EUROPEAN MEDICINES AGENCY

Promoting the authorisation of alternatives to veterinary medicinal antimicrobials in the EU

3rd International Symposium on Alternatives to Antibiotics - ATA 2019
16-18 December 2019, Bangkok, Thailand

Presented by Dr. Javier Pozo on 18 December 2019
European Medicines Agency

An agency of the European Union

Content of the presentation

- Alternatives to antimicrobials - a key priority
- Reflection paper promoting alternatives to antimicrobials
- Current situation and gaps analysis of measures to promote authorisation
- Looking ahead - Opportunities
- Key messages

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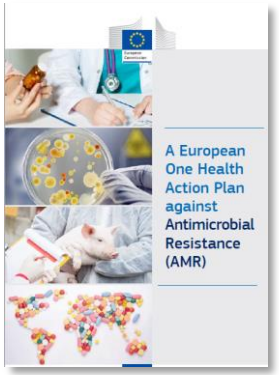
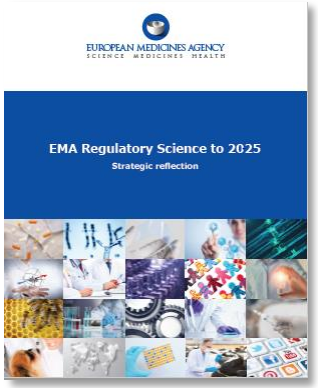
Alternatives to antimicrobials – A strategic priority in the EU

- AMR recognised as a **global threat** to human and animal health
- Fostering the development, authorisation and use of alternatives to antimicrobials is one of the pillars of fighting AMR
- **Strategic priority** for the EU and the European Medicines Agency (EMA)





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Alternatives to antimicrobials – A strategic priority in the EU

- Alternatives products that have the potential to reduce and/or replace the current use of antimicrobials include:
    - Vaccines
    - Immunoglobulins
    - Immunostimulants of the innate system
    - Bacteriophages
    - Bactericidal compounds
    - Probiotics
    - Gene-editing products

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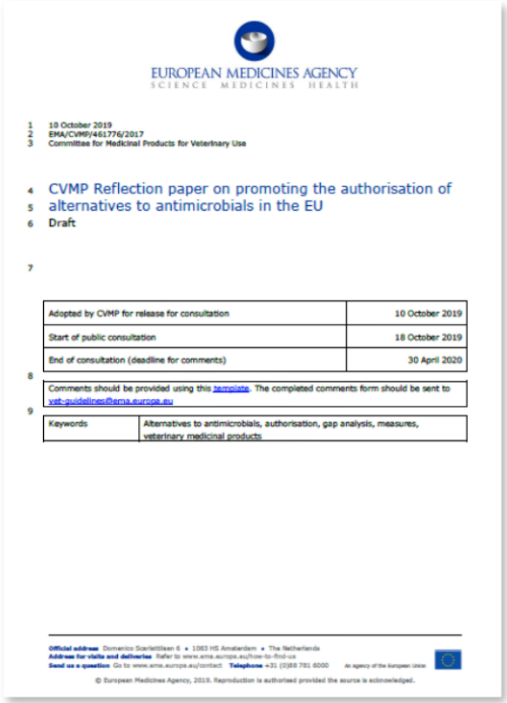
Reflection paper on promoting the authorisation of alternatives to antimicrobials in the EU



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SCIENCE MEDICINES HEALTH

10 October 2019
EMA/CVMP/461776/2017
Committee for Medicinal Products for Veterinary Use

CVMP Reflection paper on promoting the authorisation of alternatives to antimicrobials in the EU
Draft

Adopted by CVMP for release for consultation	10 October 2019
Start of public consultation	18 October 2019
End of consultation (deadline for comments)	30 April 2020

Comments should be provided using this template. The completed comments form should be sent to vet-guidelines@ema.europa.eu

Keywords	Alternatives to antimicrobials, authorisation, gap analysis, measures, veterinary medicinal products

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- Aim:
  - Perform a gap analysis of measures in place to support the authorisation of alternatives to antimicrobials
  - Identify possible actions and activities to address those gaps
  - Scope limited to veterinary medicinal products in line with the mandate of the CVMP
  - Reflection on experience, discussion with regulators, feedback from stakeholders, outcome of previous conferences

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Reflection paper on promoting the authorisation of alternatives to antimicrobials in the EU

Gaps were identified in:

- EU current regulatory framework for VMPs
- support given to developers and applicants
- strategic collaboration and communication with stakeholders

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Gaps in the regulatory framework

