IRISH MEDICINES BOARD
NON-TECHNICAL PROJECT SUMMARY

NON-TECHNICAL PROJECT SUMMARY DETAILS
Project reference number: V033/2013Q4
Project title: Regulatory study for the determination of the potency associated with the manufacture of specific neurotoxin products, using mice
Duration of the project work (months): 48 months
Project keywords: Neurotoxin; mouse; potency testing
Purpose of the project under Article 5 of Directive 2010/63/EU: Regulatory use and routine production
Project objectives, scientific unknowns or scientific or clinical needs being addressed: The objective of the project is to determine the potency value of biological neurotoxins used in medicinal products. As required by EU medicines legislation, in order to meet the quality, safety and efficacy parameters, potency testing of neurotoxins must be performed before batches of the medicines are deemed safe for use in humans.
Potential benefits likely to derive from this project: The studies are required in order to comply with the European medicines legislation, as it relates to the quality, safety and efficacy of medicinal products containing botulinum toxin. These products are used to treat a range of medical conditions e.g. severe neurological or urological conditions, where frequently no direct alternative treatments exist.
Species and approximate number of animals expected to be used: 720,000 mice
Expected adverse effects on the animals, the expected level of severity and the fate of the animals: Due to the nature of the procedures involved in these studies, adverse effects are expected which are classed as being severe. However, the animals will be frequently monitored, and humane endpoints will be applied where possible, to enable animals to be removed from study at an earlier stage than has been historically the case for testing of this nature. At the end of the procedures, all remaining mice will be humanely euthanised.

APPLICATION OF THE 3RS

Replacement - why animals need to be used for this project and why non-animal alternatives could not be used:

Although in vitro (non-animal) tests are available for certain neurotoxins, there are still no suitable and internationally validated alternative in vitro for the purpose of evaluating the quality, safety and efficacy of other test substances. Until the validation of a suitable replacement test method for the remaining test substances, in accordance with EU medicines regulatory requirements the potency values of the neurotoxin must be still be assessed in live animals. However, humane endpoints will be applied in order to reduce any suffering to the animals.

Reduction - how the use of minimum numbers of animals can be assured:

Statistical methods were used to ensure the minimum numbers of animals are involved in these studies. While test group sizes are determined based on the requirements of the European medicines legislation, manufacturers of the medicines have been able to reduce the number of tests performed by e.g. increasing batch sizes thereby reducing the relative number of test subjects required per batch.

Refinement - justification for the choice of species, why the animal model(s) used are the most refined and general measures to be taken to minimise harm to the animals:

The species (mouse) involved is that required by the legislation. The procedures are only performed by trained and experienced personnel. Humane endpoints will be applied where possible in order to reduce suffering. A veterinarian will be available for consultation over the course of the study should any non-test related animal welfare issues arise.