Applications of the 3Rs to challenge tests used in vaccine development

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A procedure frequently performed frequently in development and quality control of immunobiologicals is to challenge immunised animals with the relevant virulent micro-organism or toxin to demonstrate induction of protective immunity. Challenge tests might be statutory required in case of getting marketing authorization or for routine vaccine batch release testing.

Challenge tests are characterised by significant pain and distress for non-protected animals and, as such, should be high on the priority list for finding Three R alternatives. In vitro alternatives are preferred. Even replacement of the challenge procedure by bleeding the animal and titrating for protective antibodies means a significant Three R progress. However, these approaches are not always available and require pre-information about the kinetics of the immune response.

In case challenge of the animals is unavoidable a strict programme of animal welfare assessment must be implemented. This programme should include elements of protocol review, clearly defined responsibilities, identifying humane endpoints, frequent monitoring for animal behaviour and welfare by well trained people and using clinical score sheets.

In this presentation I will provide examples of challenge tests and discuss the various strategies for Three R optimisation. Particularly, I will focus on humane endpoints and the conditions that might guarantee the optimum implementation of these endpoints.