environmental Risks (SCHER) agrees with the widely accepted guiding "three Rs" principle, which aims at reducing the number of animals being tested, refining the methodologies used and replacing the use of animals with alternative methods for research and testing. It considers that animals should only be used in medical research when it is unavoidable and when appropriate and validated alternative methods are not available.

SCHER also recognises that the results of tests on animals cannot predict accurately all the likely effects on humans. The use of non-human primates (NHPs) is therefore considered essential in certain cases because there are crucial differences between other species and humans, which make any results of studies on other animals of limited use.

Replacing animals in medical research is a long and difficult process and alternative testing methods are often not yet feasible. At present, non-animal testing methods are usually developed as complementary methods which answer questions at the level of single cells or limited numbers of cells, and cannot be applied to the highly complex problem of whole organs or interactions between different organs. Therefore, at this stage, these methods cannot completely replace methods involving animal testing. There are however, new, promising techniques that use laboratory tests and other animal species such as genetically modified mice, instead of primates.

Experiments are also carried out on human volunteers. There should be a constant feedback between human and animal research, as well as laboratory studies on cell cultures, to improve our knowledge and to make animal and human experiments more meaningful.

3.1 Are there alternatives to the use of primates in safety testing of pharmaceuticals?

At present it is impossible to totally replace animal experiments when testing pharmaceuticals for their safety and effectiveness, because laboratory studies cannot yet predict how a drug will affect real, living humans; and it is still necessary to establish below which dose no harmful effects are observed (NOAEL).

Because of scientific reasons, testing of new pharmaceuticals on non-human primates is a very small but almost compulsory part of the global testing procedure. The reason is that primates are usually the species that match humans more closely in terms of how drugs affect them and tests on other species are not adequate. Drugs involving the immune system can often only be tested on primates. In certain cases, genetically modified rodents may replace them but this is usually not yet accepted by regulators, who consider this alternative as a source of supportive data rather than as a means to replace the use of primates.

Microdosing, where people are given extremely low quantities of the pharmaceutical being tested to study how the substance behaves in the body, has been proposed as an alternative

to animal testing. However, to make sure that the dose given is safe the toxicity of the drug must first be tested on animals. In any case, it is not obvious whether or not microdosing would lead to a reduction in the number of animals used.

Recently, the US National Academy of Sciences has proposed a combination of techniques that reduces the need for animal experimentation. These include testing cells in the laboratory, computer modelling and innovative tools in molecular biology. Animal testing should only be used when the results are unclear or where there are specific concerns. However, this method was developed for testing environmental chemicals where daily human doses are much lower than those used in medicines and is not suitable for testing the safety of pharmaceuticals.

3.2 Are there alternatives to the use of primates in research on infectious diseases?

There is no small mammal ideally suited for testing **HIV vaccines and drugs**. For instance, mice do not get infected with HIV. Despite this, some advances have been made to observe human immune reactions by introducing human immune cells into wild mice. Although this cell transplant does not last long, it has been used to investigate short-term immunity and to do quick screenings of candidate HIV vaccines.

It is very difficult to produce genetically modified mice susceptible to HIV infection. Recently, experiments have been carried out by combining the HIV-1 virus with another virus that infects mice. This method allows scientists to study how candidate vaccines and drugs work inside the body for longer periods of time. However, testing such vaccines still requires additional studies on non-human primates (NHPs).

Despite intensive research, no HIV vaccine developed so far has been successful in clinical trials on humans even though they had been tested on non-human primates beforehand. Some people claim that this shows that such testing on primates is ineffective. However, this research has increased our knowledge of how the immune system interacts with the virus both in humans and in primates. There have also been studies in cells grown in the laboratory which have improved our understanding of fundamental reactions in individual cells. However, these cannot explain how the whole body reacts to HIV infection. At present, laboratory studies on cells are complementary and cannot replace testing on primates in this area of research.

