EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

THE LATEST DEVELOPMENTS' IN SCIENTIFIC REVIEW, REGULATION AND MARKETING AUTHORISATION PROCEDURES

Scientific developments:

Update on specific points from Immunologicals WP

2015 European Medicines Agency/IFAH-Europe Info Day
12-13 March 2015

Contents

- Guideline on data requirements for changes to the strain composition of authorised equine influenza vaccines in line with OIE recommendations
- Reflection paper on the replacement of cell lines used for the production of IVMPs
- Reflection paper on the use of heat treatment to inactivate retrovirus RD114 in live immunological IVMPs
- Public statement – Routes of administration of vaccines to poultry
- CVMP discussion document on approach to updating EU guidance on testing of IVMPs for freedom from EAs
- Immunological WP - Work plan 2015

Guideline on data requirements for changes to the strain composition of authorised equine influenza vaccines in line with OIE recommendations

- Replaces NfG: Harmonisation of requirements for equine influenza vaccines – Specific requirements for substitution or addition of a strain or strains (EMEA/CVMP/112/98-9 FINAL). ***Effective date 05/2015***
- Include removal, replacement or addition of viral strains.
- Applicable to existing, authorised inactivated equine influenza vaccines containing antigens produced by 'conventional' methods and vaccines produced using recombinant technologies where the active substance is non-replicating in the target species.

Guideline on data requirements for changes to the strain composition of authorised equine influenza vaccines in line with OIE recommendations

Quality data

- Production process of new strain(s) - same principles as for original strain(s).
- Inactivation kinetics data/inactivation control test(s) for new strain(s).
- Preparation & testing of the MS & WS.
- Methods for antigen content of each influenza component & potency of reformulated vaccine (batch potency test the same) + validation of tests.
- 1 pilot scale size batch (2 commercial later), shelf-life.

Guideline on data requirements for changes to the strain composition of authorised equine influenza vaccines in line with OIE recommendations

Safety data

- No increase in number of strains: no specific safety studies, monitor systemic & local reactions in efficacy studies, compare safety profile of modified vaccine with authorised formulation.
- Increase in number of strains: safety testing according to vaccination schedule in a minimum of eight horses (3rd dose after 2 weeks post 2nd vacc.), compare safety profile of modified vaccine with authorised formulation.

Guideline on data requirements for changes to the strain composition of authorised equine influenza vaccines in line with OIE recommendations

Efficacy data

- Immunogenicity of reformulated vaccine according to testing requirements of Ph. Eur. monograph 249 'Equine influenza vaccine (inactivated)' - challenge for at least one of the strains in modified vaccine.
- Other strains present in modified vaccine - correlation between antibody levels and protection – serology sufficient - no challenge required.
- Duration of immunity data required (commitment possible).

Guideline on data requirements for changes to the strain composition of authorised equine influenza vaccines in line with OIE recommendations

Field data

- Performance of vaccine under field conditions – evaluation as part of routine pharmacovigilance monitoring. (change in PSUR schedule).

Removal of a strain(s)

- No safety or efficacy data if no other differences to formulation, evaluation of absence of any impact of the removal on the induction of protection, for at least one of the retained strains, challenge data are available.

Reflection paper on the replacement of cell lines used for the production of IVMPs

Replacement of a MCS by a MCS of the same cell line

- Equivalence of the two MCSs: document & compare history & performance of the two MCSs.
- Control of the new MCS according to Ph. Eur. 5.2.4. 'Cell culture for the production of veterinary vaccines' & for freedom of EAs (including RD114).
- Compare manufacturing process.
- Consistency of production - two pilot batches & one full scale batch.
- No additional safety or efficacy testing necessary if specifications of finished product unchanged & there only minimal change to manufacturing process.

Reflection paper on the replacement of cell lines used for the production of IVMPs

Replacement of a MCS by a MCS of different cell line

- Confirmation - finished product unchanged re quality, safety, efficacy.
- Changes to starting materials, in process & finished product controls - restricted as much as possible.
- MCS characterisation, consistency & shelf-life.
- Laboratory safety & efficacy tests required - challenge trials can be replaced by valid alternative methods.
- Field trials in exceptional cases only.

For consultation 31/03/2015

Reflection paper on the use of heat treatment to inactivate retrovirus RD114 in live immunological IVMPs

- Data requirements to introduce heat treatment to inactivate retroviruses & to show absence of negative impact on the IVMP.
- Heat treatment: define parameters & provide evidence that this treatment will effectively inactivate the replicative retrovirus RD114.
- Possible impact: higher amount of antigen, may induce selection of live virus mutants (quasispecies).
- No negative impact on quality (no change in manufacturing process & specifications), safety (overdose testing) & efficacy (under laboratory conditions according to immunogenicity test in Ph.Eur. monographs).

For consultation 31/03/2015

Public statement – Routes of administration of vaccines to poultry

- Inconsistencies in different legal provisions for routes of administration for IVMPs in poultry (Dir. 2009/9/EC, Ph.Eur. monograph 0062, Regulation (EC) No 1234/2008).
- To clarify the regulatory requirements for proving safety & efficacy for the different routes of administration of IVMPs in poultry (e.g spray, drinking water).
- Safety & efficacy data supporting all proposed administration routes required to determine the risk/benefit balance for all administration routes.

CVMP discussion document on approach to updating EU guidance on testing of IVMPs for freedom from EAs

- Table of extraneous agents to be tested for in relation to the GL on requirements for the production and control of IVMPs – draft for consultation (end 05/2013).
- March 2013 (EMA-IFAH Info day): Intensive discussions with industry including bilateral discussion & recommendations – ongoing.
- Further discussions in CVMP/IWP & together with Group 15V of EDQM.
- Split the current Table (7BIm10a) into two parts
  - Describing the general approach & principles for testing for EA together with lists of agents per species for which testing should be carried out.
  - Document on tests found to be suitable within the EU for EA testing.

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Reflection paper on the risks that should be considered prior to the use of unauthorised vaccines in emergency situations	Release for public consultation
GL on data requirements for IVMPs intended for MUMS/limited markets as well as the accompanying table listing the limited markets for IVMPs & a document on inclusion & exclusion criteria for this accompanying table	Release for public consultation
Veterinary allergens	Reflection paper
Guidance on statistical principles for veterinary clinical trials for IVMPs	Reflection paper

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Guideline on regulatory acceptance of 3Rs (replacement, reduction, refinement) testing approaches	Multidisciplinary project led by JEG 3Rs involving other WPs
Review and update of guidelines to implement best practice with regard to 3Rs (replacement, reduction and refinement) in regulatory testing of medicinal products	
Guidance on transferring quality control methods validated in collaborative trials to a product/laboratory specific context	
VICH GL on the harmonisation of criteria to waive TABST for live vaccines for veterinary use	Reflection paper

Thank you for your attention