EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

News bulletin for small and medium-sized enterprises

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This news bulletin is published four times a year by the SME Office of the European Medicines Agency.

The news bulletin aims to bring to the attention of SMEs, and their stakeholders, documents and activities related to the European regulatory environment.

IN THIS ISSUE:

Non-clinical and clinical guidance

A guideline on the evaluation of drugs for the treatment of gastro-oesophageal reflux disease (GORD) was released on 14 March 2011 (EMA/CHMP/EWP/342691/2009). It intends to assist applicants during the development of products for the treatment of GORD in adults and children. It will come into effect on 1 October 2011.

A reflection paper on non-clinical studies for generic nanoparticle iron medicinal product applications was released on 7 May 2011 (EMA/CHMP/SWP/100094/2011). For these generic dossiers, a pharmacokinetic comparison of different products based on plasma concentrations measurements may only reflect the clearance from plasma and may fail to detect to which extent nanoparticles are taken up by different target organs. Additional non-clinical studies of target tissue concentration will therefore be needed. The paper outlines the data that may be used to support the claim of essential similarity for these products.

The following questions and answers documents were released on:

- Pharmacokinetics dated 14 March 2011 (EMA/618604/2008 Rev. 3)
- Photosafety testing dated 11 April 2011 (EMA/CHMP/SWP/336670/2010)
- EudraLex – Volume 9A dated 29 March 2011 (Version 5.4)
- A document on 'Guideline on the environmental risk assessment of medicinal products for human use' released on 11 April 2011 (EMA/CHMP/SWP/44609/2010).

Pharmaceutical development guidance

A paper on the new EMA-FDA pilot program for parallel assessment of Quality by Design applications was released on 16 March 2011 (EMA/172347/2011). It details the background, objectives, and steps that will be taken to coordinate the parallel review and related GMP inspections. Quality by Design should be considered as a means to move toward a more proactive, risk-based approach to pharmaceutical development. It promotes the understanding of the product, its manufacturing process from product development, with quality built into it rather than being tested.

An ICH guidance on *'Topic Q3C (R5) Impurities: Guideline for residual solvents'* was released on 25 March 2011 (EMA/CHMP/ICH/82260/2006). It recommends use of less toxic solvents and describes levels considered to be toxicologically acceptable for some residual solvents. It was updated to include Part IV (Permitted daily exposure for cumene) which will come into operation in August 2011.

A draft concept paper on *'process validation of medicinal products containing biotechnology-derived proteins as active substance'* was released on 6 June 2011 (EMA/CHMP/BWP/25360/2011). Guidelines related to the quality of biologics have been developed at EU level, and several harmonised through the ICH process. However, these documents do not address aspects related to validation. The document proposes to develop a guideline in this field. It is released for consultation until 31 August 2011.

Paediatric guidance

A guideline on the *'pharmaceutical development of medicines for paediatric use'* was released on 19 May (EMA/CHMP/QWP/180157/2011). As a result of the introduction of the 'Paediatric Regulation', the number of paediatric formulations that will be developed in the future will increase. The document addresses the need for specific guidance in this field. It applies to the development of paediatric medicines in initial marketing authorisation applications and variations thereof. It is released for consultation until 31 December 2011.

GMP and GCP inspections guidance

A compilation of *'Community procedures on inspections and exchange of information'* was released on 11 March 2011 (EMA/INS/GMP/459921/2010 Rev 12 Corr). The document is a tool developed to facilitate the co-operation between the GMP inspectorates of the Member States and a means to achieve harmonisation. Although primarily directed to authorities, the document may be of interest to departments in pharmaceutical companies handling inspections.

A draft concept paper on *'Revising chapter 8 of the European Commission guide to good manufacturing practice to introduce risk-based concepts and to provide for more effective investigations and CAPA [Corrective Action and Preventative Action]'* was released on 12 April 2011 (EMA/INS/GMP/263759/2011). Chapter 8 of the EC Guide to GMP deals with complaints and product recalls. An update is proposed to reflect the need for quality risk management principles to be applied when investigating quality defect/complaint issues and when making decisions in relation to product recalls. The revision would also include reporting timelines of quality defect/complaint to the authorities in line with Directive 2003/94/EC. It is released for consultation until 30 June 2011.

