

## **Animal Research at Roche**

### **Roche's Position**

Before any medicine can be brought to market, clinical trials must be conducted to establish that the medicine is both efficacious and well tolerated. Before human clinical trials for new medications can proceed, regulatory bodies worldwide require efficacy and safety data from preclinical studies which are conducted on animals whenever scientifically justified. As research seeks new treatment solutions to complex diseases like, for example, cancer, autoimmune and neurodegenerative disorders, animal testing remains necessary in order to facilitate these developments.

Roche recognises that the use of animals in biomedical research is a sensitive issue. We strive to use animals only where absolutely necessary, for example where no scientifically accepted alternatives exist or where the required information cannot be generated by other methods. When the use of animals is the only option available for necessary investigations to advance biomedical research, we conduct experiments in compliance with the highest international standards for animal welfare. This also includes rigorous reviews of planned studies that include animals, as it is essential that we minimise animal use but also optimise the data collected if animal use is required.

We are also actively exploring and evaluating alternatives to the use of animals based on in silico technologies such as computational modelling and simulation models and in vitro techniques (in a test tube or artificial environment; for example, a cell culture or innovative microphysiological organ-on-a-chip systems).

Our global governance body for animal research is called Ethical Committee of Animal Welfare. It advises on strategic matters related to animal welfare practice and policy, reviews and, where necessary, proposes changes and actions related to animal testing. It advances the 3Rs (Reduce, Refine, Replace) within Roche and also assists in communications with external governance and regulatory bodies.

Furthermore, Roche adheres to a number of industry standards governing the use of animals in laboratory research and testing. For example, all Roche Pharma research centres, as well as Genentech and Chugai, maintain full accreditation status by AAALACi. This non-profit organisation enhances life sciences by promoting the responsible treatment of animals used in research, teaching and testing through voluntary accreditation and assessment programmes.

All accredited Roche sites are obliged to prepare an annual report for AAALACi in order to maintain accreditation. In addition, AAALACi evaluation teams visit Roche research sites every three years and conduct a comprehensive review of our animal care and use programmes.

## Roche's Principles for Care and Use

The following principles have been developed to outline the measures in place for the care and use of all animals for which Roche is responsible:

### **Compliance with laws, regulations, scientific and ethical standards**

- Roche is in compliance with existing international (e.g. the ICH Guidelines), regional (e.g. the EU Directive on the Protection of Animals used for Scientific Purposes) and national laws (e.g. U.S. Animal Welfare Act) and regulations, as well as with applicable industry standards, for animal research. In addition to the applicable local laws and regulations, every Roche research site conforms to or exceeds the standards established by the International Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALACi).
- Procedures involving animals are designed and performed with respect to their relevance to human or animal health, advancement of knowledge, state of the art methodology and techniques and the benefit to society.

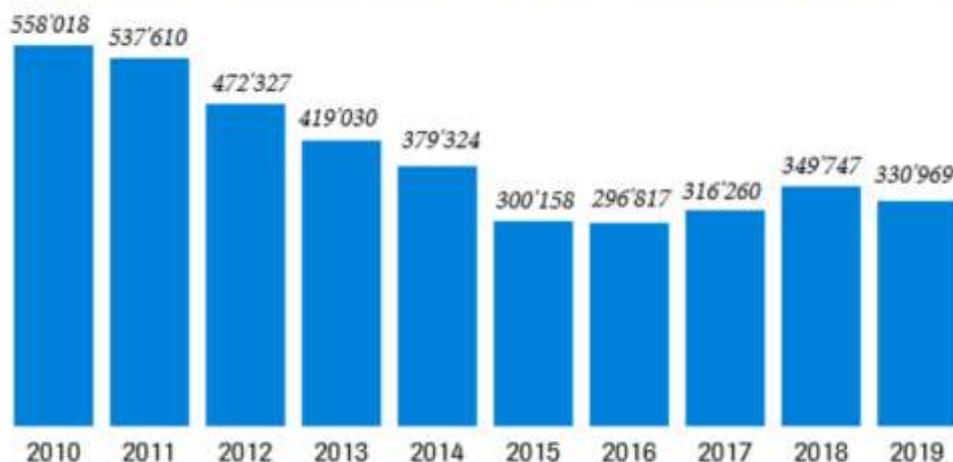
### **Reduce, Refine and Replace - the 3Rs**

