Press release

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Phasing out animal testing for in-process control of veterinary vaccines: *Clostridium septicum* as a proof of concept

On 9 and 10 March 2021, a workshop aimed at facilitating the implementation of replacement *in vitro* toxicity and antigenicity assays for *Clostridium septicum* vaccine antigens was jointly held by the European Directorate for the Quality of Medicines & HealthCare (EDQM/Council of Europe), the European Partnership for Alternative Approaches to Animal Testing (EPAA) and the European Commission's Joint Research Centre (JRC). Also on the agenda was a discussion of the regulatory consequences of the related revisions to veterinary vaccine monographs undertaken by the European Pharmacopoeia Group of Experts on Veterinary Vaccines and Sera (15V) and the potential for international harmonisation.

This workshop is the follow-up of a collaborative study (BSP130) conducted under the Biological Standardisation Programme (BSP), co-funded by the European Union and the EDQM/Council of Europe. Fourteen manufacturers and public-sector control laboratories were enrolled in an international study run under the common aegis of the EDQM and the EPAA. The study allowed the validation of Vero cell-based assays as alternatives to the mouse tests currently in use for in-process quality control of *Clostridium septicum* vaccines (toxicity: Minimum Lethal Dose; antigenicity: Total Combining Power). The results demonstrated that optimised Vero cell-based assays represent valuable toxicity and antigenicity indicators as alternatives to the corresponding *in vivo* methods. Implementation of such cell-based testing for this and other cytotoxic antigens, using this study as a model, could ultimately result in large reductions in animal usage in the quality control of veterinary vaccines. Experimental work toward the extension of the concept to other clostridial toxins was presented.

As a consequence of the study outcome, the experts of Group 15V of the European Pharmacopoeia launched the revision of monographs *Clostridium septicum vaccine for veterinary use (0364)*, *Clostridium novyi (type B) vaccine for veterinary use (0362)* and *Clostridium perfringens vaccine for veterinary use (0363)*. The key elements of the proposed revised texts, as submitted for public enquiry in 2020, were presented and discussed at the workshop, as was practical information obtained during the collaborative study and from a field enquiry.

In an effort to foster international harmonisation for the implementation of the replacement methods, the workshop brought together manufacturers and regulators from all over the world. Well over 200 attendees from some 43 countries participated in each workshop session, representing quality control laboratories in both the private (veterinary vaccine manufacturers) and public (OMCLs) sectors, regulators and experts, researchers and students.

Opening the workshop, Laurent Mallet, Head of the Biological Standardisation, OMCL Network and HealthCare Department at the EDQM, expressed his gratitude to the BSP project leaders, participants and EDQM scientific project co-ordinator. He praised the results as "a testimony to how cross-sectoral co-operation has delivered a great step forward in promoting animal welfare, by identifying the potential for reduction of *in vivo* testing in the field of veterinary vaccines".

During the workshop, the importance of conducting collaborative studies, as well as the implementation of *in vitro* methods for the quality control of clostridial vaccines, was supported by the representatives of national and regional authorities, along with the scientists active in the field.

The study results have demonstrated that cell-based assays can be more sensitive and accurate, have high reproducibility, can shorten the duration of tests and provide huge advantages in terms of saving animal lives and reducing costs, while ensuring safety and public health are not compromised.

Find out more

- Alternatives to animal testing (3Rs): www.edqm.eu/en/alternatives-animal-testing
- Biological Standardisation Programme (BSP) for 3Rs: www.edqm.eu/en/BSP-programme-for-3Rs-1534.html
- Download the workshop presentations and register to watch the recordings: www.edqm.eu/en/proceedings-international-conferences#3R

Contact: Caroline Larsen Le Tarnec, Public Relations Division, EDQM, Council of Europe
Tel.: +33 (0) 3 88 41 28 15 – E-mail: caroline.letarnec@edqm.eu

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 the development, supporting the implementation and monitoring the application of quality standards for safe medicines and their safe use. Its standards are recognised as a scientific benchmark worldwide. The European Pharmacopoeia is legally binding in member states.[1] The EDQM also develops guidance and standards in the areas of blood transfusion, organ transplantation and consumer health issues.

The **EPAA** is a unique voluntary collaboration between the European Commission, European trade associations and companies from seven industry sectors. The partners are committed to pooling knowledge and resources to accelerate the development, validation and acceptance of alternative approaches to animal testing at national, European and global levels. The overall aim is the replacement, reduction and refinement (3Rs) of animal use in regulatory testing.

The **JRC** is the European Commission's science and knowledge service which provides independent scientific advice and support to EU policy. It runs the EU Reference Laboratory for alternatives to animal testing (EURL ECVAM).

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1. There are 40 members of the European Pharmacopoeia Commission: *Austria, Albania, 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, Netherlands, North Macedonia, Norway, Poland, Portugal, Romania, Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, 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.