# Immunologicals – Industry perspective

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# Immunologicals – Industry perspective

## *2012 Highlights*

- Revision of monographs and guidelines
- Document on the efficiency of steam heat sterilisation to inactivate viruses
- Removal of TABST
- Procedure to modify the restricted list for OCABR
- EPAA activities and alternatives to animal testings
- VICH guidelines
- Perspectives on alternatives to thiomersal
- Variations regulation 1234/2008

# 2012 Highlights
## *Revision of monographs and guidelines*

- **Revision of monograph on rabies vaccines (live, oral) for foxes**
  - Suggestion made to change the title so that the monograph covers oral vaccines for wildlife
  - Feed-back on high number of animals used for safety studies; use of wild rodents

- **GL on the requirements for combined vaccines and associations of IVMPs**
  - IFAH-Europe provided feed-back on 3 remaining major issues :
    - A demanding level of requirements leading to a systematic full clinical redevelopment,
    - Underdeveloped approaches for the reduction of animal use,
    - Lack of consideration for alternative approaches

# 2012 Highlights
## *Revision of monographs and guidelines*

- **Ph. Eur. Monograph 'Infectious Bovine Rhinotracheitis Vaccine (inactivated)'**
  - IFAH-Europe provided feed-back on the in-process control tests and the consistency approach mentioned in this monograph
    - Manufacturing of this vaccine is simple without much downstream processing or in process testing
    - Support to replace the in vivo bath potency test by in vitro potency tests. As this approach is not specific to IBR vaccines, suggestion was made to draft a general part within section 5 of Ph.Eur. (or monograph 62)
    - Proposals were made for modifications of other points (residual live virus testing methodology, requirements to demonstrate immunogenicity..)

# 2012 Highlights
## *Extraneous Agents Testing (1)*

- **Lists of bibliographic references for cell systems to detect EA were sent to IWP and discussed**

- **A decision tree was also prepared:**
  - List of possible EA (species of origin, tissue of origin, target species, ..)
  - Reduction of list to final test list (exclusion of agents based on criteria such as country of origin of the seed, absence of growth,...)
  - Selection of cell systems (general or specific tests, for which viruses and which cells a general test is possible (CPE and/or HA)

- **Decision to focus on porcine species as an example**

# 2012 Highlights
## *Extraneous Agents Testing (2)*

- **Discussions with the regulators to determine if testings for EA (seeds, raw materials of biological origin) is done by general or specific methodology**

- **Guidance was provided by the regulators on the prerequisites for specific or general testings for the porcine EA list**

- **A presentation was made to IWP by IFAH-Europe**

# 2012 Highlights
## *Extraneous Agents Testing (3)*

- **IFAH-Europe provided a list of cells used for CPE, HA detection and is preparing a list of porcine viruses and possible tests to detect them with a summary of the implemented tests (information and implemented tests coming from the registered dossiers)**

- **No need for validation would be required when using a test from this list**

- **The information will be reviewed by IWP during their June meeting**

# 2012 Highlights
## *Extraneous Agents Testing (4)*

- **With regards to the use of new technologies, such as Massive Parallel Sequencing for the detection of EA, we acknowledged the EMA/CHMP/267815/2011 assessment report :**
  - *…'The detection of sequences of endogenous virus in the manufacturing of vaccines…was not an unexpected finding. Endogenous viral sequences are present due to heredity and the sequences from ALV or SRV as referred in the published article do not raise any concerns.'*
  - *'The use of new technologies may lead to the detection of unexpected findings; however a flexible approach based on a proper benefit-risk assessment and appropriate regulatory processes would likely need to be applied on a case-by-case basis'*

# 2012 Highlights

## *Documents on the efficiency of steam heat sterilisation and gamma irradiation*

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- **A document entitled 'Viral inactivation related to steam heat sterilisation of biological products' was finalised, it contains:**
  - Exhaustive bibliographic references as well as description of experimental conditions to inactivate viruses by heat
  - Experimental confirmation on the efficiency of steam heat sterilisation
  - Data covering all types of viruses (AND, ARN, single stranded, double stranded, enveloped, non enveloped viruses).
- **This document was shared with the regulators (Ph.Eur. Groups 1.6, 15 & 15V and IWP)**

