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Acellular pertussis vaccines: towards the replacement of the Histamine Sensitisation Test (HIST) for residual pertussis toxin testing

The European Pharmacopoeia (Ph. Eur.) Commission is seeking public feedback on its proposal to replace the Histamine sensitisation test "HIST" (test in mice) with a standardised CHO cell clustering assay (*in vitro* cell-based test) for residual pertussis toxin testing. The replacement would affect general chapter 2.6.33 *Residual pertussis toxin and irreversibility of pertussis toxoid* and ten individual monographs on vaccines containing acellular pertussis.

The introduction of a standardised CHO cell clustering assay for residual pertussis toxin testing is based on the results of a collaborative study¹, run under the auspices of the EDQM's *Biological Standardisation Programme*², and completed in 2015.

As part of the same revision exercise, the Ph. Eur. Commission proposes to delete the test for irreversibility of pertussis toxoid. This decision is based on the history of the safe use of acellular pertussis vaccines, as well as on data confirming that the pertussis toxoid is stable and a reversion is not an issue for marketed acellular pertussis vaccines.

Based on the data collected, the requirement to test the final lot for residual pertussis toxin is also proposed for removal. Using a CHO assay, testing of the pre-adsorbed bulk (a stage where the antigens are highly concentrated and therefore detection of pertussis toxin is easier) is considered to be the most effective and robust approach.

Published in the April 2018 issue of *Pharmeuropa*³, this public consultation will run until 30 June 2018. Interested parties are invited to provide their comments through the Procedure for commenting on *Pharmeuropa* drafts⁴.

The Ph. Eur. Commission is committed to phasing out the use of animal tests by continuously reviewing the *in vivo* tests described in its Ph. Eur. texts, and applying whenever possible the principles of "3Rs" (Replacement, Reduction, Refinement) set out in the *European Convention for the Protection of Vertebrate Animals used for experimental and other scientific purposes*⁵. The proposed replacement of the HIST for residual pertussis toxin testing shows this commitment.

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Note for the Editor: Further information is available on the internet site <https://www.edqm.eu/>. The EDQM is a leading organisation that protects public health by enabling development, supporting implementation, and monitoring the application of quality standards for safe medicines and their safe use. Our standards are recognised as a scientific benchmark worldwide. The European Pharmacopoeia is legally binding in member states¹. Similarly, the EDQM develops guidance and standards in the areas of blood transfusion, organ transplantation and consumer health issues.

¹There are thirty-nine members of the [European Pharmacopoeia](#) Commission: *Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Republic of Moldova, Montenegro,*

¹ Isbruckner R, Daas A, Wagner L *et al.* Transferability study of CHO cell clustering assays for monitoring of pertussis toxin activity in acellular pertussis vaccines, *Pharmeur Bio Sci Notes* 2016:97-114

² <https://www.edqm.eu/en/Biological-Standardisation-Programme-mission-60.html>

³ *Pharmeuropa* 30.2 of April 2018. *Pharmeuropa Online*: <http://pharmeuropa.edqm.eu/home/>

⁴ More information on public enquiries is published in *Pharmeuropa Online* under "Useful information".

⁵ Council of Europe. European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes, ETS No. 123; Strasbourg, France 18 March 1986



Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, "the former Yugoslav Republic of Macedonia", Turkey, Ukraine, United Kingdom and the European Union.

A political organisation set up in 1949, the Council of Europe works to promote democracy and human rights continent-wide. It also develops common responses to social, cultural and legal challenges in its 47 member states.