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.

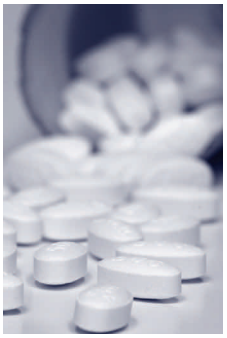
IN THIS ISSUE:

Pharmaceutical development guidance

A revised joint CHMP/CVMP guideline on the procedure for Active Substance Master File (ASMF) will come into effect on 1 October 2012 (CHMP/QWP/227/02 Rev 3; EMEA/CVMP/134/02). The objective of the procedure is to allow confidential intellectual property of the active substance manufacturer to be protected, while at the same time allowing the applicant/marketing authorisation holder to take full responsibility for the medicinal product and the quality control of the active substance. The annexes of the guideline were revised to improve the process across the European Regulatory Network.

The ICH guideline Q4B was updated to include Annex 13 (EMA/CHMP/ICH/405290/2010) which recommends that the analytical procedures described in the official pharmacopoeial texts, 'Ph.Eur. 2.9.34. Bulk Density and Tapped Density of Powders', 'JP 3.01 Determination of Bulk and Tapped Densities' and 'USP General Chapter <616> Bulk Density and Tapped Density of Powders' can be used interchangeably in the ICH regions. It will come into effect in January 2013.

A joint CHMP/CVMP guideline on setting specifications for impurities in antibiotics was released on 13 July 2012 (EMA/CHMP/CVMP/QWP/199250/2009). Antibiotics are produced by either fermentation, fermentation followed by one or more synthetic steps (semi-synthetic substances) or by chemical synthesis. Fermentation processes are more variable and the impurity profile of an active substance whose manufacturing process involves fermentation may be more complex. For this reason fermentation products and semi-synthetic substances are not included in the ICH Q3 and the VICH GL10/GL11 guidelines, which apply to impurities in active substances manufactured by chemical synthesis only. The joint guideline will come into effect on 30 June 2013.



Clinical development guidance

A revised guideline on the clinical investigation of medicinal products in Parkinson's disease came into effect on 2 July 2012 (EMA/CHMP/330418/2012 rev. 2). The document was revised to include considerations on the development of disease modifying agents.

A revised guideline on the clinical investigation of products in chronic obstructive pulmonary disease (COPD) came into effect on 1 September 2012 (EMA/CHMP/483572/2012). The changes relate to the requirements for pivotal studies, primary/secondary efficacy endpoints and the use of biomarkers.

A revised guideline on the clinical investigation of medicinal products in diabetes will come into effect on 15 November 2012 (CPMP/EWP/1080/00 Rev. 1). The main changes relate to the long-term safety assessment, the paediatric requirements and considerations for a diabetes prevention claim.

A guideline on similar biological medicinal products containing monoclonal antibodies (mAb) will come into effect on 1 December 2012 (EMA/CHMP/BMWP/403543/2010). The document complements the general guideline on biosimilars (EMEA/CHMP/42832/2005) and details the non-clinical and clinical requirements for demonstrating the comparability of two mAb-containing products from a regulatory perspective. The document may also apply to substances such as fusion proteins based on IgG Fc ('-cept' molecules).

A revised guideline on the investigation of drug interactions will come into effect on 1 January 2013 (CPMP/EWP/560/95/Rev. 1). The document is a major revision of the previous guidance. It includes information on how to study potential interactions between new medicines and medicines already on the market, and the effects of food intake. It also describes how to develop treatment recommendations based on the clinical relevance of interactions and the possibility of adjusting doses and monitoring patients during treatment.

An addendum to the guidance on the evaluation of medicinal products indicated for the treatment of bacterial infections (CPMP/EWP/558/95 rev 2) was released for consultation until 31 January 2013 (EMA/CHMP/776609/2011). It provides advice on the development of agents targeted against rare or multi-drug-resistant pathogens. The addendum also details when non-inferiority and superiority study designs are acceptable and where limited clinical data can be generated e.g. in uncommon encountered infections or (multi) resistant organisms.