In the search for a **malaria vaccine**, scientists have used alternative methods that do not require the use of primates. However, it is impossible to replicate in the laboratory the extremely complex interactions between the different malaria parasites and the human immune system. Mice can be used for preliminary testing but cannot replace testing on primates, which will be needed to develop malaria vaccines in the future.

A new method has been developed to do research on **hepatitis C** using cells grown in the laboratory instead of primates. However, to see if a candidate vaccine is effective it needs to be tested in chimpanzees which are the only species, beside humans, susceptible to the infection.

3.3 Are there alternatives to the use of primates in research on the human brain?

In humans, the brain is routinely studied using non-invasive techniques that provide images of the brain’s structure and activity and detect abnormalities:

- Magnetic resonance imaging (MRI), which uses powerful magnets and radio waves to construct pictures of the internal structures of the brain, and
- Electroencephalography (EEG), which records the electrical impulses in the brain from electrodes placed on the scalp.

Recently, a new type of MRI has been developed that measures blood flow and levels of oxygen in the brain, and gives an indirect measure of brain activity. Although such techniques are very useful, they only measure how the brain works on a large scale and are not quick enough to respond to the way in which individual brain cells process information. Therefore, they cannot replace studies made by placing small electrodes in the brain. This latter technique is invasive but gives much more precise information on how different parts of the brain work because that can measure variations in the time range of milliseconds at which neurons process information.

New non-invasive techniques based on MRI have been developed and may greatly help to study how different nerve cells are connected both in healthy and in diseased brains. Although promising, these techniques still need to be developed further and have to be validated.

Computer modelling is rapidly improving but even the best attempts cannot simulate a functioning brain, partly because we still know little about the structure of the brain itself. The "Blue Brain project" has attempted to create a biologically accurate simulation of how the brain works. In the surface of the brain, nerve cells are organised in "columns" of thousands of interconnected nerve cells (neurons). The "Blue Brain project" managed to recreate a model of one of these columns of about 10 000 neurons of a rat brain but this took the full computational power of a supercomputer. A realistic model of a primate brain needs to have about 100 billion nerve cells so we do not know if and when such a model would be technically feasible.

3.4 Are there alternatives to the use of primates in research on organ transplants?

Studies on cells grown in the laboratory are useful in the initial stages of research to find out if an organ from an animal is likely to be rejected by the human immune system. Rodents are also used to see if drugs developed to prevent transplant rejection are effective. However, these cannot replace long-term studies on how transplanted organs will function in living animals, including non-human primates (NHPs).

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

The areas of scientific research that use non-human primates (NHPs) are highly complex and it is very difficult to predict the timing of progress in the field. Based on the scientific evidence available today, however, it is very unlikely that primates will completely be replaced in the foreseeable future by other animals or tests on cells grown in the laboratory.

Safety testing

To check that new drugs are safe, they have to be tested on animals that show a similar response to the drug as humans, and that often means testing in primates. Using alternative non-rodent species may reduce the number of primates used in tests, but it will increase the use of other species.

Infectious diseases

A genetically modified mouse that responds to the HIV virus in the same way humans do may be available in the future. However, it is not clear how the results of research on these mice will translate into real vaccines, particularly because we still do not know how to test if a person is immune to HIV. Therefore it is necessary to continue research on primates in order to learn as much as possible about the immune response.

Data from human clinical trials will help develop better ways of testing the effectiveness of vaccines in genetically modified mice and in cells grown in the laboratory. However, tests on mice cannot completely replace the use of primates. In addition, regulations make it compulsory to test the effectiveness and the safety of new vaccines on a relevant animal species such as apes or monkeys before they can be experimented on humans.

Neurosciences

Computer modelling and a wider use of modern non-invasive techniques such as magnetic resonance imaging (MRI), which allows to visualise the structure of the brain, and positron emission tomography (PET), which produces images of the brain in action, can complement but not yet replace invasive tests in primates. However, technology improves quickly so it is important to frequently assess any progress in the development of non-invasive technologies.