- **A similar document is being prepared on the efficiency of gamma irradiation to inactivate viruses in serum, based on suppliers documentation and systems used to validate effective doses**

# 2012 Highlights
## *Removal of TABST*

- **IFAH-Europe welcomes the opportunity to waive the TABST for both live and inactivated veterinary vaccines**

  - Each MAH will inform the relevant NCAs in writing of the products for which they will withdraw the TABST
  - Implementation by 1st April 2013, after this date a type IA variation will be requested to remove the test
  - Exceptions: Porcine actinobacillus vaccine (inactivated), Porcine progressive atrophic rhinitis vaccine (inactivated) and Tetanus vaccine for veterinary use

    -→ Residual toxicity tests

- **Note: there is still a requirement for TABST for non-EU countries. In the context of the Directive 2010/63/EU, will it still be legal to perform the TABST in Europe?**

# 2012 Highlights

## *VBRN: Procedure to modify the restricted list for OCABR*

- **Consideration needs to be given to the detrimental effects (delays, fees, extra animals required to perform the tests) prior to the addition of a product to the restricted list**

- **Need to review the presence of each product on the list on an annual basis**

  - Critical risk/benefit assessment (use of additional animals, number of batches failed, comparison of results, how the repetition of tests at the OMCL have improved the position)

  - The results of this review should be available to the MAH for comment

  - Based on trend analysis IVMPs may be removed from the short list

# 2012 Highlights
## EPAA activities and Alternatives to Animal testing

- **IFAH-Europe contributes to the work on serological or totally in vitro potency tests for inactivated rabies, clostridial and leptospirae vaccines and to the EPAA initiatives**

- **For rabies potency testing, we lack clarity on the validation package required in order to waive animal testing**

- **We participated in several workshops on the development of in vitro methods to implement the 3Rs**

# 2012 Highlights
## *VICH*

**- VICH GL34 on Testing for detection of mycoplasma contamination: a few last comments were made**

- **Rabies Task Force Update**
  - Most countries/parties agree to adopt the serology approach and ultimately an in vitro approach
  - Discussions are still ongoing with the Japanese authorities
  - Difficulties to obtain feed-back from the chair

- **Removal of TABST**
  - IFAH-Europe provided numbers of animals used annually to satisfy the TABST for veterinary vaccines across Europe
  - The draft GL is being reviewed

# 2012 Highlights
## *VICH*

- **Strategies for extraneous agents testings**
  - Lack of harmonisation between US, EU, Japan and particularly Australia
  - Need to adopt common approaches
  - Progress on this GL is stalled for the time being

# 2012 Highlights

## *Perspectives on alternatives to Thiomersal*

- **IFAH-Europe provided data on the quantity of Thiomersal used per year in vaccines for veterinary use (WHO question on UNEP initiative)**
  - In the EU, vaccines may contain up to 0.02% thiomersal
- **Thiomersal is a unique substance and contributes to the inactivation or stabilisation of some antigens**
- **It complies with the legal requirements for preservatives in multi-dose presentations of inactivated vaccines**

# 2012 Highlights

## *Perspectives on alternatives to Thiomersal*

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Representing the European Animal Health Industry

- **Thiomersal is the only generally applicable preservative**

- **No alternative candidates exist today, changing to other preservatives not always possible, will take time and may not be economically viable**

- **Animal health, human health, human economic development would be compromised if thiomersal were to become unavailable**

# 2012 Highlights

## *Variations Regulation 1234/2008 and guidelines*

- **IFAH-Europe has been gathering input from all its members since 2010**

- **Major issues with the classification were proactively addressed to the Commission**

- **The Commission launched an official review process on the classification GL to which IFAH-Europe contributed further**

# 2012 Highlights

## *Variations Regulation 1234/2008 and guidelines*

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- **We had very little time to gain full understanding of the proposed changes by the EU task force and would welcome if a more transparent process was put in place for the next revision**

- **A follow-up meeting with stakeholders on the outcome of this consultation, prior to the public release of the revised GL, would be much welcomed.**

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# *Thank You For Your Attention !*