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August 2015

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

IN THIS ISSUE

Clinical development guidance

A draft guideline on the clinical development of fixed dose combination medicinal products has been released for consultation until 15 November 2015 (EMA/CHMP/281825/2015). The document provides an update on the scientific requirements for the development of fixed dose combination products, independently of the legal basis for submission of the marketing authorisation application.

A guideline on the clinical investigation of recombinant and human plasma-derived factor IX products will come into effect on 1 September 2015 (EMA/CHMP/BPWP/144552/2009 rev 1). It covers the clinical investigations to be conducted during the pre- and post-marketing authorisation phases and provides applicants with harmonised dossier requirements.

A draft guideline on the clinical investigation of medicinal products other than non-steroidal anti-inflammatory drugs (NSAIDs) for the treatment of rheumatoid arthritis (CPMP/EWP/556/95 Rev. 2) has been released for consultation until 29 November 2015. This document is a revision of the 'Points to Consider' document adopted in November 2003 and takes into account major advances in the field introduced over the last decade such as combinations of non-biologic and biologic disease-modifying anti-rheumatic drugs (DMARDs) and new diagnostic criteria for the identification and treatment of early arthritis.

An addendum (EMA/CHMP/707532/2013) to the 'Guideline on clinical investigation of medicinal products in the treatment of acute heart failure' (CHMP/EWP/2986/03 Rev. 1) on paediatric-specific aspects has been released for consultation until 30 November 2015.

A reflection paper on the assessment of cardiovascular risk of medicinal products for the treatment of cardiovascular and metabolic diseases' (EMA/CHMP/50549/2015) has been released for consultation until 30 September 2015. It aims to further clarify the requirements for the evaluation and quantification of the cardiovascular risk of new non-generic medicinal products intended for the long-term treatment of cardiovascular and metabolic diseases.

Guidance on pharmacovigilance for human medicines

Information on the new medical literature monitoring service introduced by the Agency in July 2015 is available on a dedicated webpage. It includes detailed guidance for companies on the new service, sets out the business processes, and includes questions and answer documents and videos on this new activity (Link).

The Agency has updated the 'Reporting requirements of Individual Case Safety Reports (ICSRs) applicable to marketing authorisation holders during the interim period' taking into account the implementation of the litterature monitoring service recently introduced (Link).

The Agency has published a 'Article 57 QuickCard - Use of data elements in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD)' (EMA/339616/2014), which aims to support companies with the submission of information under Article 57(2) of Regulation (EC) No 726/2004.

On 14 April, the Agency, on behalf of the European Union (EU) Regulatory Network, has released two draft good practice guides that aim to improve the reporting, evaluation (EMA/762563/2014) and prevention of medication errors (EMA/606103/2014) by regulatory authorities and pharmaceutical industry throughout the EU.
The guides are key deliverables of the EMA/Heads of Medicines Agencies (HMA) joint action plan on medication errors, which was agreed in 2013 (EMA/20791/2014).

A 'Guideline on good pharmacovigilance practices (GVP) Module XVI Addendum I – Educational materials' (EMA/61341/2015 DRAFT) will come into effect in Q4 2015. Educational programmes provide additional risk minimisation measures to the summary product characteristics (SmPC) and package leaflet (PL) (see GVP Module XVI), which usually require educational materials to provide targeted communications.

Regulatory and procedural guidance

A 'Guideline on core SmPC for plasma-derived fibrin sealant/ haemostatic products' (EMA/CHMP/BPWP/598816/2010 rev. 1) will come into effect on 1 January 2016.
Its aim is to provide applicants with harmonised guidance on the information to be included in the SmPC for plasma-derived fibrin sealant / haemostatic products.

The Agency has revised its guidelines on the implementation of accelerated assessment (MA/CHMP/697051/2014 Rev. 1) and conditional marketing authorisation (EMA/ CHMP/509951/2006 Rev.1) Accelerated assessment and conditional marketing authorisation are two key tools in the European legislation to accelerate patients' access to medicines that address unmet medical needs. The public consultations on the revised guidelines are open until 30 September 2015.

Publication of clinical data

On 1 January 2015, the new EMA policy on publication of clinical data entered into force.

Under this policy, the Agency proactively publishes the clinical reports submitted as part of marketing-authorisation applications for human medicines (Link). To update stakeholders on the implementation of this policy a webinar was held on 24 June 2015 (Link).

The Agency also published a revised Questions & answers document (EMA/357536/2014 Rev. 1).

The following EMA Q&A documents were recently updated:

- Pre- (EMA/339324/2007) and post-authorisation (EMEA -H-19984/03 Rev. 52) procedural advice (on e.g. timelines for submitting requests for eligibility, rapporteurs appointment, and contact points) ;
- Urgent Union Procedures (Article 107i of Directive 2001/83/EC)' (EMA/720443/2012 Rev. 3);
- Article 20 (EMA/108934/2014) and Article 31 (EMA/33617/2014 Rev.2) pharmacovigilance referral procedures.

