Association of Veterinary Consultants

VIEW OF THE INDUSTRY

LATEST SCIENTIFIC GUIDANCE

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Prepared jointly by:

Association of Veterinary Consultants

animalhealth europe

Access VETMED

Committed to animal well-being in Europe

Latest Topics for Guidance

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- Limited Markets, based on Art. 23 and Art. 8, Regulation EC 2019/6
- Benefit:risk balance of VMPs (EMA/CVMP/248499/2007-Rev.1)
- Phage Guideline: EMA/CVMP/NTWP/32862/2022
- Draft VICH GL60 and planned changes to Annex 21 of EU-GMP: GMP requirements for CTS
- Summary

  (Abbreviations and Listing of major Working parties' activities (on slides only))

Limited Market Art. 23

Ongoing issues

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- After 2 years of Regulation 2019/6 coming into effect, both sides, regulators and applicants gained experiences; welcome openess of CVMP for discussions, various products have been eligible for Art. 23 application

- Justification of 0.5 % prevalence for non-immunologicals, and 5 % for immunologicals? Negotiable (e.g. minor species, prevalence of >5%)?

- Exclusion of any antimicrobials and most antiparasitics, even for many „non-major species“: Why would use of life saving antimicrobial in a minor species be considered risky ? It is, after all, a “minor use”?
- Propose to revise guidance

Limited Market and Data Protection under Art. 40 (5)

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Clarification wished on the applicability of Art. 40 (5), granting additional data protection in case of variations having demonstrated:

(a) a reduction in the antimicrobial or antiparasitic resistance; or

(b) an improvement of the benefit-risk balance of the veterinary medicinal product,

the results of the concerned pre-clinical studies or clinical trials shall benefit from four years protection

- Understand that the Data Protection period also applies in case of moving an Art. 23 application to Art. 8?

Limited Market as Art. 8 application

Ongoing issues

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- Regulation provides option to grant MA for minor species under Art. 8 with potentially certain reduced datasets
- Much appreciated that CVMP is working on guidance to help applicants to better judge on the requirements for such pathway
- Hope that guidance reflects options granted by positive benefit:risk balance
- Made good experiences with CVMP under previous legislation with MUMS and hope, that future experiences will be similar.

Draft GL on Benefit:Risk balance

Initial comments

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- Legislation strengthens focus on the benefit:risk being the criterion for granting MAs
- Considered as a major tool to support innovation:
  Art. 23: „benefits should outweigh the risks“
- Agree with the „points to consider“ in principle (4.)
  - Lots of valuable explanations for all kind of products/applications
  - Worried about the introduction of the term „minor“ shortcomings in 4.1.1. and how this will influence the B:R evaluation
- 4.1.2.: e.g. AM VMPs, should also keep in mind the successes on the reduction of use in Animal Health
  - Vets need a toolbox: missing for Limited Markets

Draft GL on Benefit:Risk balance

Initial comments

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- 5. Benefit:risk principles and methodology in line with current state of the art
  - Appreciate to go for the „qualitative/structured“ method
  - Recommend to add „the availability of a VMP with a MA for the specific indication“ to the benefits

- 6. Risk assessment: follows the dossier requirements
  - Risk relating to „development of resistance“
    - This is one part to consider the benefit:risk, but not automatically leads to a negative balance
    - Propose to adjust wording here

Draft GL on Benefit:Risk balance

Initial comments

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- Impression that draft GL over-emphasizes the risks
- Permanent ongoing benefit:risk evaluation certainly a burden, in the absence of clear guidance on frequency
- Support importance to base scientific guidance on hard data and facts
- **Should not be more restrictive than regulation demands,** thus assure appropriate availability for treatment and prevention options for all animal species and indications; any other approach carries higher risks
  - Cascade should not be an argument

GMP and Clinical Trial Supplies

Use in clinical trials

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1. Test permits in certain countries

- Certain member states require GMP for CTS
- Effort for applying ever more and require more data, delaying the registration of valuable new products
- Observed certain adaptation of some NCAs, but still of concern (>50 questions, more than 30 on Quality).
- Duration for granting test permits >180 days with extensive list of questions
- Both sides learning, now down to <60-90 days

- Appreciate support by CVMP to keep EU an attractive area to conduct clinical studies

GMP requirements for CTS

Use in clinical trials

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2. GMP for API/final CTS for import of clinical supplies from 3rd territories

- VICH GL60 Section 19 contains proposal that API should have same requirements as stipulated in VICH GL9 (Good Clinical Practice) 2.7.:
  Wherever possible, investigational VMPs should be prepared, handled and stored in accordance with the concepts of GMP

- Measures under Art. 93 (2):
  - APIs for CTS not included in this advice
  - Stage of development to be considered. Applicant has to demonstrate, that product tested is „representative“ to marketed product, „follow principles of GMP acc. to stage of development“
  - **No need for further regulation**
  - **No national exemptions**, but **harmonised approach** required

