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SME Office NEWSLETTER

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IN THIS ISSUE

Quality Guidance

A revised guideline on the process validation of finished products was adopted on 10 November 2016 (EMA/CHMP/CVMP/QWP/BWP/70278/2012-Rev1,Corr.1; *Human and Veterinary*). It details the process validation data to be provided in regulatory submissions for finished dosage forms of chemical medicinal products for human and veterinary use. The general principles of the guidance also apply to active substances and biological medicinal products.

A CHMP guideline on the chemistry of active substances was adopted on 21 July 2016 (EMA/454576/2016; *Human*). It sets out the type of information required for the manufacture and control of active substances (existing or new chemical entities) used in a medicinal product. The document replaces the 'Note for guidance on chemistry of new active substances' (CPMP/QWP/130/96, Rev 1) and 'Chemistry of active substances' (3AQ5a).

An ICH guideline Q3C (R6) on residual solvents in active substances, excipients, and finished products will come into effect on 14 June 2017 (EMA/CHMP/ICH/82260/2006; *Human*). It provides recommendations for levels of solvents considered to be toxicologically acceptable for patient safety.

A guideline on setting health-based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities' has been released for consultation until 30 April 2017 (EMA/CHMP/CVMP/SWP/169430/2012; *Human and Veterinary*). It recommends an approach for deriving a scientifically-based safe threshold value for individual active substances to be applied for risk identification.

Non-clinical, Clinical and Multidisciplinary Guidance

A CHMP/CVMP guideline on the principles of regulatory acceptance of 3Rs (replacement, reduction, refinement) testing approaches was adopted in December 2016 (EMA/CHMP/CVMP/JEG-3Rs/450091/2012). It encourages all stakeholders to initiate, support and accept the development and use of 3Rs testing approaches for regulatory applications for human and veterinary medicinal products.

A guideline on the clinical investigation of medicinal products in chronic renal insufficiency will come into force on 1 April 2017 (EMA/CHMP/500825/2016). It details clinical study requirements of products intended to prevent or slow the progression of chronic renal insufficiency.

A revised multidisciplinary guideline on the pharmaceutical, non-clinical and clinical development of similar biological medicinal

products containing low-molecular-weight-heparins will come into effect on 1 June 2017 (EMEA/CHMP/BMWP/118264/2007 Rev. 1; replacing EMEA/CHMP/BMWP/118264/2007). The revision focuses on the demonstration of biosimilarity based on a physicochemical data package and comparable pharmacodynamic profiles instead of a dedicated comparative efficacy trial.

A revised guideline on the clinical investigation of products for the prevention of venous thromboembolism in non-surgical patients will come into effect on 1 June 2017 (EMA/CPMP/EWP/6235/04 Rev. 1). It clarifies the imaging tests to be used in dose-finding and confirmatory trials, and elaborates on the efficacy and safety requirements e.g. dedicated studies for specific claims, updated definition and assessment of bleeding events.

A revised guideline on first-in-human clinical trials has been released for consultation until 28 February 2017 (EMEA/CHMP/SWP/28367/07 Rev. 1). It addresses the increased complexity of protocols of first-in-human clinical trials, which combine several steps of the clinical development within a single clinical trial protocol. Guidance is also provided on non-clinical and clinical strategies to mitigate and manage risks for trial participants (Link).

A revised ICH E6 (R2) guideline on Good Clinical Practice will come into effect on 14 June 2017 (EMA/CHMP/ICH/135/1995). It was amended to encourage the implementation of more efficient approaches to clinical trial design, conduct, oversight in light of advances in electronic data recording and reporting.

A guideline on how to design and conduct post-authorisation efficacy studies (PAES) will enter into force on 1 June 2017 (EMA/PDCO/CAT/CMDh/PRAC/CHMP/261500/2015). It provides guidance on the need for such studies, methodological considerations and study conduct.

