

Frequently Asked Questions (FAQs) on Animal Research

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Purpose of and Rules for Animal Research

1. What is Roche's position as a healthcare company on animal research from an ethical perspective?

The use of animals in pharmaceutical research is a complex issue with no easy answer.

It is a fact that animal research saves human and animal lives. While we are committed to avoid unnecessary suffering of all living beings, research shows that for the majority of people, human health and well-being comes first. As a consequence, we have to accept that it is impossible to create new or more effective and safe medicines without using animals during the research phase, at least for the foreseeable future. However, it is also essential that we use as few animals as possible and avoid all unnecessary pain and distress.

2. Is animal research really necessary?

Many serious diseases (such as Alzheimer's disease, Parkinson's disease, hepatitis, cancer, cardiovascular diseases, and diabetes) are still not entirely understood and sufficiently treated. Therefore, new and more effective therapies and diagnostic tests are needed to improve the quality of patients' lives, not only those of humans, but also the quality of animal health. Many veterinary medicines that are used to treat animals are the same, or very similar to those used for human patients, and therefore rely as much on animal research as human medicines.

Before human clinical trials for new medications can be conducted, regulatory bodies worldwide require efficacy and safety data based on animal experimentation. This safety testing in a living organism prior to approval for studies with human beings helps to minimise the risks for patients in clinical trials and beyond. Pre-clinical testing is aimed at closely mimicking the functioning of a human body in a whole organism, so that clinical trials in humans may be conducted with maximum safety and efficacy.

The rationale for the use of animals as a surrogate model for humans is based on years of basic scientific research that has identified (sometimes even near identical) genetic, cellular, and physiological similarities in drug targets and physiological responses to medicines between animals and humans. Approximately 70% of severe adverse effects that would occur in humans are identified during the animal testing stage. The results of animal research enable researchers to help determine which experimental compounds in advanced development are unsuitable for use in humans (~30-40%) – either because the risk of potential toxicity is too great, or because they don't show the desired pharmacokinetic profile, thus likely rendering them ineffective.

Therefore, animal research is extremely beneficial in minimising the risks to humans in clinical trials. It should be noted that alternatives are used whenever possible (see 3Rs section below).

3. How can results from animals be applied to humans?

Humans are biologically very similar to other mammals. All mammals, including humans, have many of the same organs (such as the heart, lungs, kidneys, and liver), and these same organs perform the same functions and are controlled by the same mechanisms, e.g., the blood stream and nervous system. However, there are also some differences, which, from a scientific perspective, can actually be helpful sometimes. For instance, the revelation of why certain animals do not suffer from a human disease could lead to a new idea for a treatment.

4. What is the contribution of animal research to advances in medical science?

Animal research has played a vital role in virtually every major medical advance of the last century for human and animal health. Be it antibiotics or blood transfusions, dialysis or organ-transplantation, vaccinations or chemotherapy, bypass surgery or joint replacement - practically every present-day procedure for the prevention, treatment, cure and control of disease, pain and suffering is based on knowledge obtained through research with animals.

Ample proof of the success of animal research can be found in the range of Nobel Prize winners, 75 out of the 98 awarded discoveries for Physiology or Medicine were directly dependant on research from animals.¹ The use of animals was crucial in many discoveries made in drug development and biomedical research: monoclonal antibodies, antibiotics, anaesthesia, analgesia, and vaccines.

5. Are there concrete examples of Roche pharmaceuticals where very important results were based on animal research?

Animal research has enabled Roche to discover and develop new anticancer medications which are both far more effective as well as better tolerated than conventional chemotherapy. For example, animal research showed that a medicine used to treat disfiguring skin diseases is highly likely to cause birth defects. As a result, doctors are aware of the dangers in prescribing the drug to a pregnant woman.

Without animal research, Roche could not have developed modern, highly effective treatments, such as HIV/AIDS medications, with an acceptable safety profile that enhance

¹ Overview of Nobel Prizes awarded for Physiology or Medicine since 1901, available at <http://www.animalresearch.info/en/medical/nobelprize>

the quality of life of many patients. The same applies to a medication for preventing rejection reactions in patients who received organ transplants and many oncology products that have been brought on the market in recent years.

