27 **Issue 27**
March 2014

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

SME Office NEWSLETTER

Information for SMEs in the EU regulatory environment for medicines.
Published four times a year by the European Medicines Agency.

An agency of the European Union

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Pharmaceutical development guidance

A joint CHMP/CVMP guideline on process validation for finished products will come into effect on 15 June 2014 (EMA/CHMP/CVMP/QWP/BWP/70278/2012-Rev1). It provides guidance on process validation data to be submitted in regulatory submissions for the finished dosage forms of chemical medicinal products for human *and* veterinary use. The general principles detailed in the guidance may also apply to active substances.

A guideline on the use of porcine trypsin used in the manufacture of human biologics will come into effect on 1 September 2014 (EMA/CHMP/BWP/814397/2011). It details recommendations and guidance on the use of porcine trypsin, as cell culture reagent, in manufacture of human medicinal products.

An annex to ICH guideline Q4B (Link) on uniformity of dosage units will come into effect in June 2014.

Three documents were released for consultation in relation to the revision of the guideline on 'Excipients in the label and package leaflet of medicinal products for human use' (CPMP/463/00). The excipients are: benzoic acid and benzoates (EMA/CHMP/508189/2013), benzyl alcohol (EMA/CHMP/508188/2013), and ethanol (EMA/CHMP/507988/2013). The deadline for comments is 31 May 2014.

The EMA questions and answers webpage on Quality of medicines was updated (Link). It provides harmonised positions on issues, that can be subject to different interpretation or require clarification, arising from discussions during assessment procedures.

Clinical development guidance

A revised guideline on the clinical investigation of products for the treatment of lipid disorders will come into effect in June 2014 (EMA/CHMP/748108/2013). Revisions relate to the imaging modalities used as surrogate markers of outcome, and long-term safety data, including morbidity and mortality data.

An ICH guideline on photosafety evaluation of pharmaceuticals will come into effect in June 2014 (Link). It details strategies for photosafety assessment of products given by routes intended to produce systemic exposure or by the dermal route. It applies to new active substances, new excipients, clinical formulations for dermal application and photodynamic therapy products.

A reflection paper on the use of interactive response technologies (voice/web response systems) was released. It provides guidance to sponsors and interactive response technologies providers on the validation requirements for such systems and details their use for handling apects of the investigational medicinal product. (EMA/INS/GCP/600788/2011).

A reflection paper on the development of block copolymer micelle medicinal products was published in January 2014 (EMA/CHMP/13099/2013). Block copolymer micelles are innovative drug delivery systems aimed at improving the delivery of poorly soluble, highly-toxic or unstable

drugs. The paper provides information on the pharmaceutical, non-clinical and early clinical development aspects for block-copolymer micelle products for intravenous administration.

A qualification opinion on a statistical approach for dose response testing and estimation was adopted in January 2014 (EMA/CHMP/SAWP/757052/2013). It qualifies the MCP-Mod (multiple comparison procedure - modelling) as an efficient statistical methodology to enable more informative phase 2 study designs and to provide a more solid basis for subsequent dose selection strategies.

A draft guideline on the use of pharmacogenomics in pharmacovigilance was published for consultation until 30 July 2014 (EMA/281371/2013). It provides key recommendations on how to evaluate pharmacovigilance-related issues associated with pharmacogenomic biomarkers, and how to translate results into labelling recommendations.

A draft guideline on subgroup analysis in confirmatory clinical trials was released for consultation until 31 July 2014 (EMA/CHMP/539146/2013). It elaborates on the role of such analyses as part of the confirmatory and exploratory testing strategies and how to plan them at the time of clinical trial preparation and analysis.

A revised guideline on pharmacokinetics in patients with decreased renal function was issued for consultation until 31 August 2014 (EMA/83874/2014). The major amendments relate to the effect of reduced renal function on drugs that are primarily hepatically eliminated and further recommendations on methods for the determination of glomerular filtration rate (GFR).

A draft guideline on medicinal products for the treatment of chronic constipation was released for consultation until 31 August 2014. It addresses the clinical development of products intended for the treatment of chronic constipation, opioid-induced constipation and development aspects of purgatives products for bowel cleansing (EMA/CHMP/336243/2013).

Guidance for veterinary medicines

A guideline on efficacy studies for non-steroidal anti-inflammatory (NSAID) veterinary drugs will come into effect in August 2014 (EMA/CVMP/EWP/1061/2001, replacing guideline EMA/CVMP/237/01). It provides guidance on trial design, conduct and reporting standards for efficacy studies for new NSAID or to vary the indications of an already authorised NSAID.

Three VICH guidelines on pharmacovigilance of veterinary medicinal products will come into effect in December 2015:

- GL30 (EMA/CVMP/VICH/647/2001) which details the controlled lists of terms used for consistency in recording, searching and categorizing events.
- GL35 (EMA/CVMP/VICH/123940/2006) which specifies standards to construct a single electronic message to transmit pharmacovigilance information.
- GL42 (EMA/CVMP/VICH/355996/2005) which describes the data elements to standardise the data for submission of adverse events.

