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SME Office NEWSLETTER

Information for SMEs in the EU regulatory environment for medicines.
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IN THIS ISSUE

Pharmaceutical development guidance

A reflection paper on the requirements for the selection and justification of starting materials in the manufacture of chemical active substances (EMA/448443/2014) has been adopted. It clarifies the expectations of EU competent authorities arising from the guidance found in ICH Q11 (Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities).

A scientific guideline on the use of phthalates as excipients in human medicinal product will come into effect on 1 June 2015 (EMA/CHMP/SWP/362974/2012 corr 2). In the revision of the "Guideline on excipients in the label and package leaflet of medicinal products for human use (CPMP/463/00 Rev 1)" phthalates used in medicinal products were identified as one of the priorities among excipients under revision. The guideline provides recommendations aimed at reducing the phthalate content of medicines in all patient populations.

Two draft Q&A documents relating to the revision of the guideline 'Excipients in the label and package leaflet of medicinal products for human use' (CPMP/463/00 Rev.1) were released for consultation until 28 February 2015:

- propylene glycol and esters (EMA/CHMP/704195/2013; Background report EMA/CHMP/333892/2013)
- cyclodextrins (EMA/CHMP/495747/2013; Background report EMA/CHMP/333892/2013)

A Q&A document on the Quality by Design information in regulatory submissions was published on 10 December 2014 (EMA/59240/2014). The document clarifies the types of risk assessments (RAs), the level of detail required for a RA related to process/product design and for design of experiments to be included in a regulatory submission.

Preclinical guidance

A scientific guideline on 'Setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities' will come into effect on 1 June 2015 (EMA/CHMP/CVMP/ SWP/169430/2012). It aims to ensure the safety of patients and target animals exposed to residual active substances in medicinal products, as well as consumers potentially exposed to residual active substances present in food of animal origin as a result of treatment of food producing animals with veterinary medicinal products.

Clinical development guidance

A guideline on the pharmacokinetic and clinical evaluation of modified release dosage forms will come into effect on 1 June 2015 (EMA/CHMP/EWP/280/96). It was amended following the revision of the Note for Guidance on the Investigation of Bioavailability and Bioequivalence (EWP/QWP/1401/98). The document defines the studies necessary to investigate the efficacy, safety, biopharmaceutical and pharmacokinetic properties of modified release formulations following oral, intramuscular and subcutaneous administration and transdermal dosage forms in man and to set out general principles for designing, conducting and evaluating such studies.

A revised guideline on biosimilars will come into force on 30 April 2015 (CHMP/437/04 Rev 1). The main change brought by this revision is the possibility for medicines developers to use a comparator authorised outside the European Economic Area (EEA) during the clinical investigation of a biosimilar.

A reflection paper on clinical aspects of tissue engineered products has been adopted on 19 September 2014 (EMA/CAT/573420/2009). It includes details on therapeutic claims, pharmacodynamics, pharmacokinetics, challenges linked to dose finding strategy and safety assessment. The document also applies to cells or tissues combined with a medical device.

A compilation of individual product-specific guidance on demonstration of bioequivalence was published on 17 December 2014 (EMA/CHMP/736403/2014). It aims to facilitate the design of study programmes and allows a more transparent, consistent and robust evaluation of generic marketing authorisation procedures. Finalised guidelines for individual products are published in the updated annex of this compilation of guidance every 6 months.

A Q&A document on pharmacokinetics topics was updated on 7 October 2014 (EMA/618604/2008 Rev. 10). It includes new information on in-vitro drug interaction assessment.

A scientific guideline on the use of minimal residue disease as an endpoint in chronic lymphocytic leukaemia studies has been released for consultation until 30 June 2015 (EMA/629967/2014). It aims to describe the basis and regulatory requirements for the use of minimal residue disease (MRD) as an intermediate endpoint to predict clinical benefit in trials in chronic lymphocytic leukaemia.

Orphan medicines

On 16 December 2014, the EMA has published information on relevant sources for prevalence data for orphan conditions (EMA/452415/2012 Rev. 11). This new transparency initiative is designed to decrease the administrative burden for orphan designation applicants and encourage the development of medicines for rare diseases.

Guidance on pharmacovigilance for human medicines

On 10 November 2014, the Agency has made available a new tool to facilitate editing of key data fields by marketing-authorisation holders as part of the maintenance of information on authorised medicines that they have submitted to EMA. This tool is available to users of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) Data-Entry Tool (EVWEB). An informative user manual explaining how to use this tool has been published (EMA/623491/2014).

