

### 3. Animal experiments according to the 3R principles

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#### The principles of human experimental technique

In 1959, *W.M.S Russell (1925-2006)* and *R.L. Burch (1926-1996)* published their famous book "The Principles of Humane Experimental Technique". The book explains the 3R principles, which should be considered when planning and conduction animal experiments. The first R stands for Replacement, which means that animal experiments should be replaced by other methods (such as computer models or *in vitro* tissue experiments) whenever possible. The second R stands for Reduction. Reduction means that the needed number of animals used in experiments should be reduced to the lowest possible number necessary to achieve useful results. The third R stands for Refinement and experiments should be refined to achieve the best possible animal welfare during housing and testing.

It is no coincidence that the book was published exactly 100 years after Charles Darwin's "The Origin of Species". Every chapter begins with a quote from Charles Darwin. Furthermore, the book builds on the idea that since we are related to animals, then we should also expect animals to be capable of suffering. This is why animals should be treated as humanely as possible. The book was received well but was forgotten shortly thereafter until it was "rediscovered" in the 1970's.

#### Earlier guidelines for human animal testing

W.M.S. Russell and R.L. Burch were not the first ones to come up with guidelines for more humane animal testing. Marshall Hall (1790-1857) had already formulated five principles for the ethical use of *laboratory animals* in 1831.

However, he did not allow the five principles to be published until 1856 in the scientific journal *Lancet*. The five principles state that *animal testing* can only be conducted when (1) there are no alternatives, (2) there is a clear purpose, (3) the experiment has not been conducted previously, (4) suffering is minimized and (5) all results are published in detail. Several of these principles are reflected in modern animal testing principles, although a publishing requirement has never been enacted. Marshall Hall's principles were visionary and ahead of his time but were replaced by the 3R's.

#### The importance of the 3R's today

Nowadays, the *3R principles* are widespread and are an important aspect in EU legislation, which the different member countries (including Denmark) have implemented in their national legislation. The EU Directive 2010/63/EU from 2010 included, for the first time, the 3R's as an important part of the foundation of the directive. In reality, this means that when researchers apply for permission to test on animals, then they must include how they have implemented the 3R's in their protocol(s). In principle, permission cannot be granted to researches unless they can provide an argument for how they have implemented the 3R principles.

The 3R principles are an important part of compulsory experimental animal courses and the participants must be tested on them before they can work with animals. Denmark and a number of other countries have established their own 3R centers, whose main goal is to spread the

purpose of the 3R principles and to convey research results of different research groups to the public.

Additionally, the 3R principles are included in many research funds, and applicants for these funds must explain how they have incorporated the 3R's into their experiments.

Thus, the 3R's have become an important part for the modern use of experimental animals. However, this does not mean that animals cannot experience suffering because of these experiments. There is continuously being work done to find ways to reduce the use of animals and to give the animals the best possible care.