Animal-to-human organ transplantations

The artificial development of organs and tissues may reduce the need for non-human primates used to test drugs that prevent transplant rejection from animals (mostly pigs) to humans. However, currently, artificial organs are mostly used in life-support machines and are not an alternative to animal-to-human organ transplantation. Moreover, there are no devices at present that can carry out the complex functions of organs such as the liver.

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


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

There are several ways to reduce the use of non-human primates (NHPs) in research areas where no replacement can yet be foreseen.

- To ensure that any newly developed drug is safe, it needs to be tested on two animal species, one of which not being a rodent. Dogs are often used as the non-rodent species and primates are used when dogs are not suitable. The use of primates may be reduced by examining more carefully how drugs are transformed within the body of rats, dogs or mammals other than primates. This may also help identify the most suitable species on which to test each drug, and thus reduce the use of primates. However, this may only shift the testing to other mammals.
- Using the same animals for different tests could reduce the number of primates needed. However, there are regulations to avoid the same animals being continually re-used for experimentation. But overly restricting the re-use of primates may result in an increased number of primates being used.
- Some newly developed drugs are made of antibodies that attack a specific disease-causing agent. To ensure that these drugs do not cause malformations in foetuses, they are tested on a number of pregnant primates. But these standard tests are typically carried out early in the pregnancy, when any transfer to the placenta is very low or absent and thus when risks of malformation are very low. Carrying out these tests towards the end of the pregnancy in

combination with other tests that take place around the same time may reduce the number of animals used.

- Collaborating, sharing expertise and information between different animal-testing facilities and ensuring that safety testing procedures for drugs are similar across the world would ensure that experiments are effective and are not duplicated needlessly. Laboratories working to replace animal experiments should also be part of this information network.
- Advances in research may reduce and partly replace primates in testing of medicines and vaccines. For instance, stem cell research and tissue engineering may reduce the number of animals used in research on organ transplantation. Genetically modified rats would also reduce the number of primates used in safety testing. However, these techniques are still in the early stages of development.

In addition, there should be clear information available on how many animals of each species are used for experimentation, on the types of tests involved and on the reasons behind the choice of animal species and number of animals used.

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


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

There are several ways to reduce the level of suffering of non-human primates (NHPs) in scientific research and to enhance their welfare:

- Avoid poor housing and care standards which cause unnecessary suffering and produce animals less suitable for studies. Primates are social animals so it is important to attend to both their physical and their mental needs.
- Do more research to recognize when animals are suffering and understand the effects of pain. The welfare of animals improves if animals are acclimatised slowly, if they are helped to get used to procedures using positive training techniques such as rewards, and if they are given painkillers after painful procedures.
- Design experiments so that pain and discomfort are as low as possible. Stop experiments as soon as the objectives are met, or sooner if there is significant pain and distress. In the case of vaccine research, stop the tests as soon as it is clear that an animal has not become immune.
- Improve non-invasive technologies such as magnetic resonance imaging (MRI) to test the safety of drugs, and to check the effects of previous interventions on the brain without having to kill animals to collect samples for testing.
- Humane early objectives (or endpoints) should be established in the development of vaccines, such as the detection of early symptoms, to prevent experiments from lasting longer than necessary.

7. Conclusions and recommendations

The Scientific Committee on Health and Environmental Risks (SCHER) concludes that the use of non-human primates (NHPs) remains crucial in several important areas of research and safety testing because they have a close and sometimes unique similarity to humans. These areas of research include understanding infectious diseases, learning how complex brains are structured and how they function, developing methods to use animal organs for transplantation, and safety testing of newly developed pharmaceuticals.

Within the scope of this assessment, the scientific committee 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 reasons to stop using non-human primates for scientific research. However, this position should be reviewed frequently as new techniques are constantly being developed.

The SCHER supports the "three Rs" principle, which aims at reducing the number of animals being tested, refining the methodology used, and replacing the animals by alternative methods.

