EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Alternatives to Antibiotics - The EU Approach

International Symposium Alternatives to Antibiotics (ATA) – Challenges and Solutions in Animal Production,

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Content of the presentation

- Alternatives to antibiotics within EU antimicrobial resistance strategy
- The challenges that alternatives represent to the regulatory approach
- How these challenges are being met within the EU
- International cooperation
- Looking forward – the key messages

Alternatives to antibiotics – A strategic priority in the EU

- The European Commission Action Plan on Antimicrobial Resistance adopted in November 2011 places great emphasis on developing new antimicrobials *or alternatives to antibiotics*
  - http://ec.europa.eu/dgs/health_consumer/docs/communication_amr_2011_748_en.pdf
- The EMA/CVMP Strategy on Antimicrobials states that
  - "CVMP wishes to encourage an increased level of innovation on treatment alternatives for infectious diseases"
  - http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/07/WC500109137.pdf

Where do Alternatives to Antibiotics (ATA) fit within EU Antimicrobial Strategy?

Commission 5 Year Action Plan

- Action n° 1: Strengthen the promotion of the appropriate use of antimicrobials in all Member States.
- Action n° 2: Strengthen the regulatory framework on veterinary medicines and on medicated feed.
- Action n° 3: Introduce recommendations for prudent use in veterinary medicine, including follow-up reports.
- Action n° 4: Strengthen infection prevention and control in healthcare settings.
- Action n° 5: Introduce a legal tool to enhance prevention and control of infections in animals in the new Animal Health Law.
- Action n° 6: Promote, in a staged approach, unprecedented collaborative research and development efforts to bring new antimicrobials to patients.
- Action n° 7: Promote efforts to analyse the need for new antibiotics into veterinary medicine.
- Action n° 8: Develop and/or strengthen multilateral and bilateral commitments for the prevention and control of AMR in all sectors.
- Action n° 9: Strengthen surveillance systems on AMR and antimicrobial consumption in human medicine.
- Action n° 10: Strengthen surveillance systems on AMR and antimicrobial consumption in animal medicine.
- **Action n° 11: Reinforce and co-ordinate research efforts (including alternatives to antibiotics)**
- Action n° 12: Survey and comparative effectiveness research.

- **Developing ATA is only one of many measures required for an effective plan to combat AMR**

Summary of the CVMP strategy on antimicrobials 2011-2015

- CVMP perceives the need for effective antimicrobial treatment for relevant indications in all species.
- **CVMP wishes to encourage an increased level of innovation on treatment alternatives for infectious diseases**.
- Authorised antimicrobials should have product information recommending the products to be used in a responsible way to avoid unnecessary selection pressure for AMR.
- Pivotal clinical trials should be conducted according to responsible use principles.
- Risk mitigation measures at a proportionate level are needed to contain risks for human health.
- The need to allow off label use under some circumstances is acknowledged. However such use may constitute a non-assessed risk to public and animal health related to AMR.
- CVMP work should be seen in a context as a part of an overall EU strategy on antimicrobials.

What is the regulatory approach to ATA within the EU?

Regulatory Approach

- Treated in principle as any other application for authorisation
- In principle, ATAs have been authorised, or otherwise placed on the market, for many years in the form of vaccines, competitive exclusion products, pro- and pre- biotics, non-specific immune enhancers
- Many issues are therefore not new, just more frequent and high profile due to the urgency that exists to find alternatives to antibiotics in veterinary medicines

Regulatory approach for ATA

- Regulatory challenges are not unique to ATA but are shared with all types of innovative technologies
- Interest of authorities to promote authorisation of ATA
  - to contain risk of AMR
  - to stimulate innovation

Examples of regulatory challenges of ATA

Type of Alternative Technology	Example of regulatory challenges
Specific immune stimulation Conventional vaccines	How to design trials for acceptance of claims new to regulatory science such as 'This vaccine reduces/removes the use of (certain) antibiotics'
Non-specific immune stimulation Glycans, proteins and a variety of substances administered to stimulate non-specific immunity	Classification of the substance. This can be a complex issue depending on the nature of the substance, the way in which it is presented and the claims made. On the basis of a detailed analysis the substance may be classified as e.g. a medicine, a foodstuff, a food additive, a biocide or may be exempt from regulation.

Examples of regulatory challenges of ATA

Type of Alternative Technology	Example of regulatory challenges
Non-specific immune stimulation Cytokines, growth factors, other biologically active molecules produced by recombinant technology	Most of these molecules are being authorised for the first time in veterinary medicine and therefore guidance does not yet exist and regulatory expertise is scarce. In some regions the legislative framework has yet to catch up with scientific developments (e.g. EU)
Live biological solutions Competitive exclusion products, pre- and pro-biotics, other 'biological' alternatives to antibiotics	Classification; lack of existing regulatory guidance and expertise
GMOs	Public perception (not a regulatory issue)

Specific current activities in the EU

- European Commission request for an **opinion on new veterinary antimicrobials and alternatives** anticipated as part of Action Plan
- Proposals made to EU Commission as part **of Review of Veterinary legislation** to clarify legal status of biological veterinary products (which are not vaccines or pharmaceuticals)
- Clarifying procedure with EU Commission on procedure for **MRL status for novel biologicals** in the EU
- Encourage early engagement with applicants through the (Veterinary) **Innovation Task Force** to give a 'Soft Landing' at the EMA
- Promote the **Scientific Advice Procedure** and parallel scientific advice with the FDA
- Active engagement with **international cooperation** initiatives with FDA, Health Canada and other regulators

Key messages on ATA

- EU regulators are aware of the strategic importance of stimulating the development of ATA
- Several important initiatives are planned and in progress that will assist with authorisation of ATA in the EU
- ATA are treated as an important sub-set of innovative technologies for which a range of measure are in place to assist with access to market
- International cooperation between regulators is well established and is important to gain 'critical mass' of the limited pool of regulatory expertise in the new technologies involved