6. Which legal requirements & guidelines does Roche fulfil in animal research?

Roche is committed to act ethically and to apply high standards of care and use related to animals. A number of existing international, regional as well as national laws and regulations for animal research are, together with applicable industry standards, applied in the various countries where Roche operates, e.g.:

- All national laws, e.g., the Swiss Animal Protection Act.
- The EU Directive on the Protection of Animals used for Scientific Purposes (2010/63/EU).
- The European Convention for the protection of vertebrate animals used for experimental and other scientific purposes (ETS 123) by the Council of Europe.
- The Animal Welfare Act and Animal Welfare Regulations of the US Department of Agriculture.
- The Guidelines of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH Guidelines).
- The Institute for Laboratory Animal Research (ILAR) Guide for the Care and Use of Laboratory Animals.

7. Does Roche apply other standards in addition to the above mentioned requirements?

Industry standards also govern the use of animals in laboratory research and testing. For example, the Association for the Assessment and Accreditation of Laboratory Animal Care, International (AAALAC) accredits research animal care and use programs.

All major Roche Pharma research centers as well as Genentech and Chugai have received accreditation from AAALAC, and the goal is to have them maintain accreditation in the future. AAALAC enhances life sciences by promoting the responsible treatment of animals used in research, teaching and testing through voluntary accreditation and assessment programs.

In addition, Roche has developed a guidance document, "[Animal Research - Principles of Care and Use](#)", in order to ensure that every Roche employee working with animals acts ethically and with respect for the animals in their care. These standards require compliance with the existing laws, regulations, and guidelines, going the extra step to achieve excellence in animal care and use, as well as the implementation of alternative methods to animal research (the so-called 3Rs, see questions 25-32). These standards apply to the use of animals during experimentation, to their housing and care, to the training and education of the personnel involved in their care and use, and to the conduct of the investigative staff.

8. What external control mechanisms are in place to ensure that Roche complies with applicable laws and standards?

Roche's animal care and use programs are regularly evaluated by external bodies as follows:

- Unannounced inspections of our animal facilities by regulatory authorities, for example the US Department of Agriculture (USDA)² which issues sanctions if rules are breached. Roche fully supports and complies with these inspections.
- All animal research studies at Roche's European research sites must be approved by the authorities (Switzerland, Germany). This process includes an external ethical review.
- All animal research studies at Roche's North American research sites must be approved by an internal Animal Care and Use Committee.
- The Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) is a nonprofit organisation that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs. In order to maintain the accreditation, Roche has to deliver annual reports. In addition, AAALAC's evaluation teams visit the research sites every three years and review their procedures, including animal care and use policies and responsibilities, the environment and enrichment the animals receive, housing and management, as well as veterinary medical care.

9. What internal control mechanisms does Roche have in place to ensure the correct application of laws and standards?

In order to ensure that animal research conducted by Roche and its contractors comply with laws and standards, Roche has the following processes and functions in place:

- Roche's Ethics Committee on Animal Welfare for its research sites (Basel, Penzberg, Nutley, Shanghai and Chugai), which:
 - Provides support and ethical advice to Roche staff dealing with animals, in particular to researchers, animal welfare officers and laboratory animal personnel.
 - Provides guidance on the application of the 3Rs (Reduce, Refine, Replace; see question 25).
 - Develops recommendations for instance on the use of contractors for animal research.
 - Oversees that studies involving non-human primates are ethically justified and that potential alternatives have been considered.

² The agency within USDA dealing with the protection of animals is the Animal and Plant Health Inspection Service (APHIS).

- Receives and addresses concerns and questions related to ethical issues addressed by Roche employees or any external person.³
 - Offers the “3Rs Award” and evaluates the employees’ applications to the 3Rs Award program and the achievements in the area of new methods to reduce the number of animals used, to refine testing and to increase animal wellbeing (see question 29).
 - Furthermore, the Committee aims to develop prospective strategies for improvements in animal welfare going beyond local legislation.
- Institutional Animal Care and Use Committees (IACUCs). Each US research site has an IACUC, responsible for ensuring compliance with animal welfare laws, policies and internal guidelines. The federally mandated IACUC functions include:
 - Reviewing, at least once every 6 months, the institution's program for humane care and use of animals, using USDA Regulations and the Guide as a basis for evaluation.
 - Inspecting, at least once every 6 months, all of the animal facilities, including animal study areas/satellite facilities, using USDA Regulations/Guide, as basis.
 - Preparing reports of IACUC evaluations and submitting the reports to the Institutional Official.
 - Reviewing specific concerns or complaints about animal care or use.
 - Making recommendations to the Institutional Official regarding any aspect of the research facility's animal program, facilities or personnel training.
 - Reviewing and approving, requesting modifications (to secure approval), or withholding approval of those components of proposed activities related to the care and use of animals.
 - Suspending an activity involving animals when necessary; taking corrective action and reporting to the funding agency and USDA, when appropriate.
 - Animal Welfare Officers at Roche’s research sites in Switzerland and Germany cooperate closely with approval authorities and external ethics committees.
 - Internal procedures allow staff members to raise ethical concerns related to animal welfare. These concerns may be raised anonymously.