The SCHER made the following recommendations:

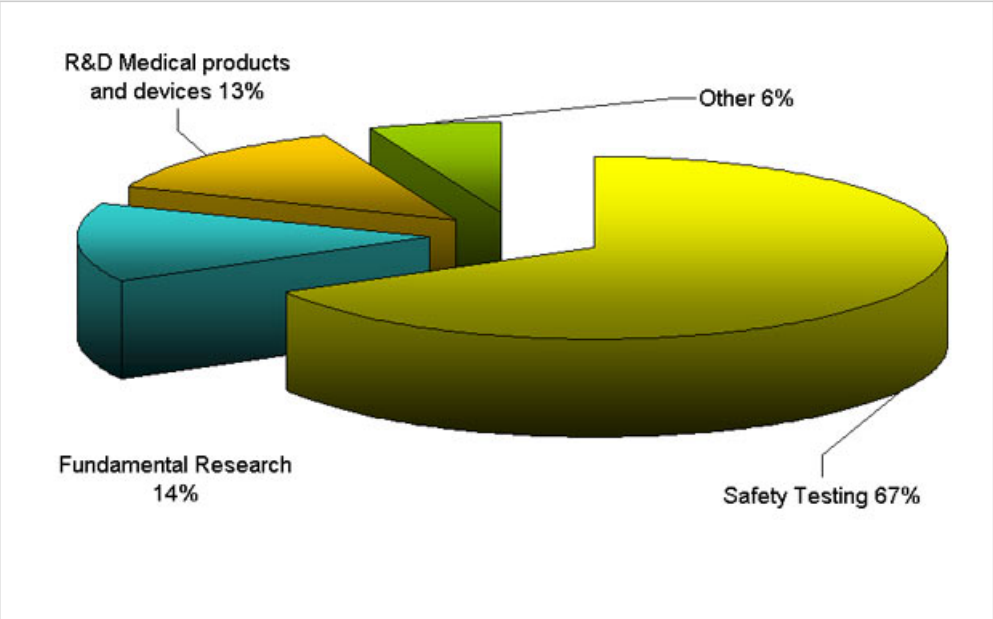
1. Non-human primates should be used only when it is scientifically justified. Justifications should be closely monitored and evaluated.
2. Improved techniques such as non-invasive methods, in vitro tests and computer models should be encouraged.
3. The potential benefits of using primates should frequently be assessed against possible alternatives so that those alternatives are adopted as soon as they are ready for use.
4. Collaboration and data sharing should be promoted in order to make further progress towards the "three Rs".
5. A network should be created between the facilities that are breeding and maintaining the primates for research purposes in order to improve knowledge and competence regarding the welfare of the animals.
6. Procedures on animals should not be too severe, and any work that would cause severe pain should be justified and approved.
7. The replacement of primates by other animal species such as genetically-modified rodents and minipigs should be further investigated and supported.
8. The use of wild-caught primates should be reduced as much as possible, for both scientific and animal welfare reasons.
9. Evaluations of the use of primates bred for research purposes should take place on a regular basis. The aspects to be assessed are impacts on animal welfare as well as scientific and economical impacts of such a use.
10. Work done outside of the EU with European support should meet European standards.
11. Global networks should be set up to exchange information on the "three Rs" among those who use primates.
12. Negotiations with countries outside the EU should be carried out to harmonize the requirements for safety testing of drugs.

Research into areas that lead to improvements in the replacement, reduction and refinement of the use of primates should be promoted. More specifically, research should focus on:

- The use of genetically modified animals to test vaccines and pharmaceuticals, while also considering the ethical aspects of this;
- Developing methods of testing the safety of drugs using laboratory grown cells;
- Understanding the similarities and differences between the immune systems of humans, non-human primates and other non-rodents;
- Understanding the social needs and housing requirements of primates that would improve their physical and mental health;
- Recognition of suffering in primates, and its classification, its avoidance, and its alleviation;
- Developing new and refined experimental techniques on primates such as non-invasive methods (e.g. new MRI-based techniques);
- The use of stem cells to avoid using primates in organ transplantation research;
- A better understanding of how the brain works;
- New methods of doing non-invasive, safe brain research in humans that could reduce and, in specific instances, replace experiments on primates.

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]