29 Issue 29
October 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

Annex 6 to ICH guideline Q4B "Evaluation and Recommendation of pharmacopoeial texts for use in the ICH Regions" came into effect in June 2014. It recommends that the official pharmacopoeial texts on uniformity of dosage units can be used interchangeably in the ICH regions subject to the certain conditions. (Link)

On 31 July 2014, a guideline on quality of oral modified release products (EMA/CHMP/QWP/428693/2013) was adopted. It addresses aspects of pharmaceutical development and in vitro testing for prolonged release oral dosage forms and delayed release oral dosage forms with the principle of gastro-resistance.

A draft reflection paper on the use of cocrystals and other solid state forms of active substances in medicinal products for human or veterinary use (EMA/CHMP/CVMP/QWP/136250/2014) has been released for consultation until 31 October 2014. It gives the current regulatory thinking on issues such as the acceptability of the Active Substance Master File (ASMF) procedure and the possibility to include different solid state forms within the same marketing authorisation.

Non-clinical and Clinical development guidance

A guideline on assessment and control of DNA reactive (mutagenic) impurities in pharmaceuticals to limit potential carcinogenic risk - Step 4 (EMA/CHMP/ICH/83812/2013) will come into effect in January 2016. It provides guidance on the assessment of the mutagenic potential of impurities for new and previously approved active substances and finished products during clinical development and subsequent post approval submissions. The document does not apply to certain types of products or conditions (e.g. biologics, excipients and advanced oncology indications).

An ICH guideline S10 on photosafety evaluation of pharmaceuticals came into effect in June 2014. It recommends international standards for photosafety assessment for clinical trials and marketing authorisations for new active substance (APIs), new excipients clinical formulations for dermal application (including dermal patches), and photodynamic therapy products. (Link)

A draft guideline on the clinical investigation of medicinal products to prevent development/ slow progression of chronic renal insufficiency (EMA/CHMP/355988/2014) was released for consultation until 1 January 2015.

It focusses on the different potential claims in relation to the kidney disorder (i.e., primary and secondary prevention), description of study populations including prognostic factors, study designs, outcome measures and data analyses including biomarkers.

A non-clinical and clinical draft guideline on influenza vaccines (EMA/CHMP/VWP/457259/2014) has been released for consultation until 31 January 2015. The revision of the guidelines aims at developing one single modular guideline that covers the regulatory, quality, non-clinical and clinical aspects. The non-clinical and clinical module reflects current understanding of the predictive value of non-clinical studies and the knowledge that individual types of influenza vaccines may differ from each other in terms of their immunogenicity, efficacy and safety.

A draft guideline on the clinical evaluation of medicinal products used in weight control (EMA/CHMP/311805/2014) has been released for consultation until 31 January 2015. The revisions clarify the requirements for the recommended methods of assessing efficacy, selection of patients, strategy and design of clinical trials, safety aspects and overall strategy of development.

A guideline on the evaluation of medicinal products for the treatment of irritable bowel syndrome (CPMP/EWP/785/97 Rev. 1) will come into effect on 1 April 2015. It replaces the "Points to consider on the evaluation of medicinal products for the treatment of Irritable Bowel Syndrome (CPMP/EWP/785/97) and includes changes relating to the patient population, primary endpoints in pivotal trials and special patient populations (gender, children and elderly).

Updated guidance on the obligations for sponsors to post results on any interventional trials registered in EudraCT has been released. EudraCT contains protocol-related information submitted by sponsors for interventional clinical trials conducted in European Economic Area (EEA) countries, as well as clinical trials conducted in third countries, when the clinical trial is part of an agreed Paediatric Investigation Plan (PIP). The notice provides general and technical guidance as well as details on the new requirements for sponsors and the timing of posting. (Link)

Guidance on pharmacovigilance for human medicines

Guidance on pharmacovigilance inspections of marketing-authorisation holders of human and veterinary medicines was released (EMA/INS/PhV/192231/2014). It applies to pharmacovigilance inspections of MAHs with centrally authorised products (CAPs), products authorised via the mutual-recognition, decentralised procedure and national procedures. Further information on Pharmacovigilance inspection procedures: Human, Veterinary.

Two guidelines on good Pharmacovigilance practices came into effect on 16 September 2014:

- Module III – Pharmacovigilance inspections Rev 1 (EMA/119871/2012 Rev 1*). The revision includes references to the new Union procedures for pharmacovigilance inspections.
- Module VI – Management and reporting of adverse reactions to medicinal products Rev 1 (EMA/873138/2011 Rev 1*). Revisions include changes to chapters on e.g. causality, seriousness and solicited reports and requirements for non-interventional post-authorisation studies.

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) has revised its guide on methodological standards in pharmacoepidemiology and pharmacovigilance (EMA/95098/2010 Rev.3). The revision added a chapter on the design and analysis of pharmacogenetic studies. These studies aim to investigate how individual genetic variations determine the response to a medicine, both in terms of therapeutic effect and adverse drug reactions.

Guidance for veterinary medicines

A guideline on the demonstration of palatability of veterinary medicinal products will come into effect on 1 February 2015 (EMA/CVMP/EWP/206024/2011). It addresses the requirements for the approval of palatability claims for new oral formulations and for existing products reformulated to improve palatability.