Roche is dedicated to following the guiding principles of the 3Rs for animal research, and encourages the development of alternatives to the use of animals in research:

- Reduce  
With careful design, sophisticated statistical techniques and modern imaging, it is often possible to significantly reduce the number of animals used in research while still generating valid results, truly adding to the knowledge base.
- Refine  
This refers to decreasing the potential for distress of animals and continuously seeking advancements in animal husbandry, care practices and environmental enrichment to provide the best possible conditions for animals.
- Replace  
Research animals are either replaced by methods not involving animals (absolute replacement) or by methods using only the cells or tissues of animals (relative replacement). Such alternative methods include cell and bacterial cultures (2D, 3D and stem cell systems), computer simulations, mathematical modelling and the use of microphysiological human or animal systems (i.e. organ-on-a-chip approaches).

The number of experimental animals required for research has fallen significantly. Since 2010, Roche has reduced the number of animals worldwide by roughly 40%. This is primarily due to the fact that we are working on modern replacement and supplementary methods and, where possible, apply these to our drug development programs.

**Fig. 1: Number of animals used in research worldwide (Roche and CROs)**



The increase in 2017 and 2018 reflects an increase in the number of projects in cancer immunotherapy and neurosciences. Advances in research in such complex areas currently still heavily depend on the use of animal models that help researchers understand disease pathology.

Percentage of species used in research (Roche and CROs) in 2019:

- 97 % Mice/rats
- 3 % Other species (e.g. Zebrafish, rabbits and large animals)

### **Principles related to the use of animals (during research)**

- Planned animal studies undergo rigorous internal and external reviews to assure that:
  - they are scientifically and ethically justified,
  - correct species are selected,
  - appropriate numbers of animals will be used
  - applied methods and techniques reflect the current state of the art in biomedical research
  - pain and distress among research animals will be alleviated or minimized.
- Research personnel (e.g. scientists, lab technicians, animal caretakers, veterinarians and animal welfare officers) place a high priority on the comfort and well-being of laboratory animals throughout the research process. Mistreatment of animals is never tolerated. Violations result in most severe disciplinary actions.
- The ethical and scientifically sound use of animals is imperative. Procedures that may cause more than momentary or minor pain or distress are performed with appropriate sedation, anaesthesia, and/or analgesia. Exceptions are rare and must be clearly defined, justified, and approved by appropriate regulatory bodies.
- Euthanasia of research animals is conducted with minimum infliction of pain and distress, using an approved method appropriate for the species and according to the current state of the art (e.g. to the American Veterinary Medical Associations (AVMA) Guidelines for the Euthanasia of Animals) .

### **Principles related to the care of animals (animal husbandry)**

- Animals for research purposes are purpose-bred and procured from reputable, approved vendors and research facilities.
- Modern, fully-equipped animal facilities and species-appropriate husbandry practices contribute to the animals' overall health and well-being.
- High priority in all Roche group animal facilities, including peer-reviewed veterinary care programmes and optimal hygienic control of housing.

### **Personnel education and training**

All research personnel (e.g scientists, lab technicians, animal caretakers, veterinarians and animal welfare officers) are appropriately educated and trained in the care and use of laboratory animals. In-service and/or external training is provided as a means for continuous improvement and according to local requirements.

### **Supervision**

- All experimentation on research animals is conducted under close supervision of qualified and experienced personnel.
- Animal welfare audits are regularly conducted to ensure high standards at Roche sites by State Veterinary Authorities or external accreditation organisations (AAALACi)
- Likewise, external contract research organisations are audited by Roche animal welfare officers and/or specialists in Laboratory Animal Science to safeguard compliance to the same standards at external partner organisations
- Procedures are submitted for approval to Institutional Animal Care and Use Committee (IACUC) and/or to appropriate governmental agencies responsible for animal welfare in compliance with local laws and regulations

*This position paper was approved by the Corporate Sustainability Committee on April 28, 2011.  
It was reviewed and updated in April 2020 with approval by the Roche Ethics Committee on Animal Welfare.*