GMP requirements for CTS import

Product produced to EU-GMP in 3rd territory

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Example:

Ask for advice to CA:	Dec 2021
Audit of GMP facilities in 3rd country:	
EU GMP acc. for human medicines, (MRA)	Oct 2022
Application for import:	Nov 2022
Application for test permit:	Jan 2023
Granting of last Test Permit:	Jul 2023
Import of product for BRT (quarantine)	Oct 2023
BRT final and Batch released for EU	Mar 2024
Labelling of clinical supplies	Mar 2024
Permit granted for GMP and use in CS	Mar 2024
Start of study: 1,25 years delay	Apr 2024

In future, with US MRA, BRT to be set-up in EU just for CTS?

Phage guideline
Ongoing issues

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- In principle much appreciated!
- Also at EFSA, the pathway of combination product appears of limited value, even with the options described in the guideline. Appropriate pathway?
- Investment considered very high, even if using all current regulatory tools: Right tool?
- Unlikely that we will see such products on the market, although being a useful technology to replace AMs
- As lytic phages considered safe, simpler approach than full MA to Art. 8 required, maybe similar to the approach of autologous vaccines: call for the COM.

Summary

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- All still learning to adapt to the new regulation and associated acts
- A lot of useful guidance has been issued in the last years: THANKS!
- As others, limited markets and benefit:risk GL important
- Concerned that risks over-addressed as compared to benefits and opportunities provided by the NVR

Thanks

Special thanks for input to

- **Animal Health Europe**
- **AccessVetMed**
- **Association of Veterinary Consultants:**
  - Anja Holm, Central VetPharma Consultancy, Denmark
  - Cornelia Huettinger, Argenta, Germany

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List of Acronyms

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Abb	Explanation
AM	Antimicrobial
API	Active Pharmaceutical Ingredient
B:R	Benefit:Risk
BRT	Batch Release Testing
C or COM	European Commission
CP	Concept Paper
CTS	Cinical Trial Supplies
CVMP	Committee for VMPs, EMA
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
GL	Guideline
MA	Marketing Authorisation
MAA	Marketing Authorisation Application

Abb	Explanation
MRA	Mutual Recognition Agreement for inspections between USA and EU: 2023
MUMS	Minor Uses Minor Species, as defined under Directive EC 2001/82
NCA	National Competent Autority
NVR	New Veterinary Regulation: Regulation EC 2019/6
VICH	www.vichsec.org
VMP	Veterinary Medicinal Product as defined in Regulation EC 2019/6
WP	EMA/CVMP Working Party

Working parties‘ activies 2024 of special interest:

Thanks to Anja Holm to put all this together

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CVMP:

- The Benefit-Risk-GL update (out for consultation: 30/6/24)
- COM-Advice regarding the list of essential VMPs for equines
- COM-Advice re. off-label use in aquaculture
- GL on Limited Market Products (those not fulfilling Art. 23)
- Increase the capability in modelling, simulation and extrapolation.

Working parties‘ activities 2024 of special interest:

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Efficacy WP:

- Revised GL for zootechnical VMPs (out for consultation now to 31/05/2024)
- GL on anticoccidials (Q2-24)
- GL on ectoparasiticides efficacy (Q4-24)
- CP for revision of the BioEquivalence GL
- CP for revision of Varroa GL (bees)
- CP for revision of anticancer VMP GL
- New VICH GL on fixed combinations
- New VICH GL on between-strength biowaivers

Working parties‘ activies 2024 of special interest

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Quality WP:

- GMP: VICH GL60 (cons to 25/03/2024)
- GL on synthetic peptides (cons to 30/04/2024)

Immunologicals WP:

- Concept Paper on CVMP GL on mRNA vaccines’ quality
- GL on live recombinant vector vaccines (cons to 31/05/2024)

Working parties‘ activies 2024 of special interest

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Safety WP:

- GL on User safety for topicals
- New GL consumer safety of IVMPs for endogenous targets.

Novel Therapy WP:

- VICH GL on monoclonals TAS (cons to 30/04/2024)
- Concept Paper on Nanomedicines safety (Q1-24).

Working parties‘ activies 2024 of special interest

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Environmental Risk Ass. WP:

- **Aquaculture VMPs**: CP on public health risk from AMR acquired via the environment
- **Parasiticidals for cats and dogs**: Risk Mitigation Measures GL review, Concept Paper for ERA

Working parties‘ activies 2024 of special interest

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Antimicrobial WP:

- Updated GL on public health risk re AMR from VMPs (Q3-24)
- **New GL on post-auth studies for AM-products**
- **Reflection Paper on diagnostic tests for AMs (2025)**
- List of candidate products for adjustment of dosage regimens (Q2-24).