A guideline on the clinical development of products intended for the treatment of pain will come into force on 1 July 2017 (EMA/CHMP/970057/2011). It replaces the guidelines on neuropathic (CPMP/EWP/252/03) and nociceptive pain (CPMP/EWP/612/00) and updates sections relating to study design, patient populations and outcome measures, as well addressing specifying requirements for children and the elderly.

A revised guideline on the clinical investigation of human normal immunoglobulin for intravenous administration (IVIg) has been released for consultation until 31 March 2017 (EMA/CHMP/BPWP/94033/2007 rev. 3). It was revised to include considerations relating to multifocal motor neuropathy, chronic inflammatory demyelinating polyradiculoneuropathy and secondary immunodeficiencies.

A paediatric addendum to the CHMP guideline on the clinical investigation of medicinal products for the treatment of acute heart failure will come into force on 1 July 2017 (EMA/CHMP/707532/2013).

An ICH E11 (R1) guideline addendum on the clinical investigation of medicinal products in the paediatric population has been released for consultation until 13 April 2017 (EMA/CPMP/ICH/2711/1999). The addendum complements and provides clarifications on a series of sections and topics of the original ICH E11 guideline.

Veterinary Medicines

Scientific Guidance

A CVMP reflection paper and a revised guideline on the production and control of immunological veterinary medicinal products were published (EMA/CVMP/IWP/251741/2015; (EMA/CVMP/IWP/206555/2010-Rev.1 coming into force in May 2017).

The VICH GL54 guidance on studies to evaluate the safety of residues of veterinary drugs in human food will come into effect in November 2017 (EMA/CVMP/VICH/699251/2010). It addresses the nature and type of data to determine a toxicological acute reference dose (ARfD) for residues of veterinary drugs.

Revised guidelines on quality (EMA/CVMP/QWP/128710/2004-Rev.1), safety and residues (EMA/CVMP/SWP/66781/2005–Rev.1), efficacy and target animal safety data (EMA/CVMP/EWP/117899/2004–Rev.1) requirements for veterinary medicinal products intended for minor use or minor species (MUMS)/limited markets will come into force on 1 July 2017. The guidelines have been revised in light of experience gained and clarify the applicability of certain data requirements.

Regulatory and Procedural Guidance

A draft QRD guidance on the use of pictograms on the packaging of veterinary medicinal products authorised through the centralised (CP), mutual recognition (MRP) and decentralised procedures (DCP) has been released for consultation until 25 February 2017 (EMA/QRD/752627/2016).

A draft reflection paper on the chemical structure and properties criteria in the evaluation of the new active substance (NAS) status of chemical substances has been released for consultation until 17 February 2017 (EMA/CVMP/QWP/3629/2016).

A statement of intent on the extension of the common repository to veterinary centralised procedure submissions by the end of 2017 has been published (EMA/715059/2016). Further information is available in a Q&A document (Link).

Electronic submission via the EMA e-Submission Gateway or Web Client became mandatory on **1 January 2017** (Link). Dossiers submitted electronically should follow the current version of the guideline on the specifications for the provision of an e-submission for a veterinary medicinal product. The VNeeS format will become mandatory for all submissions in European procedures (CP, DCP and MRP) as detailed in the annex to the eSubmission roadmap (Link). Further information is available on the veterinary eSubmission Gateway/ Web Client page (Link).

Regulatory, Scientific and Procedural Advice (Human Medicines)

A pilot EMA scientific advice procedure to support the development of new biosimilars will be launched in February 2017. It will advise applicants on a proposed biosimilar development strategy as well as performing an in-depth review of the quality, analytical and functional data available. More information can be found under EMA/756854/2016.

Guidance on the implementation of the EMA policy on **publication of clinical data for medicinal products for human use** was revised based on the experience gathered to date (EMA/90915/2016). The changes are outlined in EMA/729722/2016 and were presented in a webinar held on 9 December 2016. **SMEs are advised to contact the SME office** for any question relating to the policy on the publication of clinical data for human medicines (EMA/240810/2013). More information can be found under this Link.