On 16 September 2014, a draft policy on the classification of veterinary medicinal products indicated for minor use minor species (MUMS) / limited market was published. The updated policy has been separated out into a policy document (EMA/308411/2014) and a separate guidance document for applicants (EMA/CVMP/388694/2014). (Link to MUMS webpage)

Pre-authorisation and post authorisation procedural advice for users of the centralised procedure have been extensively revised on topics including fee incentives, validation of dossiers, variations, extensions and renewals applications, transfer of marketing authorisation, marketing and cessation notification.

- Pre-authorisation advice (Link)
- Post-authorisation procedural advice (Link)

Updates on the following EMA Q&A webpages were also published:

Renewals, Annual re-assessment, Post-authorisation measures, Post-authorisation safety studies, Annual renewal of conditional marketing authorisations, Type-IA variations, Type-II-variation and extension applications, Periodic safety update reports, Guidance on European Union periodic-safety-update-report single assessment for nationally authorised medicines, Worksharing.

Regulatory and procedural guidance

A draft reflection paper on the classification of advanced-therapy medicinal products (EMA/CAT/600280/2010 Rev.1) has been released for consultation until 31 October 2014. The revisions include considerations related to substantial manipulation, non-homologous use, vaccines and gene-therapy medicinal products classification issues and combined advanced-therapy medicinal products.

On 11 September, the Agency published guidance on its adaptive licensing pilot project (EMA/417706/2014) and a Frequently asked questions document for prospective applicants based on the initial experience gained from the pilot. (Link to FAQ)

Updated guidance on the labelling and package-leaflet obligations (EMA/24613/2014) was released on 30 July. It sets out recommendations for the implementation of the exemptions (e.g. orphan drugs) to the labelling and package-leaflet obligations in the centralised procedure.

EU news

European Commission launches a logo for online pharmacies to protect patients from falsified medicines

The establishment of this logo for online pharmacies has been introduced by the new Directive on falsified medicines (Directive 2011/62/EU). The Regulation establishing the new logo entered into force in July 2014 and Member States will have one year to prepare for its application. EU regulatory authorities will list on their websites all legally-operating online pharmacies and other legally-authorised retailers of medicines. Find more information on this new logo and on Falsified Medicines.

On 8 September, the European Commission launched a public consultation on its SME Policy to help upgrade the EU's Small Business Act (SBA). The SBA is a set of wide-ranging measures designed to make life easier for small companies.

The public consultation is open until 15 December 2014. More information, including the consultation document can be found here.

Regulation No 658/2014 on pharmacovigilance fees was published in the Official Journal of the European Union (EU) on 27 June 2014.
It provides for two types of fees to be charged:

- a procedure-based fee for the single assessment of periodic safety update reports (PSURs) and the assessment of post-authorisation-safety-study (PASS) protocols and study results, and for pharmacovigilance-related referrals.
- an annual fee that applies to nationally authorised products only.

Fee reductions and exemptions for pharmacovigilance fees are foreseen for **micro-, small and medium-sized enterprises** (SMEs) and for certain categories of medicines such as generics and herbal medicinal products.

Meetings and reports

The following upcoming meetings and workshops have recently been announced:

- **10 October:** Regulatory workshop on clinical trials designs in neuromyelitis optica (NMO) and spectrum disorders; (Link)
- **28-29 October:** Workshop on viral safety of plasma-derived medicinal products with respect to hepatitis E virus; (Link)
- **18-19 November:** Plasma Master File (PMF) Epidemiology; (Link)
- **4-5 December:** European Medicines Agency (EMA)/ European Federation of Pharmaceutical Industries and Associations (EFPIA) workshop on the importance of dose finding and dose selection for the successful development, licensing and lifecycle management of medicinal products; (Link)

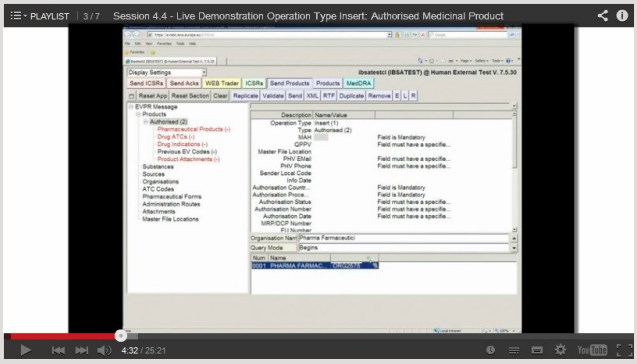
The reports and videos of the following meetings have recently been released:

- **28-29 November 2013:** Characterisation of new clotting factor concentrates (FVIII, FIX) with respect to potency assays used for labelling and testing of post infusion samples; (Link)
- **2-3 December 2013:** Workshop on risk based quality management in clinical trials; summaries of the presentations; (Link)
- **28 April 2014:** EMA workshop of pharmacovigilance in the paediatric population; (Link)
- **2 June 2014:** Paediatric osteoporosis expert meeting (Link).

Electronic submission of Article 57(2) data

E-Learning material on Electronic submission of Article 57 (2) data has been uploaded to the Agency website. (Link). A Q&A document Electronic submission of Article 57(2) data (EMA/159776/2013) was also extensively revised with new topics of interest and clarifications on issues covered in previous versions.

Session 4.4: How to insert an Authorised Medicinal Product



Registered SMEs

Currently, 1226 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.

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;
- setting up briefing meetings to discuss regulatory strategy;
- 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)

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