Opinion from National Committee for the Protection of Animals Used for Scientific Purposes (NCPAUSP)

April 29, 2016

Request for advice: A request for advice was submitted to the NCPAUSP from the HPRA.

Issue: The question asked of the Committee was: *What criteria should be used to decide when it is scientifically and ethically justified to conduct the same test procedures in two species?*

Background provided: Directive 2010/63/EU mandates the application of the 3Rs in the use of animals for scientific purposes. A central tenet is that experiments in animals should not be repeated unnecessarily.

Advice: The Committee consider that it is the obligation of the researcher to make a strong scientific argument why it is necessary to perform the same experiments in two species. We recommend the HPRA criteria on which to approve such work be based two or more on the following considerations:

1). There is consensus in the field that no single model species is sufficient or more suitable to model the core disease/condition. Specifically, there are aspects of a given species that make them suitable to study a specific disease, but also aspects that do not make them suitable. The applicants should clearly articulate what value each species provides in their application.

2). There is consensus in the field that tests of a disease model or drug/compound in at least two species is the minimum burden of scientific proof (e.g. because past use of a single species resulted in poor subsequent clinical translation).

3). There is evidence that pharmacokinetic and/or pharmacodynamic responses of the intended test treatments behave differently between the two species and that no single species faithfully represents (or can be assumed to) how that compound will perform in humans/higher species.

Additional: Even when the above criteria are satisfied, the HPRA might consider the following suggestions to improve compliance with 3Rs:

1). That design of the studies be modified to focus on the species that best reproduces the clinical/disease phenotype and that experiments in a second species be restricted to validating key findings from the first species.

2). That if studies in both species proceed together from the beginning, a decision point is included in the study design such that data are reviewed at an interim stage and, if appropriate, work be suspended in one species where there is no longer sufficient scientific justification for further replication.

In addition to the standard HPRA project evaluation procedure, we suggest that the HPRA strongly recommend to applicants that they obtain institutional ethical approval in all such circumstances.