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Current regulatory framework for veterinary medicinal products (VMPs) in the EU

- Definition of VMP in legislation (Directive 2001/82/EC; also in new Regulation 2019/6):

"any substance or combination of substances which fulfils at least one of the following conditions:

(a) it is presented as having properties for treating or preventing disease in animals;

(b) its purpose is to be used in, or administered to, animals with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action; (…)"

- Regulatory framework for VMPs:
  - Directive 2001/82/EC (new Regulation 2019/6 to be implemented from Jan 2022)
  - European Pharmacopoeia texts and monographs
  - General and specific guidelines (CVMP, VICH,…)

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Current regulatory approach for alternatives to veterinary medicinal antimicrobials

Alternative to antimicrobials products:

- Treated in principle as any other application for authorisation
- Some products have been authorised for many years e.g. vaccines
- Regulatory challenges are not unique to alternatives but shared with all type of innovative technologies or approaches
- General recognition that current regulatory framework is not well adapted to accommodate this type of products
- Interest of the authorities to promote authorisation of alternatives

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Gaps in the regulatory framework -1

- Lack of consistent terminology and definitions
- Challenges in classification – borderline products
  - Depending on presentation, intended use and claims made, products may be classified either as veterinary medicinal product, feed additive or biocide
  - Regulatory framework to be applied and the authority handling authorisation depends on classification

Authority	Type of product	Regulatory framework
European medicines agency (EMA)	Veterinary medicinal product	Directive 2001/82/EC*
European Food Safety Authority (EFSA)	Feed additive	Regulation (EC) 1831/2003
European Chemical Authority (ECHA)	Biocide	Regulation (EU) 528/2012

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Gaps identified in the regulatory framework - 2

- Regulatory framework not adapted – new approaches/paradigms needed
  - Demonstration of safety and clinical efficacy:
    - Efficacy endpoints, efficacy claims: descriptive claims acceptable?
    - How to design trial to support them?
  - Approach to benefit-risk evaluation
    - How to factor-in the positive effect in reducing the need for antimicrobials
- Lack of specific guidance increases uncertainty – explore development of specific guidance

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Gaps in support to developers and applicants

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Support tools available to developers and applicants

Advice

- **Innovation task force (ITF):** Early stages of development, general or product-specific, advice on legal, regulatory and /or scientific aspects
- **Scientific advice:** Later stages of development, pre-submission or during evaluation
- **Pre-submission meetings:** Later stages of development, product-specific
- **Advice from ADVENT (novel therapies):** General guidance e.g. Q&A documents on specific topics

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Support tools available to developers and applicants

Incentives

- **Small and medium-sized enterprise scheme (SME):** Administrative, regulatory and financial support to SMEs
- **MUMS/Limited market scheme:** Reduction in data requirements and financial incentives (food-producing species)

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Gaps in the support to developers and applicants

- Need for advice at early stages of development
  - Promote and optimise use of ITF (EMA) and innovation offices (NCAs)
- Many SMEs companies unaware of regulatory requirements and assistance provided by EMA
  - Promote EMA and NCA incentives to SMEs working in the area of alternatives
- Creation of 'pull incentives' – need for new financial models
  - Explore financial or other incentives to authorisation of alternative products

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Gaps in strategic collaboration and stakeholder engagement

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Gaps in strategic collaboration and stakeholder engagement

- Communication with stakeholders
  - Create a platform of communication and dialogue with industry, researchers e.g. a public-private partnership
  - Inclusion as priority topic in the EMA Regulatory Science Strategy to 2025
- Develop objective targets to monitor success of measures to promote alternatives
  - Draft roadmap with targets for development – identify alternatives with greatest potential
- International collaboration

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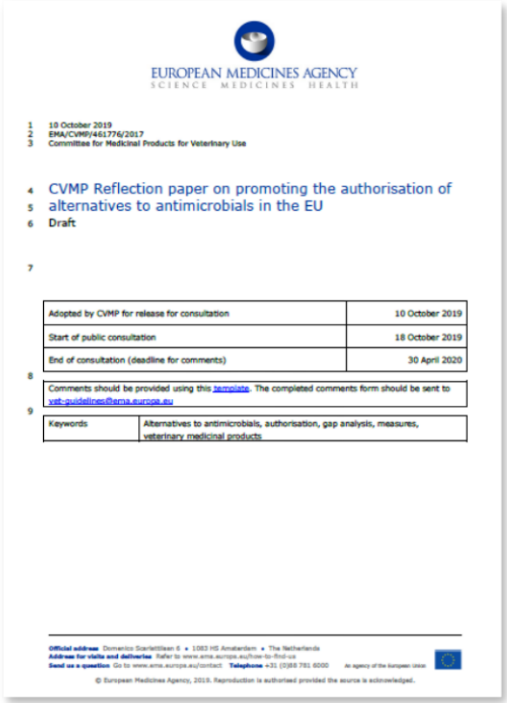
Reflection paper on promoting the authorisation of alternatives to antimicrobial veterinary medicinal products in the EU