10. What is Roche’s relationship with contractors and how do you know that animal research conducted at the contract laboratories you use is being conducted humanely and in compliance with the law?

Roche works closely with various external contractors in the field of animal research. Contractor site-visit audits are performed on a routine basis by Roche staff.

Since the proper care and use of laboratory animals is of fundamental importance for Roche, contract laboratories are typically pre-qualified prior to starting a collaboration. For

³ This statement applies to the Roche European sites only as Nutley follows a similar policy, approved by IACUC.

example, in the United States, one of several requirements is that the contract laboratory has an attending veterinarian, as well as their own institutional animal care and use committee that reviews all research proposals in compliance with all applicable laws and regulations. For non-clinical safety studies, Roche has internal teams with the specific obligation to monitor contract laboratories during the conduct of animal studies. These teams include trained personnel from the non-clinical safety department and the research quality assurance group. In addition, members of the Comparative Medicine department inspect the animal facilities of contract laboratories. Roche has developed a global audit checklist that the Roche Comparative Medicine personnel use for evaluating the contractors and animal vendors. This checklist allows us to standardise assessment criteria and determine if they are in compliance with the relevant animal welfare regulations.

Use & Care of Animals

11. What types of medicinal research use animals?

- **Basic research** helps advance our scientific knowledge about how animals and humans behave, develop and function biologically. Basic research tends to be publicly funded with some private funding from industry and medical research charities. In the EU, for instance, basic research accounts for approximately 38%⁴ of all animals used for research purposes.
- **Translational research** furthers our scientific understanding of diseases and facilitates the transition of research findings from “bench to bedside.” This type of research is both publicly and privately funded and translates, or puts into use, the discoveries obtained from basic research. Translational research is the second largest area where animals are used. In the EU this accounts for approximately 23%⁴ of animals used for research purposes.
- **Production and quality control** tests pharmaceutical compounds and medical devices for adverse reactions in animals, prior to testing in humans. This research is required by North American and European legislation and international guidelines. In the EU, 15%⁴ of all animals used are production and quality testing of human and veterinary medicines.
- A further 9%⁴ of animals are used in **toxicological or other product safety evaluations**. Of these, about half of the animals are used for medicinal testing, with the remainder used to obtain quality and safety data from household and industrial chemicals, herbicides, fertilisers, and food additives. Quality and safety tests are usually funded by private organisations.

⁴ Sixth Report from the Commission to the Council and the European Parliament on the Statistics on the number of animals used for experimental and other scientific purposes in the member states of the European Union [COM(2010) 511 final/2] available at <http://eurlex.europa.eu/Notice.do?val=545453:cs&lang=en&list=545453:cs.&pos=1&page=1&nbl=1&pgs=10&hwords=>

- The remaining 15%⁴ of animals are used for the purposes of diagnosis of diseases (1.6 %), education, training (1.7%) or other purposes (12.2%).

12. What kinds of animals does Roche use and how many?

In 2010, Roche used a total of 502,105 animals in its own research (additionally, 55,913 animals were used by contractors carrying out research on Roche's behalf). Mice and rats comprise 97% of all laboratory animals used globally. The remaining 3% include other rodents and rabbits (1.1%), dogs (0.3%), non-human primates (0.5%) and other species (fish, minipigs, frogs: 1.0%).

13. Does Roche use pound or shelter animals?

No, Roche does not use pound or shelter animals. Roche purchases all animals from selected vendors who breed them specifically for research purposes.

14. Does Roche breed animals for research?

Roche purchases all animals from professional breeders, the only exception being specific animal strains that aren't commercially available (e.g., transgenic mouse, rabbit and rat strains).

