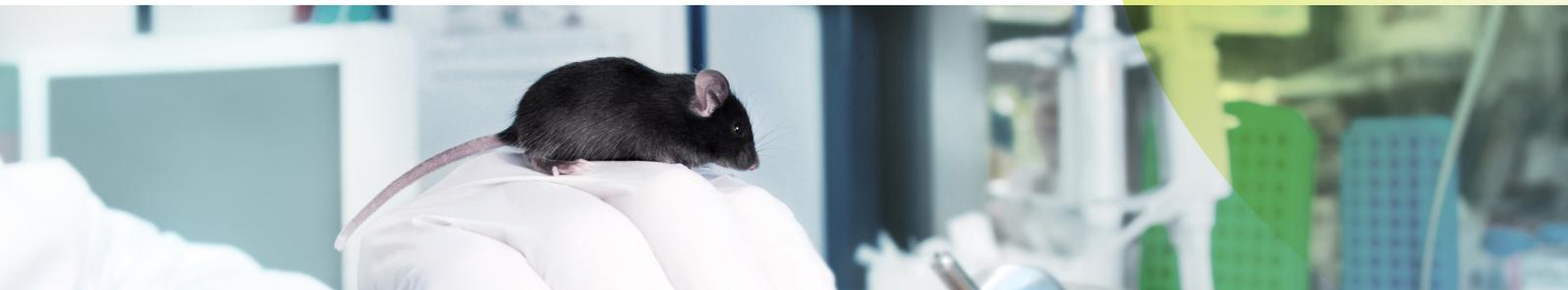




3R research: Replacement, Reduction and Refinement of animal experiments



Introduction

Intravacc is one of the leading organizations in global 3R research (Reduce, Replace and Refine), with a main focus on Reduction, Replacement and Refinement of animal use in statutory required testing for vaccine batch release.

Methods we developed have been accepted by the European Pharmacopoeia. We are a front runner in the development and distribution of a new paradigm in vaccine lot release testing, known as the consistency approach. To promote the implementation of this strategy, we participate in VAC2VAC, an IMI2-funded European research project on consistency testing (www.vac2vac.eu/).

A shift in vaccine control testing

Animals are still required for vaccine development and quality control. However, these models are nowadays challenged for reasons of ethics, economics and science. Intravacc recognizes the need for reducing the number of animals as well as for improving the welfare of these animals. Therefore, we specifically develop assays and perform studies in order to Replace, Reduce and Refine the use of animals for this purpose.

3Rs

Although animal use in vaccine research and testing cannot always be avoided, much can be done in terms of Replacement, Reduction and Refinement.

- Reduction aims at reducing numbers of animals without violating the relevance of the animal model
- Replacement aims to use alternative animal models, e.g. cell-culture models or physico-chemical methods.
- Refinement refers to reducing pain and distress in animal studies and/or improving animal welfare such as by improving housing conditions.

3Rs successes at Intravacc

Being one of the frontrunners of 3Rs research our experienced scientists are using the latest technologies to minimize the use of animals.

3R achievements:

- Several 3R developed models have been accepted by the European Pharmacopoeia
- More than 25 assays developed that could help replace, reduce or refine the use of experimental animals
- Over 20 publications in peer reviewed journals since 2013

Selected Publications

- Michiels TJM, Meiring HD, Jiskoot W, Kersten GFA, Metz B. Formaldehyde treatment of proteins enhances proteolytic degradation by the endo-lysosomal protease cathepsin S. *Sci Rep.* 14;10(1), 11535 (2020).
- Metz B, Michiels T, Uittenbogaard J, Danial M, Tilstra W, Meiring HD, Hennink WE, Crommelin DJA, Kersten GFA, Jiskoot W. Identification of Formaldehyde-Induced Modifications in Diphtheria Toxin. *J Pharm Sci.* 109 (1), 543-557 (2020).
- Hoonakker ME, Verhagen LM, van der Maas L, Sloots A, Hendriksen CFM. Reporter cell lines for detection of pertussis toxin in acellular pertussis vaccines as a functional animal-free alternative to the in vivo histamine sensitization test. *Vaccine* 22;35(8), 1152-1160 (2017).
- Westdijk J, Metz B, Spruit N, Tilstra W, van der Gun J, Hendriksen C, Kersten G. Antigenic finger-printing of diphtheria toxoid adsorbed to aluminium phosphate. *Biologicals* 47, 69-75 (2017).