EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Issues for Immunologicals for SME applicants

Veterinary SME Workshop
"Veterinary regulatory support for SMEs"
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Current Situation

me

your project

others

industry

science

regulation

administration

market

finances

you

Clear understanding ⇔ clear answers

Pathway

Project to be positioned correctly

1 Type of product

2 Market

3 Constraints

Type Of Product

Project intended to become a veterinary medicinal product (VMP)?

If so, which kind of VMP?

VMP ⇒ research phase (and proof of concept) to be done in view of granting a marketing authorization

Right from the Beginning

→ Specific rules and constraints from scientific, industrial, regulatory and administrative points of view

VMP ? (1)

What is a veterinary medicinal product ?

→ definition of Directive 2001/82/EC, Title I, article 1

“Any substance or combination of substances presented for treating or preventing disease in animals.

Any substance or combination of substances which may be administered to animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in animals is likewise considered a veterinary medicinal product.”

VMP ? (2)

Court clarification - Judgment of the Court (Fifth Chamber) of 21 March 1991, Court Case C-369/88

→ Medicinal product by function

→ Medicinal product by virtue of its presentation

VMP ? (3)

Medicinal product by virtue of its presentation :

“A product may be regarded as being a medicinal product "by virtue of its presentation"... if its form and the manner in which it is packaged render it sufficiently similar to a medicinal product and, in particular, if on its packing and in the information provided with it reference is made to research by pharmaceutical laboratories, to methods or substances developed by medical practitioners or even to testimonials from medical practitioners commending the qualities of the product”.

VMP ? (4)

Examples :

VMPs : injectables, claim for a therapeutic indication, hyperimmunization of donor animals for serum/colostrum ….

Still some grey zones : standard colostrum by oral route, product to induce a flora barrier effect …

⇒ decision on a case-by-case basis

⇒ seek advice from EMA (or national competent authorities)

We can help only for (future) VMP

VMP (1)

For VMPs, registration of virtually everything is necessary : engineering, strains, type of animals, protocols, methodology, products used, batches, amounts, results (even if not satisfactory) …

Need to trace back very frequent for VMP → could deeply impact the benefit-risk balance.

VMP (2)

Examples :

• since 1995, pharmaceutical companies asked to identify all raw material of ruminant origin used (TSE)