15. Why must non-human primates be used in biomedical research?

As independent reviews confirm, there is a moral and scientific case for the carefully justified use of non-human primates in research.⁵

The areas of biomedical research where usage of primates cannot be completely replaced include several vital research programs on infectious diseases (such as Malaria, Tuberculosis, Hepatitis, Influenza), neuro-degenerative disorders (Parkinson, Alzheimer, etc), mental disorders (schizophrenia, depression, etc.), immune based diseases (diabetes, multiple sclerosis, immunotoxicity, allergy) and on oncology (monoclonal antibodies), which is of particular importance for Roche.

Whenever non-human primates are used, the purpose, in over 90% of the cases, is to evaluate the efficacy and safety of certain drugs and vaccines, prior to the testing in humans. Such studies are required by regulatory authorities worldwide (for example the European Medicines Agency and the U.S. Food and Drug Administration). The Roche Group has been developing treatments specifically designed to mark particular molecules

⁵ Report "The need for non-human primates in biomedical research, production and testing of products and devices" by the Scientific Committee on Health and Environmental Risks (an advisory committee to the European Commission) available at http://ec.europa.eu/environment/chemicals/lab_animals/pdf/scher_o_110.pdf

in the human body and thus block their disease-causing effects for years. Such therapies are called monoclonal antibodies (MAbs). As those MAbs are very species-specific, negative and/or positive effects must be shown by testing the substances in organisms which are as close as possible to the human body, i.e. often in non-human primates. In addition, before entering into studies with non-human primates it has to be proven that other animal species can not be used to reach the study's goal.

The remaining 10% of the non-human primates used involve basic research to advance human knowledge, such as the study of the nervous system, including the brain, and inflammatory diseases, including asthma and other respiratory diseases.

16. What would happen if non-human primate use was banned in parts of the world?

Banning the use of non-human primates (in Europe, for example) will not stop this type of research. It simply means that the research will be conducted outside of Europe. While global companies can influence the standards of their research sites in those countries, they can't necessarily influence the regulations themselves.

If (non-human) primate research was banned globally, there would be areas of greater medical need that could not be met. The reputational, regulatory, logistic, and cost barriers to using non-human primates in research are high; nevertheless, regulatory requirements and overwhelming scientific need mean that their use remains essential. Therefore, until alternatives to using non-human primates are found, they will remain a vital part of the discovery and development of new medicines.

17. How do you know that animals are not experiencing pain and distress?

Most research involves only slight or momentary pain such as taking blood samples, giving a single injection, or having a change of diet.

However, just as humans might experience pain and distress caused by a disease, a research animal serving as a model for a disease might experience the same. If more invasive procedures are necessary, anesthetics and/or pain relieving drug are given in nearly all cases – unless their application would endanger the scientific validity of the experiment.

Animal welfare is of vital importance and trained animal technicians look after the animals under the supervision of veterinarians. All research activities, including measures to minimize pain and distress, are closely scrutinised before approval is given to carry out a study. They are monitored by internal and external bodies (see questions 8 and 9). Each project submitted for approval includes a detailed explanation of the animal research purpose, the likely effects on the animals, and why the research cannot be done using other methods.

It is key to ensure that pain and distress is minimised - for ethical reasons but also because it could compromise the reliability and reproducibility of research results. The prevention of undue suffering is the main task for animal welfare officers as well as animal care and use committees.

18. What does Roche do to reduce the pain and distress of animals?

Pain and distress management is addressed in every animal research proposal before the research is approved either by the Roche Institutional Animal Care and Use Committee (IACUC) or the approving state authority (Switzerland, Germany). Any animal research proposal that may potentially cause pain or distress in animals must be scientifically justified, including an assurance that alternative methods are not available. Similarly, every animal research proposal must have an assurance that the proposal does not unnecessarily duplicate other animal research.

19. Does Roche administer anesthesia, analgesics and/or tranquilisers to animals?

Anesthesia, analgesics (i.e. pain killers) and/or tranquilisers are utilised whenever possible, except in specific circumstances when this would interfere with research results. For surgical procedures, anesthesia and painkillers are always administered.

20. Why might a few procedures be carried out without anesthetics, or analgesics?

Most procedures cause no pain (or only slight and momentary one), meaning that they wouldn't require the administration of a general anesthetic or analgesic. For example, an injection, the oral administration of a medicine or the taking of blood from veins would not warrant the use of anesthetics or analgesics in animals any more than it would in people.

The regulations require that any pain or distress have to be prevented or reduced to the minimum amount possible given the nature of the research. This is realised, for instance, by using painkillers, as well as by ensuring that those doing the research have all the necessary skills to perform procedures in a way that causes as little distress as possible and, in the case of surgery, results in a favourable outcome.