A report from the workshop on *'Ethics and GCP in clinical trials outside the European Union'* was released on 17 May 2011 (Link). The meeting took place in September 2010 with international stakeholders to discuss the global framework of clinical trials. It was organised as part of the consultation process on the Agency's draft *'Reflection Paper on ethical and Good Clinical Practice (GCP) aspects of clinical trials of medicinal products for human use conducted in third countries and submitted in marketing authorisation applications to the EMA'*.

Veterinary guidance

A questions and answers document on the management and assessment of periodic safety update reports (PSURS) was published on 30 March 2011 (EMEA/126661/2009-Rev. 2). This document primarily directed at assessors from regulatory authorities assessors may also be useful to marketing authorisation holders when preparing PSURs.

A draft guideline on the production and control of immunological veterinary medicinal products was released on 30 March 2011 (EMA/CVMP/IWP/206555/2010). It outlines aspects related to the quality, safety and efficacy parts of the marketing authorisation dossier that are not clearly defined in the existing legislative requirements. It is released for consultation until 30 September 2011.

A draft guideline on the safety and efficacy of fish vaccines was released on 30 March 2011 (EMA/CVMP/IWP/314550/2010). The guideline outlines the points to consider for laboratory scale and field trials to support the safety and efficacy of such vaccines when administered in accordance with their intended use (e.g. type of fish to be used; water conditions, method of administration, use of control groups). It is released for consultation until 30 September 2011.

A guideline on determining the fate of veterinary medicinal products in manure was finalised in March 2011 (EMA/CVMP/ERA/430327/2009). It provides additional guidance to the *'Guideline on Environmental Impact Assessment [ERA] for Veterinary Medicinal Products in support of the VICH guidelines GL6 and GL38'* (EMEA/CVMP/ERA/418282/2005-Rev.1) on the studies required for the preparation of the ERA.

The following VICH guidance documents were published on 7 April 2011.

- *'Draft GL36: Studies to evaluate the safety of residues of veterinary drugs in human food: general approach to establish a microbiological acceptable daily intake'* (EMA/CVMP/VICH/467/2003-Rev.1). It provides guidance for assessing the human food safety of residues from veterinary antimicrobial drugs with regard to effects on the human intestinal flora. It is released for consultation until 14 September 2011.

- *'GL46: Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing animals: metabolism study to determine the quantity and identify the nature of residues'* (EMA/CVMP/VICH/463072/2009). It provides recommendations for these studies which are conducted in food-producing animals and are often accomplished using radiolabeled drugs. It will come into effect in February 2012.

- *'GL47: Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing animals: laboratory animal comparative metabolism studies'* (EMA/CVMP/VICH/463104/2009). The purpose of these studies is to compare the metabolites from laboratory animals used for toxicological testing to the residues of the veterinary drugs in edible tissues of food producing animals, in order to determine if the laboratory animals used for toxicological testing were exposed to the metabolites that humans can be exposed to as residues in products of food producing animal origin. It will come into effect in February 2012.

- *'GL48: Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing animals: marker residue depletion studies to establish product withdrawal periods'* (EMA/CVMP/VICH/463199/2009). Marker residue depletion studies are required to establish appropriate withdrawal periods in edible tissues including meat, milk and eggs. The guidance provides study design recommendations which will facilitate the acceptance of these studies. It will come into effect in February 2012.

Veterinary guidance continued

- *'GL49: Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing animals: validation of analytical methods used in residue depletion studies'* (EMA/CVMP/VICH/463202/2009). It provides a general description of the criteria considered suitable for the validation of analytical methods used in veterinary drug residue depletion studies. It will come into effect in February 2012.

A draft concept paper on the revision of the guideline on veterinary medicinal products containing antimicrobial substances was released on 20 April 2011 (EMA/CVMP/EWP/760764/2010). The current guideline came into effect in 2003 and attention has focused since then on the responsible use of antimicrobials and the development of antimicrobial resistance. The *'CVMP strategy on antimicrobials 2011-2015'* document and increased knowledge gained in areas relating to the efficacy of antimicrobials point to the need to revise the guideline. The concept paper on the proposed revision is released for consultation until 31 August 2011.

