Human and veterinary pharmaceuticals regulation

Towards EU accession: Serbia's regulatory challenges, expectations and opportunities

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Republika Srbija
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Ministarstvo poljoprivrede, šumarstva i vodoprivrede,
Uprava za veterinu

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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Добар дан

Immunologicals / New developments

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Directive 2009/9/EC

The updated technical requirements apply to all immunological veterinary medicinal products (IVMPs) except when the products are intended for use in some species or with specific indications as defined in Title III and in relevant guidelines or in Title IV

- Similar biological veterinary medicinal products
- Applications under exc. circumstances for Foot-and-Mouth Disease (FMD), Avian Influenza (AI) and Bluetongue (BT)
- Minor use and Minor species
- Multistrain dossier

Part I: Summary of the Dossier

Diluents may be packed together with the vaccine vials or separately

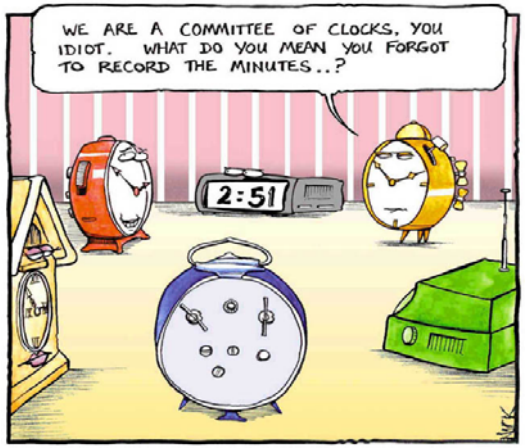
- Clarification: information on the diluents needs to be in the dossier but it is possible that different preparations of the final product can be prepared, which may be for different routes or methods of administration

Part II: Quality

E. Control Tests on the Finished Product

3. Batch titre or potency
   - A quantification of the active substance shall be carried out on each batch to show that each batch will contain the appropriate potency or titre to ensure its safety and efficacy

6. Safety tests
   - Routine application of the batch safety test may be waived in the interests of animal welfare…



Part II: Quality

G. Stability Tests

- Stability data obtained from combined products may be used as preliminary data for derivative products containing one or more of the same components

- Information on the efficacy of preservatives in other similar immunological veterinary medicinal products from the same manufacturer may be sufficient

Part III: Safety Tests

In the case of IVMPs containing a live organism the dose shall contain the maximum titre

For inactivated vaccines it should be the maximum antigen content unless justified - linked to quantification of the active substance

Part III: Safety Tests

Potential risk resulting from exposure to humans

Part III: Safety tests

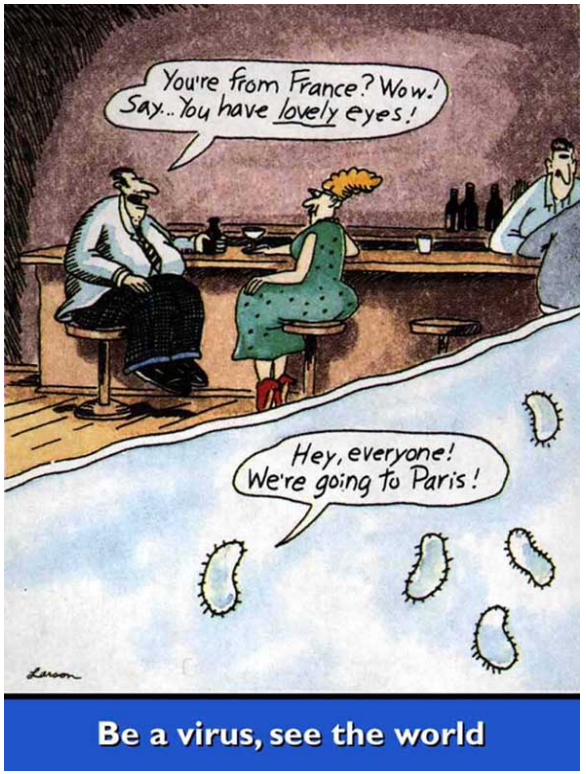
One dose study

- May be part of repeat dose study
- May be omitted if overdose study have revealed no signs of systemic or local reactions

Overdose study

- Only live IVMPs require overdose testing

Part III: Safety Tests



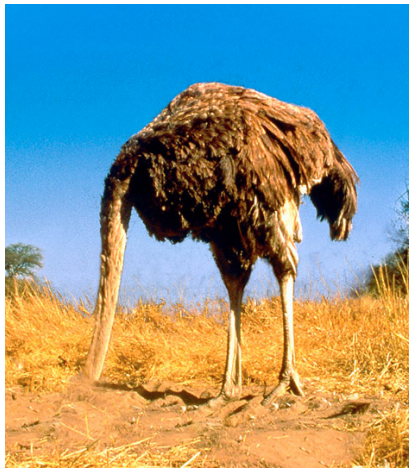
Dissemination in the vaccinated animal

- In the case of live vaccines for zoonoses the studies shall take particularly into account the persistence of organism at the injection site

Reversion to virulence

- Serial passage through 5 groups of animals

Part III: Safety tests



User safety

Interactions

- Compatibility statements in SPC shall be investigated and described

Environmental risk assessment

Genetically Modified Organisms (GMOs)

Field studies

- Standard batches may be used – both safety and efficacy in the same field studies