21. What happens to an animal at the end of an experiment?

At the end of a study, most animals are euthanised. This allows for a full examination of their tissues, which is necessary to see details of the effect of the compound being tested. Many of the non-rodent species that are used for drug metabolism or behavioral studies are re-used following a "washout period", once the compound they received has been fully metabolised and excreted. These types of studies involve the administration of compounds at dosages that are unlikely to cause adverse effects while still providing useful information regarding pharmacokinetic and/or behavioral effects, with all

procedures that are performed (i.e., injections, blood collection, etc.) judged as non-painful.

22. If scientists behave within strict guidelines, why do animal rights groups have pictures and videos of alleged misconduct and animal suffering?

Many pictures displayed by animal rights groups aren't examples of current practices; instead, they represent examples of outdated methods that are no longer considered acceptable by the scientific community. Furthermore, many are taken out of context, and are edited to elicit a negative public response about animal research. Such practices are unacceptable and undermine any trust between researchers and animal rights groups because they obstruct the pursuit of an open and factual discussion about animal research.

Researchers are concerned about the welfare of all animals they use, and their concern is both humane and scientific. They have no excuse to mistreat research animals, and many reasons for treating them well because the use of unhealthy, stressed or frightened animals reduces the reliability of experimental results. The veterinary staff is responsible for ensuring that research animals are well fed, free of infections and other illnesses and kept in an appropriate environment.

23. Is Roche willing to have a dialogue with animal welfare organizations?

Yes. Roche welcomes constructive dialogue on this complex issue and has regular contacts with animal welfare organisations. We take public concerns about using animals in scientific procedures very seriously.

Animal Welfare & Alternative Methods

24. What is Roche doing to actively promote and contribute to animal welfare?

Roche has established mechanisms to ensure high standards of animal care and is committed to using animals appropriately and responsibly. We comply with international, regional and national laws and regulations, as well as meeting or exceeding industry standards. All employees within Roche, and all external contractors who perform animal research for Roche, are required to obey these laws and standards at all times and to conduct their research by acting with respect for the animals. Moreover, all Roche employees involved in animal research continuously receive training in standards of care and ethics on the use of animals in research.

Roche is committed to the 3Rs principles (alternative methods to animal research, i.e. Reduce, Refine, Replace; see questions 25-32) and actively promotes such methods.

One example of Roche's efforts for animal welfare is Roche's Ethics Committee on Animal Welfare, which provides support and guidance on ethical issues raised by Roche employees or external persons, as well as on the application and promotion of the 3Rs within the Roche Group. The Committee develops recommendations and oversees in particular that studies involving non-human primates are ethically justified and that potential alternatives have been considered. In addition, the Committee aims to develop prospective strategies for improvements in animal welfare going beyond local legislation.

Roche was one of the founders of the new Swiss Charter on Animal Welfare, adopted in 2010 by Interpharma, the association of research-based pharmaceutical companies in Switzerland. The Charter commits Interpharma's members to join efforts for consistently applying high standards of animal welfare, for discussing and working on internal and external auditing processes, for further fostering employee training, stakeholder dialogue and promotion of the 3Rs. We will report annual progress in implementing the Charter. So far, a working group on auditing has been initiated to exchange best practices and join forces in external auditing efforts. Further, various workshops are organised to promote the education and training of employees who work with animals, e.g., the "Primate Day", with the goal to exchange new findings about training, handling, or stress reduction in lab animals. An interactive tri-lingual E-learning tool about the 3Rs in collaboration with the University of Marburg is currently under development.

25. What are the alternatives to using animals?

There are three main alternative methods which are known as the "3Rs"⁶:

- Reduction
- Refinement
- Replacement

Reduction means ensuring the fewest possible number of animals used in a given study. With careful experimental design, sophisticated statistical techniques and modern imaging techniques, it is often possible to significantly reduce the number of animals needed for a study while still getting valid results.

If Reduction is not possible, there is the option to Refine existing testing procedures by decreasing any potential for suffering and continuously looking for advancements in husbandry, animal care practices and environmental enrichment .