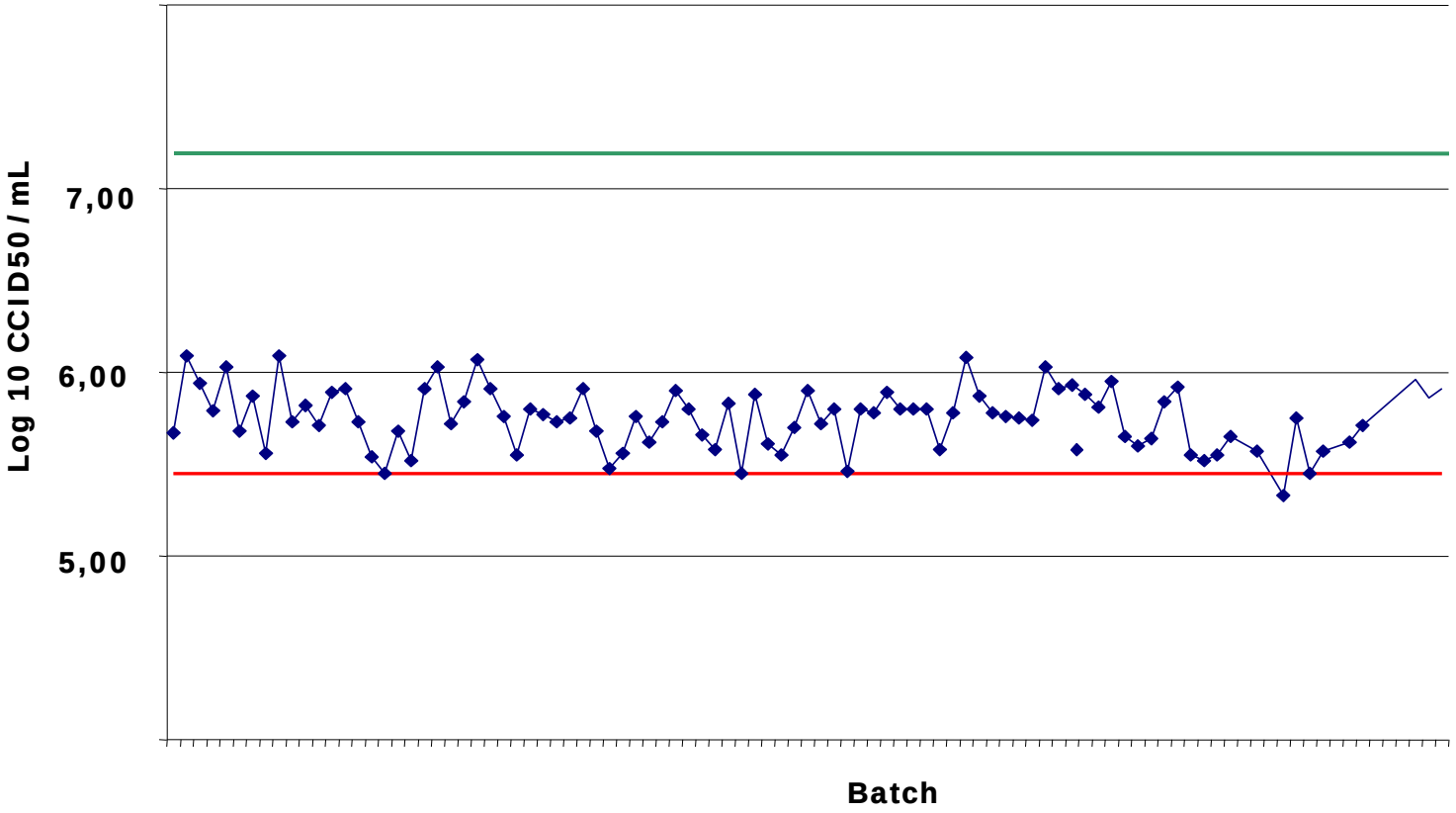
→ Master seeds sometimes established 30-40 years before 1995.

• use of batches of non-conforming bovine serum in production processes – identified in 2013, traced back to 2001.

VMP (3)

Examples (cont'd):

- control charts



Which Kind of VMP ? (1)

Immunological VMP : “a veterinary medicinal product administered to animals in order to produce active or passive immunity or to diagnose the state of immunity” (definition of Directive 2001/82/EC, Title I, article 1)

Chemical VMP : defined as opposed to Immunologicals (Directive 2001/82/EC, Annex I, Title I: “the following requirements shall apply to VMPs other than immunological VMPs…”)

⇒ Both covered by Directive 2001/82/EC
(modified by Directives 2004/28/EC & 2009/9/EC)

Which Kind of VMP ? (2)

Both chemical and immunological VMP

for example : cytokins (chemically defined, but immunological functions).

⇒ mixture of requirements as laid down

by Directive 2001/82/EC & co.

Neither chemical nor immunological VMP

for example : stem cells for therapeutic use.

⇒ no official guidance yet

Which Kind of VMP ? (3)

Is it innovative ? ⇒ different situations:

→ really and completely new, almost no experience gained (if any), nowhere (human sector, other countries, …)

Ex: use of bacteriophages as VMP, most of cytokines, …

⇒ Measures to accompany and support evolving knowledge

not available…

Which Kind of VMP ? (4)

→ really new, but only on few aspects

Ex: GMO strain for a vaccine against a standard infectious disease.

→ new only for the EU veterinary sector, knowledge do exist elsewhere

Ex: blood products (a lot of knowledge do exist on EU human side).

Which Kind of VMP ? (5)

⇒ In the 2 latter cases, EMA & CVMP can provide some guidance

BUT

Experience gained in one species is not systematically applicable to another one !!!

- in particular with regard to the immune system

Market (1)

- What is achievable with your product?
- With which targets?

target species (subpopulation: laying hens, fattening pigs, …), therapeutic indication(s),…

- In which countries?

diseases/needs not homogeneously distributed throughout the world or within EU.

