

# VACCINES CONSISTENCY APPROACH

## Workshop#5: Clostridial Vaccines

flash



The European Partnership  
for Alternative Approaches to Animal Testing

Brussels, Belgium, September 11<sup>th</sup> 2013

### APPLICATION OF THE 3RS AND THE CONSISTENCY APPROACH FOR IMPROVED VACCINE QUALITY CONTROL

>>> EPAA workshop on Validation of In Vitro Alternatives for In-process Control of Veterinary Clostridial Vaccines

The EPAA project on Application of the 3Rs and the Consistency Approach for Improved Vaccine Quality Control is currently working in parallel on four priority areas - DTaP (diphtheria, tetanus and acellular pertussis) vaccine, rabies vaccine for human and veterinary use and finally, clostridial vaccines for veterinary use. These priorities were agreed by the project's Technical Committee as those with the most pressing animal welfare concerns and flash reports on progress in these areas are available on the EPAA website.

Of the four areas, the clostridial vaccine project is the most advanced as explained in the [flash report](#) of the project's expert working group meeting on 19<sup>th</sup> March 2013. Briefly, MSD Animal Health, with the financial support of the UK National Centre for the 3Rs, has developed cell culture tests as alternatives to two animal methods used as in-process controls for manufacture of a vaccine against *Clostridium septicum*.

These tests measure the toxicity of the toxin, the residual toxicity of the inactivated toxin (toxoid) and the antigenicity of the toxoid. All these tests rely on the measurement of residual toxicity, and while this has relied conventionally on mice, the new tests aim to replace these with cell culture.

The aim of the project is to bring together an expert group of manufacturers, regulatory and standards bodies to design and carry out a collaborative study overseen by EDQM, the European Directorate for the Quality of Medicines and HealthCare. Collaborative studies

run under the Biological Standardisation Programme of EDQM, if successful, lead to validation of new methods and their inclusion in the European Pharmacopoeia as approved alternatives.

The expert group consists of scientists from laboratories in the USA, New Zealand, Turkey, Spain, Hungary, Germany, Switzerland, France and the UK. They met, together with representatives from EDQM, on September 11<sup>th</sup> 2013 in Brussels to agree on the final details. Eleven laboratories from the nine countries will be involved in the study and to ensure the validity of the study it is essential that each contributing lab adheres strictly to the agreed experimental protocols for carrying out and reporting the work.

Six toxins and six toxoids donated by the participants will be coded to ensure that no-one knows their origin, and distributed to the various labs together with a reference toxin and antitoxin so that results from different labs can be normalised to these standards. Each lab will undertake to test the toxicity of toxins and the antigenicity of the toxoids in vivo and/or in vitro.

The data will be collated and analysed by an EDQM statistician to look at the performance of the tests in different hands and the comparison between the in vivo and in vitro results. The data, still coded, will be shared with the participants through teleconferences and a final workshop towards the middle of next year. The workshop will outline the study report to be published in the EDQM journal, *Pharmeuropa Bio* and *Scientific Notes*.

**“Bring together manufacturers, regulatory and standards bodies from Europe and beyond”**

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ALTERNATIVES  
to ANIMAL TESTING

The eventual inclusion of these tests in the European Pharmacopoeia will be a milestone for the whole Consistency Approach project, but this rests in the hands of EDQM and its advisory experts. However, the work of the Clostridial expert group will continue. In addition to looking for means to extend the methodology to other Clostridial species, the group intends to publish the findings in a standard peer-reviewed journal to promote the uptake and acceptance of these new methods, but also to encourage manufacturers to think about how they could adopt the general methodology to their current manufacturing quality control for Clostridial vaccines.

successful collaborative study results in an enormous amount of work whose completion relies on the support and goodwill of the participating organisations. More important perhaps to success is the enthusiasm and commitment to the 3Rs shown by the individual members of the expert working group.

The two workshops have shown that even for a study limited to two related tests for one Clostridial species, the meticulous attention to detail needed to ensure a

## Participating Organisations

- Bornova Institute, Turkey
- Ceva, Hungary
- CZV (CZ Veterinaria), Spain
- EPAA
- EDQM (European Directorate for the Quality of Medicines and Healthcare), France
- MSD Animal Health, UK
- NEBIH (Nemzeti Élelmiszerlánc-biztonsági Hivatal), Hungary
- PEI (Paul Ehrlich Institute), Germany
- USDA APHIS (US Department of Agriculture, Animal and Plant Health Inspection Service), USA
- Syva, Spain
- Zoetis, Belgium

## Previous Workshops reports

Reports from the previous Consistency Approach Workshops (DTaP and Human rabies vaccines) workshops are available for download on the EPAA website:



EPAA DTaP vaccines Workshop

EPAA Human Rabies vaccines Workshop

EPAA Veterinary Rabies vaccines Workshop

EPAA Clostridial Rabies vaccines Workshop #1

## About...

The Vaccines Consistency Approach project is one of the flagships 3Rs projects of the EPAA. Further information is available in the dedicated factsheet.

>>> Download it from the EPAA website



## CONTACT



entr-epaa@ec.europa.eu  
www.epaa.eu.com  
+32 (0)2 29 52 014