Replacement is how most people interpret the term "alternatives to animal testing": research animals are replaced by using either methods that don't involve animals at all (absolute replacement) or by methods that use only the cells or tissues of animals (relative

⁶ Russell, W.M.S. and Burch, R.L., "The Principles of Humane Experimental Technique", London, 1959.

replacement). Such Replacement alternatives include cell and bacterial cultures, computer simulations, mathematical modeling and the use of isolated animal organs. Irrespective of their level of sophistication, these methods are not able to simulate the complexity and level of coordination and integration of an entire organism with all its cells, tissues and systems working together and are therefore not always a realistic option. For the foreseeable future, any research that has reached a certain stage will require studies of the whole living organism in order to acquire as much information as possible about a potential new medicine before taking it into human clinical trials. Therefore, while focusing on replacement as an overall goal, it is equally important to promote validating ways of reducing the number of animals used and refining testing procedures.

26. Have alternative methods lead to a significant change in the number of animals used for research?

Yes. As the following examples show, the number of experimental animals required for research has already been significantly reduced:

- The statistical data in Switzerland (industry and academia) show that the number of research animals has been reduced by over 70% since 1980.⁷ This includes figures from Roche where we can see a similar evolution.
- In the US, for species covered by the Animal Welfare Act⁸, the total number of animals used by research in FY (Fiscal Year) 1973, versus research animals used in FY 2007, has decreased by 38%.⁹

27. Which alternative methods are implemented at Roche?

Roche is dedicated to implementing the 3Rs - Reduction, Refinement, and Replacement. Where regulations allow, and where it is scientifically possible and ethical, Roche employs medical testing procedures that do not require animals.

Alternative techniques are incorporated wherever possible, and we continue working on projects designed to identify compounds with specific therapeutic action. We also discontinued the screening of large numbers of compounds on various species of animals, a technique that was much more prevalent in the past. Roche continues to improve upon and uses automated *in vitro* (“*in a test tube or artificial environment*”) screening methods to identify promising compounds before they are tested in animals. These screening methods help ensure that the compounds that end up being tested in animals are much more likely of being made into useful new pharmaceutical products. *In vitro* screening, as well as other alternative methods, help minimise the number of animals being used to test compounds in the early phases of development.

⁷ Statistics published by the Swiss veterinary authorities available at <http://www.tv-statistik.bvet.admin.ch/BasicStatistics.php>

⁸ Mice and rats are not included in the USDA covered species

⁹ Animal Care Annual Report of Activities (Fiscal Year 2007), Appendix 5 available at http://www.aphis.usda.gov/publications/animal_welfare/content/printable_version/2007_AC_Report.pdf

In addition, all Roche research sites have implemented a computer program that predicts the absorption of active substances in humans without animal tests. The program utilises data on solubility and cell permeability.

Determining whether a drug is safe without the aid of animal tests is a major scientific challenge due to the complexity of the processes involved. Roche is a worldwide promoter of computerised techniques for determining pharmacokinetics and tolerability using data from cell tests and clinical studies in humans.

28. Does Roche actively support the development of new alternative methods?

Yes. Around the world, Roche is supporting the development of experimental models that will help replace animal tests both during and after the initial screening phase. One of the objectives of Roche's global Multidimensional Medicines Optimisation program is to develop new cell-based tests producing results that can be reliably applied to humans.

Roche is also at the forefront of research in toxicogenomics, a technology that will enable us to use information on genetic predispositions to determine drug tolerability — with the promise of reducing the need for some animal toxicology testing in the future.

Recently, Roche began to work on a 3Rs database for sharing good practices throughout the Roche Group. It will start in 2011 to empower Roche colleagues to share and communicate the techniques or procedures that address the 3Rs methods. The ultimate goal is to help researchers to avoid or reduce further animal testing or to apply better methods or techniques.

29. What is Roche doing to educate and motivate its employees on alternative methods?

Roche is committed to advance alternative methods (see questions 25-32). All Roche employees involved in animal research follow the guiding principles of the "3Rs" and receive training in standards of care and ethics on the use of animals in research.

Another approach of Roche to advance alternative methods is the internal global "Roche 3Rs Award", which was launched in March 2008 and includes a financial incentive for the applicants. The aim is to increase awareness among employees and scientists about the 3Rs, to encourage the discovery of alternative methods, and to make Roche a more innovative and productive company. The "Roche 3Rs Award" is offered every second year to all Roche sites; so far, 39 entries were submitted over the first 2 rounds from all Roche Pharma research sites, including Chugai. This high global participation demonstrates Roche's steadfast commitment to work on the 3Rs.

