

APPLICATION OF ALTERNATIVE METHODS THROUGH THE CONSISTENCY APPROACH FOR IMPROVED VACCINE QUALITY CONTROL

STRONG INTEREST OF INDUSTRY AND REGULATORS IN NEW EPAA PROJECT

At the occasion of a Workshop organised by the EPAA on April 7, 2011, representatives from industry and regulators (including EMA, EDQM, UK, Netherlands, France, Belgium, Germany, US and Canada) agreed to participate in a project on the application of alternative methods through the consistency approach for improved vaccine quality control. The consistency approach is already used for the release of vaccines of the most recent generation of vaccines. The purpose of the project is to successfully implement the approach for the routine release of conventional vaccines.

Participants took note of the strong support of the EU Commission for the EPAA and its role in the EU policy context. For **John Dalli**, speaking at the 2011 EPAA conference, EPAA is a «model of how to work effectively across different sectors, and in co-operation between regulators, industry and other stakeholders». In recent interviews, **Antonio Tajani** stressed the need «to explore the full potential of the virtuous circle of innovation resulting in better animal welfare, and animal welfare resulting in better science»). **Janez Potocnik** suggested «to try to improve the outreach of EPAA to the regulatory risk assessors and risk managers»

1 MAJOR SCIENTIFIC, ANIMAL HEALTH AND ECONOMIC FEATURES OF THE CONSISTENCY APPROACH

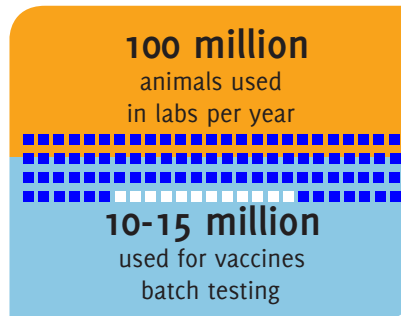
Control of batch release of vaccines for human and animal is one of the biggest use of animals for testing in the pharmaceutical sector. Estimates suggest that worldwide more than 100 million animals are used in laboratories, of which between 10 – 15 % for vaccines batch release testing. The majority of these animals are utilized for compliance to regulatory requirements.

There have been great achievements in the validation and implementation of alternative methods to animal testing used for routine quality control over the last years and today in vitro testing is developed for new candidate vaccines and implemented in their routine release quality control at licensure.

Whilst there have been evolution of the release process approach both on the side of Control Authorities and manufacturers, there is still room for improvement: at the level of regulatory authorities for facilitating the introduction of new release concept on the basis of the consistency approach, at the level of test “users” to engage on alternatives development.

Implementation of the consistency approach in batch release testing is expected to result in scientific, economic and animal welfare benefits without jeopardizing the quality, safety and efficacy of the vaccines:

- More powerful and reliable analytical tools for lot release
- Less cumbersome and time consuming Quality control (a few days instead of 2 months)
- Faster access of vaccine lots to the patients/animals



PARADIGM SHIFT

2

Acceptance of the consistency approach will imply a major shift in current thinking. Current alternative approaches are too often characterized by the replacement of individual quality control tests (1 by 1 replacement), fitting in the established practice of the final lot as a unique product with emphasis on final lot testing.

« In vitro tests do not provide and do not have to provide the same information as in vivo tests »

Consistency testing starts from the idea that subsequent lots produced can be compared to an earlier (reference) lot (clinical lot, historical lot) which is thoroughly characterised with regard to quality, safety and efficacy. This requires consistent production, tight in-process control and strict application of GMP and Quality Assurance. Lot release is then based on equivalence with the reference lot. This shift in the lot release paradigm implies the acceptance that in vitro tests do not provide and do not have to provide the same information as in vivo tests.

INTERNATIONAL SUPPORT

3

Since the majority of EU vaccines production is exported outside the EU, representatives of EU manufacturers highlighted the need for convergence at the international level. Representatives of the EDQM highlighted their interest in the project, explained EDQM expectations, and suggested conditions and mechanisms to move forward. Authorities from US and Canada confirmed their interest in participation.



4

FOCUSED APPROACH

In conclusion, participants agreed to embark on this challenging project, diversifying activities between vaccines for human and for veterinary use. Authorities and representatives of vaccine manufacturers, will cooperate to issue guidance and advice on priorities, validation and acceptance criteria and to select the pilot cases.

The project will focus on the establishment of the proof of concept for the replacement of specific tests to the level necessary for submission to the Biological Standardisation Programme of EDQM in charge of the formal validation process. It will avoid duplication with existing projects and organizations.

Emphasis will be put at this stage on:

- Inventory of existing initiatives (prevent duplication)
- Promotion and support to existing initiatives (quick wins)
- New projects to be initiated (hard wins)

This approach implies a joint effort from manufacturers and Release Authorities and a stepwise globally harmonized action. Work will be coordinated by specifically dedicated expert consultants engaged by the EPAA.

Vaccines Project Committee

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Jean-Michel Chapsal, Sanofi Pasteur
Fabrizio De Mattia, Intervet/Schering Plough
Marlies Halder, European Commission Joint Research Centre
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Tanya Scharton-Kersten, Novartis Vaccines and Diagnostics
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The European Partnership
for Alternative Approaches to Animal Testing

For further information:

Visit http://www.ec.europa.eu/enterprise/epaa/index_en.htm

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