EMA boosts EU transparency with online publication of suspected side effect reports

Since 6 October 2014, public and private stakeholders can obtain information on suspected side effects of nationally authorised medicines through a single website: http://www.adrreports.eu/. The website launched in 2012 previously only contained information on suspected side effects reported with centrally authorised medicines. Its expansion now also allows the public to access the relevant information for medicines approved by national authorities in the EU.

Regulatory and procedural guidance

A pre-authorisation regulatory and procedural guideline for users of the centralised procedure was updated in November 2014 on similar-biological-product applications (Questions 1-10), fee incentives (Questions 11 to 20), and environmental-risk assessment (Questions 41 to 50).

Post-authorisation procedural advice for users of the centralised procedure (EMEA-H-19984/03 Rev 45) and their related Q&A webpages were updated on:

- Type-IA variations (veterinary);
- Type-IA variations (human);
- Type-IB variations (human);
- Withdrawn-product notification;
- Submission of Article-46 paediatric studies.

In addition the Agency has published a a practical guidance on the application form for centralised type IA and IB variations (EMA/233564/2014). It should be read in conjunction with the EMA/CMDh Explanatory Notes on Variation Application Form (CMDh/EMA/133/2010).

Guidance for veterinary medicines

A scientific guideline VICH GL23 'Studies to evaluate the safety of residues of veterinary drugs in human food: genotoxicity testing' will come into effect in October 2015 (EMA/CVMP/VICH/526/2000). The objective of this guideline is to ensure international harmonisation of genotoxicity testing for veterinary medicines.

A guideline on data requirements for changes to the strain composition of authorised equine influenza vaccines in line with World Organisation for Animal Health recommendations will come into effect on 7 May 2015 (EMA/CVMP/IWP/97961/2013). The modifications include the removal, replacement or addition of viral strains used to produce the antigenic components of authorised equine influenza vaccines.

Two reflection papers on immunological veterinary medicinal products have been released for consultation until 31 March 2015 on the data requirements to be submitted by the marketing authorisation holder (MAH) for:

- the replacement of cell lines used for the production of immunological veterinary medicinal products (EMA/CVMP/IWP/37620/2014).
- the use of heat treatment to inactivate retrovirus RD114 in live immunological veterinary medicinal products (EMA/CVMP/IWP/37924/2014).

The Agency's Committee for Medicinal Products for Veterinary Use (CVMP) has established a new Ad Hoc Expert Group on Veterinary Novel Therapies (ADVENT) aimed at providing more guidance on new classes of veterinary medicines, such as stem cell-based therapies or monoclonal antibodies. (Link)

Policy guidance

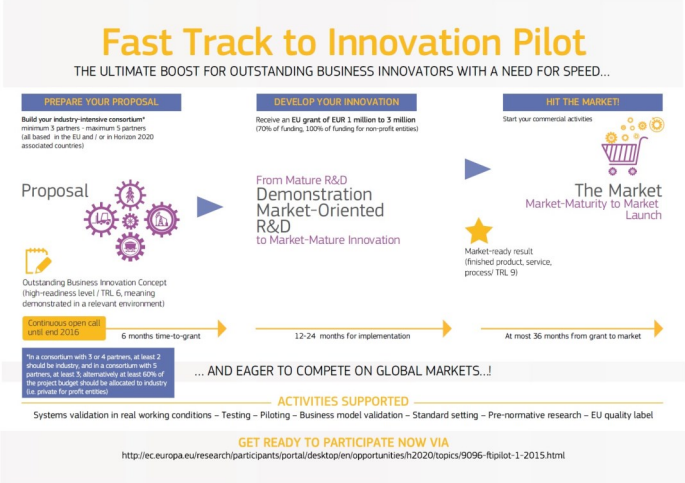
On 2 October 2014, the EMA Management Board adopted a new policy on the publication of clinical data for medicinal products for human use. The policy applies to clinical reports contained in all applications for centralised marketing authorisations submitted after 1 January 2015. (Link to website; Link to policy; Link to Q&A document)

Meetings and reports

The reports and videos of the following Workshop have been published:

- **17 September:** European Medicines Agency Human Scientific Committees' Working Parties with Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP) joint meeting - Workshop on benefit-risk communication; (Link)

Building a new innovation fast track to bring ideas to market quicker



The European Commission has aunched the new, €200 million Fast Track to Innovation (FTI) pilot initiative to promote innovation by reducing the time it takes to bring innovative ideas to market. Over the next two years, the pilot initiative will be open to all types of participants, particularly from industry, while stimulating first-time applications from industry and SMEs to Horizon 2020, the EU's research and innovation funding programme. Projects funded under the pilot are to be 'business-driven' to ensure promising innovative ideas are exploited faster. (Link)

Registered SMEs

Currently, 1302 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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