The Award is given in 2 categories and will be offered again in 2011. The 2009 winners are as follows:

- Category “Scientific Progress Fostering the 3Rs Idea”
 - Winner 2009: A new in-vitro test for detecting toxic compounds before testing new drugs on animals. Roche’s Diagnostics business developed the test, which is now available for pharmaceutical preclinical research.
- Category “Laboratory Animal Care and Management”
 - Winner 2009: A method to gradually rehabilitate monkeys that had been housed individually back into larger groups, increasing their social interaction and improving their wellbeing.

In line with the commitment and responsibility to animal welfare, Roche Basel hosted in 2010 the “3Rs Day” for the first time, a full training day inviting employees to look at the 3Rs concept in detail. Internal as well as external speakers presented various angles of the topic. Break-out sessions provided an opportunity to discuss various aspects of the 3Rs in depth. Employees from the Penzberg site were also invited to attend. It is planned to extend the scope of the 3Rs-Day and will be hosted also at other Roche Pharma research sites in 2011.

30. What organisations does Roche interact with to further promote animal welfare as well as the 3Rs?

We work with a number of external organisations, e.g.:

- Roche was a founding member of the Swiss 3Rs Research Foundation, which was set up more than 20 years ago and we continue to support. The objective of the foundation is to promote research into alternatives and improvements to animal studies by funding research projects for new methods in line with the 3Rs principles of reduction, refinement and replacement.
- Roche is a partner of the European partnership for Alternative Approaches to Animal Testing (EPAA), aimed at promoting the development of new 3Rs-based methodologies and modern alternative approaches to the use of animals in safety assessment in Europe.
- Roche was one of the founders of the new Swiss Charter on Animal Welfare, adopted in 2010 by Interpharma, the association of research-based pharmaceutical companies in Switzerland. The Charter commits Interpharma’s members to join efforts for consistently applying high standards of animal welfare, for discussing and working on internal and external auditing processes, for further fostering employee training, stakeholder dialogue and promotion of the 3Rs. We will report annual progress in implementing the Charter.

31. How long will it take to develop and validate alternatives?

Nowadays, researchers are continuously striving to improve the alternative techniques and processes in use. The overwhelming majority of R&D (Research & Development)

expenditure by the pharmaceutical industry goes towards non-animal methods. Many alternative methods employed in non-regulatory areas are used in the R&D process as soon as they are developed.

Different criteria apply to the field of regulatory testing. Here, testing methods are used for getting the market authorisation of a product. In order to be accepted by regulators, the development of a method has to be followed by a scientific validation process. Altogether, a process like this can take more than 10 years.

32. Should there be more data sharing to minimise duplication of animal experiments?

The pharmaceutical industry is involved in applied research (toxicology and safety evaluations, research & development, production and control of human and veterinary drugs and vaccines), usually performed on novel patented compounds. Therefore, the likelihood of duplicated experiments is fairly small.

Consequently, full open disclosure prior to publication won't have much of an effect on the number of research animals, yet it would endanger the competitive base of companies and academia. This being said, the industry supports pre-competitive data sharing. It has been realised for large projects such as the Innovative Medicines Initiative, and it is also implemented in cases such as the sharing of information on non-active substances.

There are also other mechanisms established to avoid the duplication of animal tests, such as the publication of peer-reviewed research in scientific journals and presentations at conferences.

Useful Links

Related Roche documents

Roche Position on Animal Research

http://www.roche.com/ar_pos.pdf

Animal Research – Principles of Care and Use

http://www.roche.com/ar_principles.pdf

EU

Statistics on Animal Research in the EU

http://ec.europa.eu/environment/chemicals/lab_animals/reports_en.htm

EU Directive on the Protection of Animals used for Scientific Purposes (2010/63/EU)

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:276:0033:0079:EN:PDF>

Organisations

About animals in biomedical research and development of alternatives

www.animalresearchforlife.eu

Association for the Assessment and Accreditation of Laboratory Animal Care, International (AAALAC)

<http://www.aaalac.org/>

Biotechnology Industry Association

<http://www.bio.org/>

European Federation of Pharmaceutical Manufacturers and Associations (EFPIA)

www.efpia.org

European Partnership for Alternative Approaches to Animal Testing (EPAA)

http://ec.europa.eu/enterprise/epaa/index_en.htm

3Rs Research Foundation Switzerland

<http://www.forschung3r.ch/>

Swiss Charter on Animal Welfare

<http://www.interpharma.ch/de/pdf/Charter-animalwelfare-E.pdf>