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10 October 2019
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Next steps

- Public consultation open until 30 April 2020
- Comments from stakeholders sought
- Document and instructions on how to send comments available at: https://www.ema.europa.eu/en/documents/scientific-guideline/cvmp-reflection-paper-promoting-authorisation-alternatives-antimicrobials-eu_en.pdf

Set priorities and define next steps and actions based on the results of gap analysis and feedback from consultation

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Opportunities – Looking ahead

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Opportunities – New regulatory framework

- New Veterinary Regulation 2019/6 on veterinary medicinal products

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English edition — Legislation — Volume 62, 7 January 2019

Contents

REGULATION (EU) 2019/6 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC (Text with EEA relevance)

https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32019R0006&from=EN

Ref. Ares(2019)5494385 - 30/08/2019

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SCIENCE MEDICINES HEALTH

29 August 2019
EMA/CVMP/351417/2019
Committee for Medicinal Products for Veterinary Use

Advice implementing measures under Article 146(2) of Regulation (EU) 2019/6 on veterinary medicinal products – Scientific recommendation on the revision of Annex II to Regulation (EU) 2019/6 on veterinary medicinal products

https://ec.europa.eu/food/sites/food/files/animals/docs/ah_vet-med_imp-reg-2019-06_ema-advice_art-146-2.pdf

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New Regulation (EU) 2019/6 - Highlights

- Adapt regulatory framework to scientific progress
- Reduce administrative burden and increase availability
- Tackle AMR and incentivise the development of new antimicrobials
- Protection of data documentation for new products
- Mandate NCs to support SMEs
- Open the centralised route to all products

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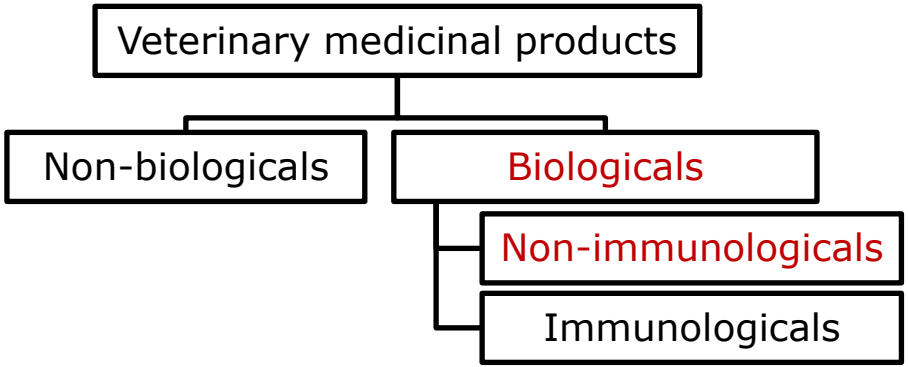
Reg. (EU) 2019/6 - Impact on authorisation of alternatives

- Classification of VMPs: Coordination group of MSs to provide recommendations on classification of borderline products
- New categories of VMPs with general data requirements defined for each category: Easier to accommodate alternative products, allows more flexibility



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Reg. (EU) 2019/6 - Impact on authorisation of alternatives

- New technical requirements for novel therapies
  - General requirements on quality, safety and efficacy
  - Specific requirements for certain products e.g. phage therapy, RNA antisense therapy and RNA interference therapy products

- Increase availability of vaccines
  - Vaccine antigen master file
  - Vaccine technology platform master file
  - Revision of multi-strain dossier
  - Limited markets

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Key messages

- Fostering the development, authorisation and use of alternatives to antimicrobials is an effective way to reduce antimicrobial use and must be a key priority
- Main regulatory challenges: uncertainty on classification and the approach to demonstrate safety, efficacy and the overall positive benefit/risk balance
- Early dialogue and collaboration between researchers, industry and regulators essential
- The new Regulation (EU) 2019/6 offers a more flexible, accommodating regulatory framework for alternative products. This potential should be further developed.
- Gaps analysis will be used to establish priorities and define next steps and necessary actions to address the key gaps identified.

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Thank you for your attention

Further information

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