



Replacing, reducing and refining the use of animals in biomedical research: case studies

Almost every major breakthrough in human and veterinary medicine has depended on the use of animals in research and development, or the testing of new therapies.

At this time, research involving animals remains an essential tool to increase our understanding of how human and animal bodies work, how diseases affect them, and how diseases can be prevented or treated.

European Directive 2010/63/EU, which promotes both animal welfare and high-quality scientific research, was adopted in 2010 after a rigorous process of discussion and negotiation.

These case studies show a range of novel and innovative projects that are helping to reduce, replace and refine the use of animal models. Each is helping meet the goals of the Directive and enhance animal welfare while maintaining public benefit

Replace

Organs-on-a-chip *Netherlands*

A consortium, led by the Philips Research Institute in the Netherlands, is making progress on growing human blood vessels in the laboratory. This research could ultimately lead to the reduction of animals needed in biomedical research. They are heart cells cultures on a chip designed to simulate the mechanics of a beating heart. These models are being further expanded to other organs and tissues for example the human airway. Animal models provide scientists with an understanding of how whole biological systems work and respond to treatments. Growing cells, blood vessels and working organs means scientists may not have to use whole animal structures to conduct vital research in the future.

Innovation of the 3Rs in drug development *Denmark*

Novo Nordisk has established a centralised department to drive innovation with a focus on animal welfare, improving laboratory animal science and seek to identify possible replacement opportunities. Greater emphasis on for example access to human cells in vitro can provide effective opportunities to reduce animal use in safety and efficacy testing of new medicines. By setting a strategy and dedicating the necessary resources it has been possible to remove 11 tests involving animals in the drug approval process.

Reduce

International Primate Brain Consortium (IPBC) *Across the EU*

The IPBC aims to preserve valuable material that shapes our understanding of the make-up and workings of the primate brain. To do this are creating a digital, open-access data bank of primate brain material. They will also develop a 3D atlas of the primate brain to generate new questions and ideas about brain function and diseases. By using the 3D atlas and biobank, scientists will be able to conduct some research without animals.

New models and innovations in Cancer Research *Germany*

Progress in cancer treatment would not have been possible without research involving animal models. However, the results of preclinical therapy experiments often do not translate well in humans, with current approaches limiting our ability to study cancer. New research involving novel mouse-based models holds great promise in overcoming many of the limitations of currently established animal tumor models. These models better mimic human tumour samples and improved standardisation will greatly enhance their relevance to understanding and treating cancer. They could help reduce animal use in cancer research by improving the likelihood of finding the right answer with fewer experiments.

The International Mouse Phenotyping Consortium (IMPC) *United Kingdom*

The scientific community has taken advantage of mice's genetic similarity to humans. In 18 centres worldwide, the IMPC is generating a comprehensive catalogue of mammalian gene function for the first time. This method can reduce animal use by systematically cataloguing and sharing all mouse gene function and their role in disease. This means researchers may not have to use mice in future studies. Using genetically modified mice in this way is improving our understanding of disease and biology.

Deciphering the Mechanisms of Developmental Disorders [DMDD] *United Kingdom*

The goal of DMDD is to identify which genes are essential for the development and survival of mouse embryos. The project, based at Wellcome Trust Sanger Institute, will use many approaches, such as imaging and tissue analysis, to identify problems that cause death in mice. Developmental biologists and clinicians from across the UK are using this to further our understanding of human development.

All data will be made freely available via their web site, enabling individual researchers to identify information relevant to their own research. By building a database of available and applicable evidence, researchers are able to reduce their use of animals by using data from other studies.

Refine

Improved housing for rabbits *France*

Recently there has been greater emphasis on group housing of social animals, including rabbits, to improve animal welfare. However, the introduction of social groups needs to be managed carefully to ensure animals are safe and compatible.

Covance Research Products, in partnership with a large academic institution, conducted an innovative project involving the housing and transport of paired rabbits. Rabbits were introduced to each other at a younger age and kept in a purpose built, friendly environment. It included the introduction of a novel nesting box that could accommodate both animals, as well as toys and hay cubes for enrichment.

The majority of rabbits were successfully paired in their new environment after transportation and successful adaptation. Refining the care of rabbits helps to improve animal welfare, while protecting the legal requirement for testing of new drugs.