- With which formulation?

live/inactivated vaccine, protein, adjuvant, number and way(s) of administration, …

- etc….

Market (2)

- Similar products already existing?
- Restricted to limited market/MUMS?
- Compliant with company's commercial choices? (range of products, specializations, …)
- VMP economically viable?
- etc …

Constraints - Industrial

→ important, but not for EMA & CVMP : production costs, easiness to produce and to control, yields …

Good Laboratory Practice (Directive 2004/9/EC): not compulsory as such for research phase and for proof of concept, but might become relevant if corresponding data presented in a dossier for marketing authorization.

Constraints – Administrative & Procedures (1)

- Directive 2001/82/EC as amended
  - norms and protocols
- Regulation (EC) 726/2004
  - EMA & GMOs
- Regulation (EC) 470/2009
  - MRLs
- Directive 2001/18/EC
  - deliberate release of GMOs

Constraints – Administrative & Procedures (2)

Definitions of GMO ≠ when Regulation (EC) 726/2004 is compared to Directive 2001/18/EC.

Roughly : for VMPs using recombinant DNA technology, Directive 2001/18/EC is part of Regulation (EC) 726/2004, but fully applicable only if continued propagation of host organism.

Constraints - Scientific (1)

- GMO constructs plasmid carrying drug resistance gene(s)

→ to be chosen adequately (MRL, antibioresistance, antibiotics of 3rd generation, …)

- Transmissible Spongiform Encephalopathy

→ note for guidance minimizing the risk (EMA/410/01 rev.3)

Constraints - Scientific (2)

- Interference with diagnosis, control or eradication programs

→ community & national law

- Epidemiologic evolution

Ex: vaccines against avian Influenza

- Import of biological material, implementation of clinical field trials

→ national competence

Constraints - Scientific (3)

Linked to practical constraints:

number of injections to be limited for beef cattle …

Linked to technical constraints:

injectables not always useful….

Constraints - Scientific (4)

- Linked to environmental constraints:

→ integration of plasmid DNA into the genome of injected animals.

→ spread by uncontrolled means (fleas carrying virus for wild rabbits)

- Linked to biological constraints:

live Aujeszky vaccine in ovines

→ all animals died (2400)…

(Res.Vet.Sci., 2013,AOP, 4p.-DOI 10.1007/s11259-9568-8)

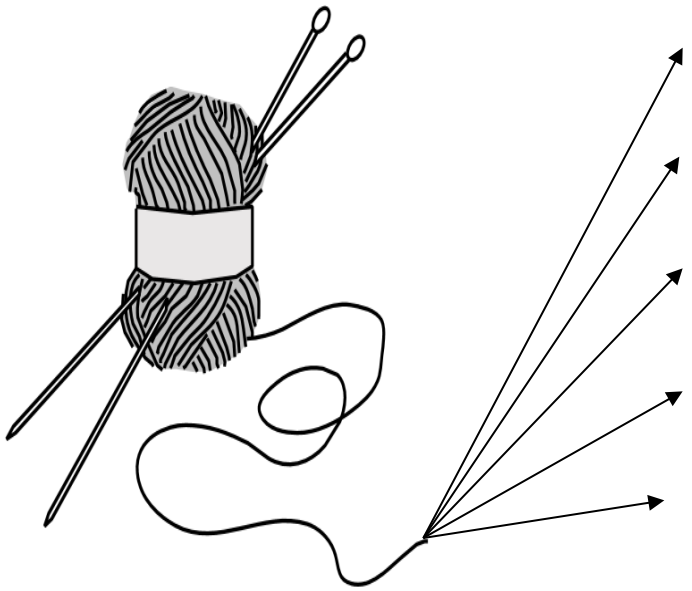
Constraints - Scientific (5)

Linked to immunological constraints:

Ex : vaccines against avian Influenza

- chicken : 1 injection sufficient
- duck : 2 injections needed
- goose : 3 injections needed
- Ratites : nothing happens after injections
- prey birds : quick and high seroconversion, but non-lasting

Situation After the Workshop?



regulation
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others

yippee

Thank You for Listening!

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