A draft VICH GL52 on bioequivalence studies for veterinary products was released for consultation until 31 May 2014 (EMA/CVMP/VICH/751935/2013). It details the design variables to consider when developing a bioequivalence study and the information to include in the final study report.

A draft recommendation on pharmacovigilance and signal detection of veterinary medicinal products was released for consultation until 30 June 2014 (EMA/CVMP/PhVWP/901279/2011). It provides practical modalities for the development of a framework for signal detection in veterinary pharmacovigilance.

A VICH guidance on file format requirements for the electronic exchange of regulatory documents concerning veterinary medicinal products was published for consultation until 20 July 2014 (ICH reference GL53, EMA/CVMP/VICH/758781/2013).

A reflection paper on pharmacovigilance communication for veterinary products was announced (EMA/CVMP/PhVWP/536313/2013). It provides an overview of the communication tools and methods to ensure effective pharmacovigilance communication to users of the veterinary medicinal products.

A major update of the pre-authorisation guidance for centralised dossiers for veterinary medicines was recently released (Link).

Guidance on pharmacovigilance for human medicines

GVP Module XVI on risk minimisation measures (EMA/204715/2012) came into effect on 1 March 2014. It provides guidance on the development of additional risk minimisation measures (e.g. educational programmes, controlled access programmes) and the evaluation of their effectiveness.

The Questions and Answers webpage on periodic safety update reports (PSUR) was recently updated on topics such as: the EURD implementation date, the submission of updated risk management plan within PSUR/PSUSA (Periodic Safety Update Single Assessment) procedures and review timelines (Link).

Regulatory and procedural guidance

An update on the maintenance of information on authorised medicines by marketing authorisation holders ('Art. 57') was announced on 31 January 2014. It sets out the updated data submission requirements and the implementation roadmap for the overall project (Link).

Updates of the following guidance documents were published on:

- Pre-authorisation guidance for centralised applicants on topics related to active substance master file, dossier requirements and risk management plan (Link).
- Post-authorisation guidance for centralised marketing authorization holders on topics related to European Union reference (EURD) dates, PSUR, Article 46 paediatric studies submission (Link).
- Questions and Answers on variations guidelines in the centralised procedure, related to categories of variations for Article 46 paediatric study submission, environmental risk assessment (ERA) and changes to due dates of the conditions of a marketing authorisation or of measures in a risk management plan (Link).
- Questions and answers on paediatric investigation plans on topics related to modifications of an agreed PIP and compliance aspects (Link)

eCTD

The eSubmission Gateway or web client is mandatory for all eCTD submissions for human medicines to the centralised procedure since 1 March 2014.

It applies to all types of procedures for human medicines, including active substance master file (ASMF) submissions (Link). The *eSubmission Gateway* was launched in 2012 as an electronic submission tool for all types of eCTD applications for human medicines. The *eSubmission web client* is a specific tool aimed at applicants with lower transmission volumes.

From 1 April 2014, the use of the eSubmission Gateway and web client will be extended to all referral procedures, veterinary medicine submissions and paediatric submissions. Submissions on CDs/DVDs for these procedures may be accepted during a transitional period.

Meetings

The reports and videos of the following meetings have been released:

- EMA/Health technology assessment bodies workshop on parallel scientific advice in drug development (Link).
- EMA/EDQM meeting on characterisation of new clotting factor concentrates (factor VIII and factor IX) with respect to potency assays used for labelling and testing of post-infusion samples (Report)
- Harmonising the approach to VeDDRA coding workshop (Link)
- EMA/Parenteral Drug Association Quality-by-Design workshop (Link)

Registered SMEs

Currently, 1143 companies have SME status assigned by the Agency. The names and profiles of these companies are published in the Agency's public SME Register.

If you would like to have your company details included in the SME Register, you must first apply for SME status at the Agency. See the How to apply section of the SME Office pages on the Agency's website for information on how to do this.

Procedural announcement on unique product identifiers (UPIs) for orphan designation, paediatric development or scientific advice.

Since February 2014 new medicines have to receive a unique product identifier (UPI) by the EMA, in order to track them through pre-authorization procedures such as orphan designation, paediatric development or scientific advice.

Further information on the process is included under Link.

About the SME Office

The SME Office was set up within the European Medicines Agency to address the particular needs of smaller companies.

The Office has dedicated personnel who can help SMEs by:

- responding to practical or procedural enquiries;
- monitoring applications;
- organising workshops and training sessions.

Need more information?

Visit the European Medicines Agency website:

http://www.ema.europa.eu

In particular, these sections may interest you:

SME Office
Pre-authorisation (human medicines)
Pre-authorisation (veterinary medicines)

Contact the SME Office

E-mail: smeoffice@ema.europa.eu
Tel: +44 (0)20 7418 8575/8463
Fax: +44 (0)20 7523 7040

European Medicines Agency

7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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