In search of acceptable alternatives to the murine histamine sensitization test (HIST): What is possible and practical?

4-5 March 2015, London

The NC3Rs is hosting a workshop to bring together scientists from government, industry, academia, and research institutions to discuss and evaluate alternative methods to the murine histamine sensitization test (HIST) for monitoring of residual pertussis toxin activity in acellular pertussis vaccines.

Background

Pertussis, also known as whooping cough, is a highly contagious bacterial disease caused by *Bordetella pertussis*. Pertussis was once a major cause of childhood morbidity and mortality, but its incidence has decreased substantially with the development of vaccines. Regulatory authorities require testing prior to the release of each production lot of pertussis component vaccines. The murine histamine sensitization test (HIST) is a key assay performed to ensure sufficient inactivation of pertussis toxin in acellular pertussis vaccines has been effectively inactivated and that no reversion of toxoid to active pertussis toxin has occurred. However, such testing uses many mice, some of which can experience significant unrelieved pain and distress. In addition, the HIST has technical challenges and requires frequent retesting, thereby increasing both vaccine testing expense and animal use.

Recently, *in vitro* methods have been developed that may be considered as alternatives to the HIST. One of these methods is currently undergoing international evaluation for its sensitivity to pertussis toxin and inter-laboratory transferability. It is hoped that the data from this study will help in the adoption of this method by vaccine manufacturers and international regulatory authorities.
Key objectives

The workshop is organized by the ‘International Working Group on Alternatives to the HIST’, a consortium of interested stakeholders representing government, industry, and research institutions. The key objectives of the workshop will be to:

- Review and discuss data generated from an international collaborative study sponsored by the European Directorate for the Quality of Medicines and Health Care (EDQM) to determine if a cell-based assay is a suitable alternative for replacement of HIST.
- Review recent scientific advances that can be applied to acellular pertussis vaccine testing to provide greater accuracy and precision of results, improve testing efficiency and to reduce or ultimately replace the use of animals in this area.
- Discuss issues associated with assay design and validation, effect of product toxoiding and adjuvanting on testing outcome, and preparation and calibration of reference standards for alternative methods.

Registration

Attendance is free but advanced registration is essential. There are a limited number of places available and registration closes on 6 February 2015.

Further queries should be directed to Katie Lidster at the NC3Rs katie.lidster@nc3rs.org.uk.