A guideline for the conduct of bioequivalence studies for veterinary medicinal products was released on 20 April 2011 (EMA/CVMP/016/00-Rev.2). It specifies requirements for the design, conduct, and evaluation of bioequivalence studies for pharmaceutical forms with systemic action. In addition, guidance is given on how in-vitro data may be used to allow bridging of safety and efficacy data. It will come into effect on 1 November 2011.

A revised guideline on *'Target animal safety and efficacy of veterinary medicinal products for use in farmed finfish'* was released on 17 May 2011 (EMA/CVMP/EWP/459868/2008). This revision takes into account recent developments in the field and feedback obtained from users of the previous guidance. The revised guideline only addresses finfish, as these are the main species kept under farmed conditions in Europe. It will come into effect on 1 December 2011.

A draft reflection paper on risk mitigation measures related to the environmental risk assessment of veterinary medicinal products was released on 17 May 2011 (EMA/CVMP/ERAWP/409328/2010). It provides a review of the adequacy of risk mitigation measures included in current marketing authorisations of veterinary medicinal products. The paper takes into account the current legislation and existing guidelines, as well as the experience gained formulating risk mitigation measures in line with the criteria specified in the VICH guidelines GL6 and GL38. It is released for consultation until 31 August 2011.

Regulatory guidance

Fees payable to the EMA by applicants and marketing authorisation holders for human and veterinary medicines increased by 2.1% on 1 April 2011. Details of the new fees are available in the revised fee regulation, its implementing rules and the corresponding explanatory note on fees. These new fees apply to all types of procedures handled by the Agency, including marketing-authorisation applications, post-authorisation procedures, scientific advice and inspections. Information on fee reductions for designated orphan medicinal products has also been released and is available under EMA/229775/2011.

The following questions and answers documents for human Medicines were released:

- Updated *pre*-submission guidance for the centralised procedure (EMA/339324/2007; 19 May 2011). The updates relate to invented names, dossier submission requirements, PIM.

- Updated *post*-submission guidance for the centralised procedure (EMEA-H-19984/03 Rev 19; 19 May 2011). The update relates to type 2 variations

- A revised document on generic medicines released on 29 March 2011 (EMA/393905/2006 Rev. 1)

News on EC framework programme

On 9 June 2012, the European Commission held an open day to highlight the priorities, novelties and special features of the 2012 work programme for innovative health research funding through the 7th Framework Programme. The research priorities include ageing, medical technologies and rare diseases. There will be specific support for clinical trials and a strong emphasis on the participation of SMEs in most areas. Publication of the final work programme is foreseen on 20 July 2011. Further information is available under Link.

What is new on the EMA website?

The Agency's website updated with new pages including Frequently asked questions on a variety of topics raised by stakeholders, Disease areas bringing together information related to specific diseases and a feature enabling the results of searches of human and veterinary medicines to be downloaded to a spreadsheet (Link). A section dedicated to audiovisual content has also been released compiling links to workshops and conferences organised by the Agency (Audio and video). Also of interest is a document titled 'Introduction to EU Telematics Programme'. One of its objectives is to describe the main European pharmaceutical IT systems and how they interact with each other (EMA/147558/2010).

Information on meetings

Reports and presentations of the following meetings were released:

- 'Veterinary pharmacovigilance question time: better regulation for electronic reporting and periodic safety update reports (PSURs)' (EMA/166976/2011)
- Workshop on antibacterials (EMA/257650/2011)
- SME Workshop on 'Regulatory and Scientific Advice (Link)

SME companies registered with the Agency

533 companies currently have SME status assigned by the Agency. The companies are published in the Agency's public SME registry at: http://fmapps.emea.europa.eu/SME/

Contact the SME Office

The SME Office has been set up within the Agency to address the particular needs of smaller companies. The Office aims to facilitate communication with SMEs through dedicated personnel who will respond to practical or procedural enquiries, monitor applications, and organise workshops and training sessions for SMEs. Any comments or queries on this news bulletin can be forwarded to the SME Office:

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