EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

CVMP ad hoc veterinary expert group on novel therapies “ADVENT”

A new group dedicated to novel therapies

Presented by Fia Westerholm on 16 April 2015
Development and evaluation of veterinary medicines

Presentation objectives

Why establish a new CVMP ad hoc expert group for veterinary novel therapies (ADVENT)?

- Novel therapy products
- Challenges posed by novel therapy products
- EMA guidance and advice to support development of novel therapy products – availability and gaps

What is ADVENT?

- Structure and organisation
- Expectations and working methods
- Priority topics

Why establish ADVENT?

Why establish ADVENT?

- Increasing number of requests for advice related to therapies that are entirely new to the veterinary domain
  - do not easily fit within the framework of existing legislation.
- Requests for advice have to date been channelled through scientific advice and more recently the innovation task force (ITF).
- Experience shows there is need to provide guidance on novel therapies that
  - is publicly available,
  - sets a precedent to be followed for future applications based on the same technology,
  - is detailed that it is useful yet flexible, not to constrain innovation or access to market.

What are veterinary novel therapies?

- Wide range of products, e.g.:
  - **new concepts** for active substances in veterinary medicine
  - **new technologies** in manufacture applied to products that may contain “classic” active substances (e.g. nanotechnology)
  - **new types of active substances** of biological origin, such as growth factors, cytokines, recombinant hormones, monoclonal antibodies and other biologically active molecules
    - as a result of advances in biotechnology, industry is increasingly developing new types of veterinary medicinal products.

What are the challenges posed by novel therapy products?

Challenges posed by novel therapy products

- For the development of new products companies need predictability in respect to data requirements and outcome of an application in order to allow time and budget planning.
- Many uncertainties with novel therapies
  - Definitions
  - Data requirements
    - Marketing authorisations
    - Maximum residue limits
  - Guidance
  - Assessment of dossier

Challenges posed by novel therapy products - product definition

- Neither pharmaceutical nor immunological veterinary medicinal product.
  - Active substance can be “biological” by nature and intended for a “pharmaceutical” indication
  - Active substance can be chemically defined molecule thus fit to the specification of a pharmaceutical but have immunological properties and immunological indication
- New therapies can concern very different types of active substances and concepts thus making it difficult to extrapolate approach for one type of product to another.
- The exact qualitative and quantitative composition may be difficult to define.

Challenges posed by novel therapy products - data requirements

- No “one fits all” set of requirements
- Tailored requirements:
  - the dossier requirements need to be tailored to the specific active substance and product
- It is often useful to review requirements step by step for the identification of suitable tailored data requirements
  - Dialogue with responsible authority recommended
  - Scientific and regulatory advice recommended

Challenges posed by novel therapy products - data requirements for marketing authorisation applications

- Data requirements under the Titles of Annex I of Directive 2001/82/EC are in general not directly applicable.
  - Often elements from both Title I (pharmaceuticals) and Title II (immunologicals) of Annex I are applicable
  - Requirements depend very much on the properties of the active substance and the specific product.

Challenges posed by novel therapy products - data requirements for maximum residue limit applications

- Legal requirement (Art 6(1) of Directive 2001/82/EC) that *pharmacologically active substances* contained in a veterinary medicinal product intended for food producing animals have maximum residue limit (MRL) classification (included in Table 1 of the Annex to Regulation 37/2010).
  - Regulation 470/2009 does not apply to "*active principles of biological origin intended to produce active or passive immunity or to diagnose a state of immunity*" (Article 1(2) of Regulation 470/2009).
  - However, active principles of biological origin, whose intended use is not to produce immunity or to diagnose a state of immunity, are not exempted by this definition.

Challenges posed by novel therapy products - data requirements for maximum residue limit applications

- The scientific rationale of the exemption rule seems to apply equally for many of these biologicals
  - e.g. stem cells.
- Other biologicals are likely to require residue and consumer safety assessment/MRL evaluations
  - e.g. some types of cytokines.
- Upon request, and with agreement of the Commission, the CVMP included exceptionally stem cells as active substance in the list of substances not falling within the scope of Regulation 470/2009 ("Out of scope list")
  - new list heading *"Biologically active constituents"*.

Challenges posed by novel therapy products - data requirements for maximum residue limit applications

- A single approach cannot be applied to this class of products as a whole.
  - Case-by-case considerations necessary.
- Recommendations by CVMP to include such biological active substance in the “Out of scope list” will continue to require approval by the Commission.
- If an MRL evaluation is necessary, the data requirements will need to be tailored to the characteristics and profile of the specific active substance.

Challenges posed by novel therapy products - status of existing guidance

- Specific guidance for veterinary products only available to a very limited extent.
- Challenging to develop guidelines without experience of assessments.
- Difficult to prioritise guideline developments and difficult to identify types of products most likely to be developed.
- More guidelines are available for human advanced therapy medicinal products.
  - In how far can/should they be applied for veterinary products?

Challenges posed by novel therapy products – assessment issues

- Regulators to prepare for submissions:
  - make available / find / develop specific expertise,
  - provide regulatory and scientific advice to specific product developments,
  - develop general guidance
- Assessment concepts developed for pharmaceuticals and immunologicals are not directly applicable.

