

The Danish 3R-Center thinks that a broader understanding of the concept of Replacement of experiments on animals is needed (2019)

The Board of the Danish 3R-Center

Sixty years have passed since William Russell and Rex Burch introduced the 3Rs in *The Principles of Humane Experimental Technique* (1959). The principles have been particularly successful, considering that they are currently integrated into animal research legislation in many countries.

Quite a number of scientific reports conclude that the volume of information currently obtained per laboratory animal used is far greater than was the case in 1959, which is one of the fundamental features of Reduction. The housing of laboratory animals has also vastly improved and procedures have become more humane, resulting in Refinement. In addition, a number of routine tests for safety assessments of chemicals and drugs have been superseded by non-animal methods, leading to Replacement. Approval procedures for new chemicals and medicines have also begun to utilise non-animal methods. This is exemplified by the adoption by the OECD (which harmonises testing guidelines) of the Adverse Outcome Pathways concept, specifying guidelines for mechanistic studies without laboratory animals. The Danish 3R-Center expects to see great benefits from sharing of experimental findings to maximize the level of knowledge.

Yet research itself has changed, too, and research results are in far greater demand today than previously. Basic research at universities and the initial development of new candidate drugs are areas that are particularly increasing in scope. These types of research are based far less on routine trials that repeatedly use the same laboratory set-up. Accordingly, there is still a great demand for targeted projects to implement the 3Rs, and for research into non-animal methods to make it possible for the more formative experiments in basic research to be replaced with non-animal methods as well.

Basic research and development is usually founded upon on a scientific question that seeks to be answered, after which an experiment that can answer the question is planned from scratch. Since no one else has probably answered the question previously, there is usually no previous experiment to which a new experiment can be considered to be a direct alternative. Therefore, the use of non-animal methods will largely be dependent upon the researcher, and not least the researcher's organization, who have multiple options when attempting to answer a research question. This means that a researcher will not only tend to think along the lines of animal research. The entire palette of research methods, including cell cultures, computer simulation and interdisciplinary analyses of research data, should therefore be considered whenever research questions need to be answered in basic research.

The concept of Replacement, as defined by Russell and Burch in 1959, i.e. substituting a single well-defined experiment on animals with a similarly well-defined experiment without animals, cannot at present be considered to be the only indicator if there is an overarching wish to obtain more knowledge using fewer animals in the most basic areas of research. This means that society, institutions and companies conducting the research and, not least, the Danish 3R-Center, need to support in a wider sense an existing infrastructure which addresses research questions using non-animal methods. These methods must be fundamental to the mindset of a research organisation. Accordingly, the Danish 3R-Center aims to widen the extent of its activities to support not only positive trends in the sector which conducts experiments on animals, but also in the communities which, in an overarching perspective, have the capacity, expertise and infrastructure to answer research questions without experiments on animals. The Center's vision is that from now on researchers will include a wide range of options when planning how to answer specific research questions, gradually enlarging their experience base and thus narrowing the area within which animal experiments are deemed to be the best way to answer the question concerned.