A draft guideline on the clinical investigation of products in atrial fibrillation was released for consultation until 15 February 2013 (EMA/CHMP/450916/2012). It provides guidance on how to develop medicinal products in prevention of stroke and systemic embolic events (SEE) in patients with non-valvular atrial fibrillation.

Guidance for veterinary medicines

A VICH guideline GL36(R) on the safety evaluation of veterinary drug residues in human food and the establishment of a microbiological acceptable daily intake came into effect in May 2012 (EMA/CVMP/VICH/467/2003). The document provides guidance for assessing the human food safety of residues from veterinary antimicrobial drugs with regard to their effects on the human intestinal flora.

A guideline on the production and control of immunological veterinary medicinal products (IVMPs) will come into effect in January 2013. It outlines important considerations related to the quality, safety and efficacy parts of the marketing authorisation dossier that are not sufficiently defined in the veterinary dossier requirements included in Directive 2001/82/EC and the European Pharmacopoeia (Ph. Eur.). The document replaces a series of product specific guidance documents relating to live/inactivated, mammalian/bacterial/viral vaccines intended for several species.

A guidance on the assessment of *P*ersistent, *B*ioaccumulative and *T*oxic (PBT) or *v*ery *P*ersistent and *v*ery *B*ioaccumulative (vPvB) substances in veterinary medicines was released for consultation until 1 February 2013 (EMA/CVMP/ERA/52740/2012). PBT or vPvB are properties which give substances the potential to accumulate in remote environments, which is difficult to reverse as cessation of emission will not immediately result in a reduction in chemical concentration due to the long half-life. The guidance details the criteria for identification

Pharmacovigilance guidance

The first set of guidelines on good pharmacovigilance practices (GVPs) were finalised (Link). GVPs have been drawn up to facilitate the performance of pharmacovigilance activities. They apply to marketing authorisation holders in the EU, the EMA and Member States competent authorities. Each of the modules covers one major process in the safety monitoring of medicines:

- I – Pharmacovigilance systems and their quality systems
- II – Pharmacovigilance system master file
- V – Risk management systems
- VI – Management and reporting of adverse reactions to medicinal products
- VII – Periodic safety update report
- VIII – Post-authorisation safety studies
- IX – Signal management

In addition explanatory documents on the implementation of the Pharmacovigilance legislation were released:

- New European Union pharmacovigilance legislation – Key concepts (EMA/186974/2012).
- Questions and answers on the implementation of the pharmacovigilance legislation (EMA/228816/2012 – v.2).
- Extended EudraVigilance medicinal product report message (XEVPRM): Frequently asked questions and answers (FAQs) (EMA/945380/2011).

Regulatory and procedural guidance

The following updated documents were released:

- Policy on changes in scope of paediatric-investigation-plan decisions (EMA/472551/2012).
- Questions and answers on ICH guideline E3 Guidance, Structure and Content of Clinical Study Reports (Link).
- Guideline on the processing of renewals in the centralised procedure (EMEA/CHMP/2990/00 Rev.4).
- Post-authorisation procedural advice for the centralised procedure (EMEA-H-19984/03 Rev 24).
- Updated guidance on the electronic submissions of dossiers for veterinary medicinal product or MRL applications (EMA/613295/2011-Rev.1).

News from the European Commission

The European Commission adopted in July 2012 a proposal for a regulation on clinical trials for medicinal products for human use (Link). The regulation proposes to introduce a simplified authorisation procedure allowing the submission of applications to a central electronic portal and a coordinated assessment by Member States resulting in one single assessment outcome; ethical issues will still be assessed nationally. It will also introduce simplified reporting requirements for sponsors as well as controls by the Commission in Member States and third countries. The proposal has been submitted to the European Parliament and the Council which will now engage in the legislative procedure.

Meetings

The report of the following meetings was posted:

- Joint EMA/EDQM workshop on improved potency assays for inactivated influenza vaccines held on 12 December 2011 (Link)

The following workshops have been announced:

- Workshop on multiplicity issues in clinical trials, EMA, London, 16 November 2012 (Link)
- Workshop on clinical trial data and transparency, EMA, London, 22 November 2012 (Link)

SME companies registered with the Agency

1006 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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