Part IV: Efficacy tests

Field trials to be conducted in accordance with established principles of Good Clinical Practice (GCP)

Maternally derived antibodies (MDA) *if appropriate*

Onset of Immunity (OOI) and Duration of Immunity (DOI) *unless justified*

Part IV: Efficacy Tests

Concurrent or simultaneous use may be allowed if supported by appropriate studies

For marker vaccines where efficacy claim is reliant on *in vitro* diagnostic tests, sufficient data needed to allow adequate assessment

Part IV: Efficacy tests

Laboratory trials

- For live vaccines min titre/potency unless justified, for other products the minimum active content

Field studies

- Standard batches may be used – both safety and efficacy in the same field studies

Vaccine Antigen Master File

Stand alone part of the dossier for a vaccine

All relevant information on quality concerning each of the active substances

May be common to one or more monovalent and/or combined vaccines presented by the same applicant or Marketing Authorisation Holder (MAH)

Multistrain dossier

FMD, AI and BT – antigenically variable viruses

Single dossier containing the data of the different options of strains/combinations of strains for the authorisation of vaccines

New Developments

Biologics = biological medicinal products

A product, the active substance of which is a biological substance. A biological substance is a substance that is produced by or extracted from a biological source and for which a combination of physico-chemical-biological testing and the production process and its control is needed for its characterisation and the determination of its quality.

What are they?

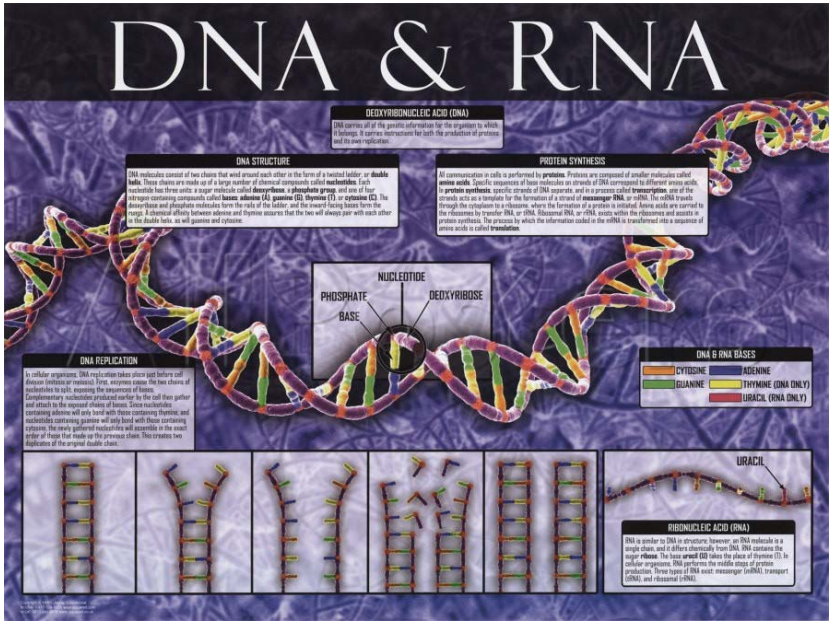
Recombinant proteins, monoclonal antibodies, blood products, immunological medicinal products such as sera and vaccines, allergens, and advanced technology products such as gene and cell therapy products.

In addition, on scientific grounds, a number of other products should be considered biological medicinal products, because they meet the aforementioned legal criteria of biological origin and complexity.

But no biological veterinary medicinal product definition or legal basis!

Medicinal products containing active substances of biological origin

Committee for Medicinal Products for Veterinary Use (CVMP) analysis of the functioning of current veterinary legislation and proposals for its evolution and comments on the Commission paper (EMA/CVMP/38660/2010)



Why discuss biologics on the veterinary side now?

Number of centrally authorised products (except vaccines): to date **2**

Virbagen Omega for cats and dogs– Recombinant Omega interferon of feline origin

Improvac for male pigs - Gonadotropin releasing factor (GnRF) analogue-protein conjugate (a synthetic peptide analogue of GnRF conjugated to Diphtheria Toxoid)

Veterinary biologics - GMOs

Suvaxyn Aujeszky 783 o/w live attenuated gene deleted Aujeszky disease virus strain

ProteqFlu; ProteqFlu-Te equine influenza recombinant canarypox virus

Equilis StrepE live deletion mutant *Streptococcus equi* strain TW928

Purevax FeLV; Purevax RCPCh FeLV; Purevax RCP FeLV, Eurifel RCP FeLV FeLV recombinant canarypox virus

Vaxxitek HVT + IBD live recombinant vaccine against infectious bursal disease and Marek's disease

Scientific Advice applications

8 confidential but including

- Plasmid **DNA** vaccine
- **recombinant** hormones
- **rDNA** produced highly immunogenic protein
- double stranded **RNA** for treatment of an infectious disease
- pegylated **granulocyte** stimulating factor

What are the main discussion points

- Are they veterinary medicinal products?
- What about Maximum Residue Limits (MRLs) for products intended for food producing species?
- Are they a GMO?
- What are the technical requirements for these products?
- How to assess?
- Guidance needed?

Guidance will be needed

Who has the expertise/experience to provide such guidance?

What should the guidance focus on?

- Quality
- Safety
- Efficacy

Hvala vam / Thank you

The new technical requirements explained in this talk as well as the new developments discussed show a continued need for an up-to-date, functioning and pro-active regulatory framework for immunological/biological veterinary medicinal products…