Available EMA guidance and advice

Applicable to existing types of veterinary medicines and novel therapies

Overview of advice available	Scope
Innovation task force	Forum for *early dialogue* with applicants Novel veterinary initiatives http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000334.jsp&mid=WC0b01ac058074f177
Pre-submission meetings	Regulatory advice on intended product applications *prior to submission* http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000171.jsp&mid=WC0b01ac058002d9ab
Scientific advice	Scientific advice on product *development* of prior to submission http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000250.jsp&mid=WC0b01ac058002d4ef
EMA website	Procedural, regulatory and scientific guidance both for initiatives and products http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/landing/veterinary_medicines_regulatory.jsp&mid=
ADVENT ***new***	General advice on topics/requirements for novel veterinary medicines not related to a particular application or product http://www.ema.europa.eu/ema/index.jsp?curl=pages/contacts/CVMP/people_listing_000125.jsp&mid=WC0b01ac05808625e1

What is ADVENT?

Setting the expectations

What is ADVENT?

- ADVENT is a group of experts established under CVMP in December 2014
- Objective: to provide guidance to CVMP on the requirements for authorisation of novel veterinary medicines.
- Composition:
  - ‘core’ group of experienced regulators with a wide knowledge of the regulation of veterinary medicinal products
  - supplemented by topic groups involving experts chosen on the basis of their specialised knowledge on particular technologies
- Work programme:
  - First ADVENT work plan adopted by CVMP on 12 March 2015 including initial priority topics (EMA/CVMP/ADVENT/630656/2014)

Main objectives of ADVENT

- Main objective to *provide advice* to the CVMP on all issues relating to veterinary novel therapies, including
  - General advice on scientific and technical topics on the requirements for authorisation of therapies that are new to the veterinary domain.
  - Support dossier evaluation and referrals for novel therapies as required by the CVMP.
  - International cooperation on novel therapy related issues.
  - Advice to the European Commission on novel therapy related issues.
  - Contribution to novel therapy related workshops and training.

Advice by ADVENT

- Advice on particular topics
  - Sufficiently detailed to be useful
  - Sufficiently flexible that it does not constrain innovation or access to market.
- Objective of advice:
  - Describe an approach to development;
  - Based on the current state of scientific knowledge;
  - Advice to be updated on basis of scientific developments;

Advice by ADVENT

- Form of advice
  - Initially Questions and Answers
  - Formal guidelines later when experience has been gained.
- Availability of advice
  - Published on the Agency's website.
- Other support available for confidential advice on a particular application or product.

Identification of topics for ADVENT

- Topics are chosen on the basis of emerging and expanding interest in the society, brought to the knowledge of EMA, CVMP and ADVENT via various routes
  - Proposals and suggestions for topics from stakeholders are welcome for consideration (email: ADVENT@ema.europa.eu)
- Priority topics chosen for initial consideration
  - stem cells
    - sterility, tumourigenicity, extraneous agents
  - monoclonal antibodies and
  - cancer vaccines

More details on other EMA guidance and advice available

- Innovation Task Force (ITF)
- Scientific Advice (CVMP SAWP-V)
- Pre-submission meetings
- Guidance and guidelines on EMA website on procedural, regulatory and scientific issues.

Innovation Task Force (ITF)

- Multidisciplinary group for preparatory dialogue and orientation with applicants on innovative medicines, technologies and methods.
  - Provide a forum (soft landing zone) for innovation.
- ITF members are scientific and legal administrators appointed from different departments of the Agency including scientific, regulatory and legal competencies.
- To fulfil its task the ITF involves as appropriate experts from EMA scientific Committees and Working Parties or individual experts.
- For enquiries regarding suitability of the ITF in respect to their product or requests for ITF briefing meetings, applicants for innovative veterinary medicines are invited to send all potential applications to: vet.applications@ema.europa.eu

Innovation Task Force (ITF)

- Briefing meetings aiming to provide an early guidance and information.
- Open for veterinary medicines.
- Scope of the ITF activities encompasses:
  - emerging therapies (i.e. gene therapy, cell therapy and engineered tissues),
  - emerging technologies (i.e. new development strategies, new manufacturing approaches),
  - borderline therapeutics (i.e. combination of pharmaceuticals and devices) for which there is no established EMA scientific, legal and regulatory experience, and
  - biomarkers and new technology platforms.

Scientific Advice

- Scientific advice particularly useful for novel therapy products to provide advice to companies on the appropriate tests and studies in the development of a veterinary medicine.
- Areas for scientific advice: quality, safety, efficacy; data requirements for minor use minor species (MUMS) products; the establishment of new MRLs or extrapolation of existing MRLs.
- Scientific advice helps the applicants to ensure that the appropriate tests and studies are performed and to support predictability of outcome of an intended application.

Scientific advice

- For veterinary medicines, scientific advice is given by the CVMP on the recommendation of its Scientific Advice Working Party (SAWP-V).
- Independent of route of authorisation.
- Possibility for parallel advice with FDA: may be of particular interest for novel therapy products.
- Free scientific advice for products classified as MUMS/Limited market with fee incentives.
- 90% fee reduction for SMEs.

Summary

- Challenges posed by novel therapy products have been acknowledged concerning definitions, requirements and assessment.
- ADVENT is established to provide general advice to CVMP on scientific and technical topics on the requirements for authorisation of therapies that are new to the veterinary domain
  - First topics in consideration: *stem cells, monoclonal antibodies, cancer vaccines for animals*.
- Advice will initially be developed and published in the form of Questions and Answers on chosen topics; updated in accordance with scientific developments
- Other support is available for specific applications and products
- Stakeholders are welcome to send suggestions for *topics*

Email: ADVENT@ema.europa.eu

Thank you for your attention