Revised recommendations on the exemptions to the labelling and package leaflet obligations in the centralised procedure (EMA/617541/2016 rev.3*) were released on 9 December 2016.

Pre- and post-authorisation procedural advice for users of the centralised procedure has been updated on topics such as multiple applications, batch release, orphan related type-II variations or extensions, PIP compliance statement and transfers (Link to the pre-authorisation guidance; Link to the post-authorisation guidance).

Guidance on the application form for centralised type IA and IB variations has been updated (EMA/233564/2014; see also EMA/CMDh Explanatory Notes on variation application forms CMDh/EMA/133/2010/Rev.7).

A new EudraVigilance system with enhanced functionalities is planned for release in November 2017. Details about the changes are available under Link.

The questions and answers webpage on pharmacology and pharmacokinetics were recently updated (Link).

Common European Single Submission Portal (CESSP) -Human and Veterinary

EMA and Heads of Medicines Agencies (HMA) have published a statement of intent (EMA/666963/2016) on replacing electronic application forms (eAFs) for human and veterinary medicines applications with a Common European Single Submission Portal (CESSP). It will integrate the HMA's Common European Submission Platform (CESP) and EMA's eSubmission Gateway into a single system. The first version will cover initial and extension applications, and will be available by Q1 2018. At a later stage, CESSP will replace all other eAFs for variation and renewal applications.

Reports, Workshops and Meetings

An **EC public consultation** to support the drafting of a 10-year report on the **Paediatric Regulation** is ongoing until 20 February 2017 (Link).

- A 10-year report on conditional marketing authorisations has been published (Link). It highlights that such authorisations enable timely access to medicines for patients with unmet medical needs. Since 2006, conditional marketing authorisations were granted to a total of 30 medicines that target seriously debilitating or life-threatening conditions such as HIV infection, breast cancer, severe epilepsy in infants or multi-drug resistant tuberculosis. The main findings are also available in an infographic.
- Report on the outcome of the EMA survey on centralised post-authorisation procedures 2015 (EMA/156890/2016).
- CVMP strategy on antimicrobials 2016-2020 (EMA/CVMP/209189/2015).
- Enpr-EMA newsletter - December 2016 (Link).

Selection of upcoming events

- Veterinary medicines info day– 16 & 17 March 2017 (Link).
- SME Info Day 'The new clinical trial regulation' – 20 March 2017 (Link).

Reports, presentations and/or videos of the following meetings have been published:

June 2016

- Report of the 2016 annual workshop of the European Network of Paediatric Research (Enpr-EMA) – 2 & 3 June 2016 (EMA/408587/2016).

September 2016

- Second annual scientific workshop: Applying regulatory science to neonates – 12 & 13 September 2016 (Link).
- EU-USA strategic meeting on the future of paediatric medicines – 28 September 2016 (Link).

October 2016

- PSUR info day – 28 October 2016 (Link).
- Patient registries workshop – 28 October 2016 (Link).

November 2016

- CAT workshop: scientific and regulatory challenges of genetically modified cell-based cancer immunotherapy products - 15 & 16 November 2016 (Link).
- Workshop on identifying opportunities for 'big data' in medicines development and regulatory science - 14 & 15 November 2016 (Link).
- Workshop on qualification and reporting of physiologically-based pharmacokinetic modelling and simulation – 21 November 2016 (Link).
- Spinal muscular atrophy workshop – 11 November 2016 (Link).
- Webinar on type-I variations – 15 November 2016 (here).

December 2016

- Webinar 'How can clinical research networks support developers of medicines for children?' – 1 December 2016 (Link).
- Workshop on adaptive pathways – 8 December 2016 (Link).

Registered SMEs

Currently, 1562 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 their regulatory strategy;
- organising info days 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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