The following EMA webpages were recently updated:

- Paediatric investigation plans (Link); update on procedural guidance, Q&A, templates and deadlines for submission;
- Orphan designation (Link); update on procedural guidance;
- Quality of medicines (Link); update on eye drops and veterinary medicinal products ;
- Information and guidance on invoicing, terms and conditions of payment and how to set up a customer account with the Agency (Link);

The Agency has updated the following guidance on labelling and package-leaflet:

- Recommendations for the implementation of the exemptions to the labelling and package leaflet obligations in the centralised procedure (EMA/276177/2015 rev.2*);

- Draft questions and answers on 'sodium' in the context of the revision of the guideline on 'Excipients in the label and package leaflet of medicinal products for human use' (EMA/CHMP/338679/2014) have been published for consultation until 30 September 2015. It includes proposals for the label and package leaflet based on a review of safety. The main aspects were summarised in a concept paper published on 25 March 2012 (Link);
- List of details of national competent authorities to contact for requests of translation exemption falling under Art. 63.3 of Directive 2001/83/EC and cases of shortages (EMA/182949/2015 rev. 2);
- Labelling exemption requests under article 63 of Directive 2001/83/EC examined by the QRD group (EMA/266315/2015 rev.1*).

Advanced Therapies

The Agency has released a draft guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products (EMA/CAT/80183/2014) for public consultation until 31 August 2015. The revision takes stock of the experience gained with gene therapy in recent years and provides detailed guidance on both the development aspects of this type of medicine, and on the regulatory requirements that companies need to fulfil, including quality good manufacturing practice.

Quality Guidance

A series of draft product specific guidance documents in relation to the 'Compilation of individual product-specific guidance on demonstration of bioequivalence' (EMA/CHMP/736403/2014 Rev 2) have been released for public consultation until 1 November 2015 for: asenapine (EMA/CHMP/PKWP/269533/2015), prasugrel (EMA/CHMP/PKWP/36761/2015), sitagliptin (EMA/CHMP/PKWP/36869/2015) and zonisamide (EMA/CHMP/PKWP/253507/2015).
Carglumic acid product-specific bioequivalence guidance has been published in Annex B of the guidance and will come into effect on 1 October 2015.
Guidance on sunitinib and capecitabine have been published in Annex C to the guidance and will come into effect on 1 November 2015.

A draft guideline on the chemistry of active substances (EMA/CHMP/QWP/96664/2015) has been released for public consultation until 24 October 2015. Its purpose is to set out the type of information required for the manufacture and control of new and existing active substances used in a medicinal product. This guideline replaces the 'Note for guidance on chemistry of new active substances' 52 (CPMP/QWP/130/96, Rev 1) and 'Chemistry of active substances' (3AQ5a).

A guideline on the adventitious agent safety of urine-derived medicinal products (EMA/CHMP/BWP/126802/2012) will come into effect in December 2015. It addresses specific aspects, which should be taken into consideration in the evaluation of viral safety of medicinal products derived from human urine and provides guidance on the process validation of steps for virus inactivation/removal.

A draft guideline on epidemiological data on blood transmissible infections (EMA/CHMP/BWP/548524/2008. rev 1) has been released for public consultation until 31 August 2015. It outlines the scientific data requirements for epidemiological data to be included in applications for Plasma Master File certification submitted to the EMA and offers guidance to PMF holders on residual risk calculation and epidemiological data requirements for approval of blood establishments.

Guidance for veterinary medicines

A revised guideline titled 'Principles on assignment of defined daily dose for animals (DDDvet) and defined course dose for animals (DCDvet)' (EMA/710019/2014) has been adopted on 8 June 2015. The aim of establishing DDDvet and DCDvet for antimicrobial veterinary medicinal products is to provide standardised fixed units of measurement for the reporting of data on consumption by species that take into account differences in dosing.

A guideline titled 'Recommendation on pharmacovigilance surveillance and signal detection of veterinary medicinal products' will come into effect on 1 October 2015 (EMA/CVMP/PhVWP/901279/2011). Its purpose is to provide an initial framework that will allow further development of signal detection in veterinary pharmacovigilance, including practical modalities relating to the signal management process and the determination of the post-authorisation surveillance interval.

eApplication Forms

Since 1 July 2015, the use of electronic application forms is mandatory for all centralised marketing authorisation applications for human and veterinary medicines (Link). Further information on the new requirements can be found on the eSubmission website and in a new information leaflet.

Workshops, meetings and reports

On 25 September 2015, the Agency's Committee for Advanced Therapies (CAT) and the International Society for Cellular Therapy (ISCT) are organising a workshop to discuss how to facilitate the development of advanced therapies. It will offer attendees the opportunity to interact directly with regulators and learn more about quality development, manufacturing issues and non-clinical testing of ATMPs and specificities of clinical development of ATMPs. (Link)

The reports and/or videos of the following meetings have been published:

- **October 2014:** Workshop on viral safety of plasma-derived medicinal products with respect to hepatitis E virus (Link)
- **December 2014:** Report from the European Medicines Agency/European Federation of Pharmaceutical Industries and Associations workshop on the importance of dose finding and dose selection for the successful development, licensing and lifecycle management of medicinal products (Link);
- **December 2014:** Expert meeting on the clinical investigation of medicines for the treatment of paediatric hepatitis C (Link);
- **April 2015:** SME workshop: Focus on chemistry, manufacturing and controls (CMC) regulatory compliance for biopharmaceuticals and advanced therapies (Link).

Registered SMEs

Currently, 1392 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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