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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

SME Office NEWSLETTER

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

United Kingdom's withdrawal from the European Union ("Brexit")

Guidance to aid pharmaceutical companies developing human and veterinary medicines to prepare for the United Kingdom's withdrawal from the EU has been updated (Link). The EC/EMA questions and answers document (Link) and the 'practical guidance for industry' (Link) outlines the steps that companies should follow to make sure that the necessary changes to their marketing authorisations are made by the end of March 2019.

A report summarising the feedback received on the Brexit preparedness survey of centrally authorised MAHs carried out by EMA in January 2018 has been published (Link).

Reports of the Industry Stakeholders meeting on Brexit and the operation of the centralised procedure for human medicinal products (Link) and of the EMA Info Day on Brexit regulatory preparedness for veterinary medicines in the centralised procedure (Link) have been published. A recording of the EMA Info Day is also available.

Orphan medicines

EMA has launched a new secure online portal, named IRIS, for orphan designation applications (Link). It provides a single interface where applicants can manage the information and documentation related to applications for orphan designation. Applicants are encouraged to start using the new portal before the implementation date on 20 September 2018 (see updated guidance EMA/710915/2009 Rev. 14 and IRIS Quick guide to registration (EMA/416538/2018).

PRIME

The Agency has published a report which provides an overview of the first two years of implementation of the PRIME scheme (Link). The report explains how the criteria for PRIME eligibility have been applied and details the type of support applicants have received so far.

New guidance for applicants on opportunities for regulatory interactions in the context of PRIME (EMA/205771/2016) (i.e. 'kick-off meetings') has also been published. The guideline on enhanced early dialogue to facilitate accelerated assessment of PRIority MEdicines (PRIME) (EMA/CHMP/57760/2015, Rev. 1) has been revised to reflect the initial experience since the launch of the scheme.

Paediatric investigation plans

A revised EMA Decision on class waivers for paediatric investigation plans (PIP) (CW/0001/2015) came into effect on 28 July 2018. Initial applications and variations will be

validated against this decision from this date. The request form for confirmation of the applicability of the Agency's decision on class waivers has been updated to reflect this change (Link). Further information on class waivers can be found on the EMA website (Link).

Clinical trials

EU clinical trial portal and database

Updated information on the EU clinical trial portal and database project planning has been released (Link).

Clinical trials guidance

- A guideline on requirements for quality documentation concerning biological investigational medicinal products in clinical trials has been revised to provide guidance on the quality of comparator and placebo products used in clinical trials (EMA/CHMP/BWP/534898/2008 Rev. 1).

- An ICH guideline E17 on the general principles for the planning and design of multiregional clinical trials (MRCT) came into effect on 14 June 2018 (EMA/CHMP/ICH/453276/2016).

- A draft guideline on the responsibilities of the sponsor with regards to handling and shipping of investigational medicinal products for human use in accordance with good clinical practice and good manufacturing practice (EMA/202679/2018) has been released for public consultation until 31 August 2018.

- A questions & answers document on Good Clinical Practice (GCP) (Link) has been updated (e.g. on level of validation/ qualification needed to be performed by a sponsor when using an electronic system previously qualified by a provider).

Good Clinical Practice (GCP) for advanced therapies

The European Commission has launched an online targeted public consultation on the draft guidelines on good clinical practice for Advanced Medicinal Products addressed particularly to SMEs, academia, hospitals and patient organisations (Link). Comments may be sent to sante-pharmaceuticals-B5@ec.europa.eu until 31 October 2018.

Pharmacovigilance

Public data from Article 57 database

EMA now publishes data from the Article 57 database on all medicines authorised in the EEA in the form of an excel document (Link). Only products that have a valid marketing authorisation are included. The objectives of publishing this data are to provide a complete list of medicines authorised in the EEA alongside the dedicated contact points for pharmacovigilance enquiries and to enable applicants to better assess their potential invented names.

EudraVigilance

The EudraVigilance Operational Plan - milestones 2018 to 2020 has been published (EMA/100194/2018). It describes key factors that will impact EudraVigilance and its stakeholders from a technical and operational perspective until 2020.
A series of guidance documents on EudraVigilance training have been published. These include step-by-step guides, user manuals and questions and answers documents (Link). Updated versions of other EudraVigilance training documents can also be found here. The EudraVigilance user manual for marketing authorisation holders (EMA/167839/2016) has been updated and a questions and answer document on EudraVigilance (EMA/390861/2018) has been published.

Good Manufacturing Practice

EU-US mutual recognition of inspections of medicines manufacturers

The mutual recognition agreement between the EU and US has made further progress with FDA confirming the capability of two additional EU Member States (Lithuania and Ireland) to carry out GMP inspections at a level equivalent to the US (Link).

Shortages due to GMP non-compliance/quality defects

EMA has updated the defective product report template to incorporate Medical Dictionary for Regulatory Activities (MedDRA) terminology (Link). The criteria for classification of critical medicinal products (EMA/24304/2016) and the points to consider for the overall assessment of a supply shortage of a

medicinal product due to GMP non-compliance/quality defects (EMA/352178/2013) have been updated to include veterinary medicinal products as well as products for human use. The corresponding regulatory and procedural guideline has been updated (EMA/INS/GMP/35037/2017).

Regulatory

Duplicate marketing authorisation of biologicals

The European Commission has opened a public consultation until 10 September 2018 regarding the impact of duplicate marketing authorisations of biological medicinal products on the availability of biosimilar medicines to healthcare professionals and patients (Link). The consultation will assess whether there is a need to clarify the current wording of Annex I, Section 1 of the note on the handling of duplicate marketing authorisations applications (Link).

Regulatory guidance

The following guidance has been updated:

- Pre-authorisation guidance (EMA/821278/2015) (on e.g. attribution of EMA application/procedure number, oral explanation);
- Post-authorisation guidance (EMEA-H-19984/03 Rev. 7) (on e.g. grouping of variations, article 46 paediatric study submission, transfer of Marketing Authorisation, change of Qualified Person for Pharmacovigilance);
- User guide on how to generate PDF versions of the product information and other annexes – human (EMA/524020/2007 rev.5);
- Information package for certificates of medicinal products issued by the European Medicines Agency (EMA/119843/2013 Rev 13).

The following questions and answers (Q&A) have been updated:

- Classification of quality changes to marketing authorisations: questions and answers (Link);
- Grouping of variations: questions and answers (Link);
- Type-IA variations: questions and answers (Link);
- Submission of Article-46 paediatric studies: questions and answers (Link).

Substance, product, organisation and referential (SPOR) master data

A webinar was held at EMA to provide an overview of the Organisations Management Service (OMS) data services, the impact of the integration of OMS with the electronic application form (eAF) and the Common European Single Submission Portal (CESSP). It also covered the OMS change request process and data quality aspects; see presentation here and guidance on using Referential and Organisation master data in eAF (EMA/819524/2017 version 2).

The following guidance has also been updated:

- Referentials Management Services (RMS) operating model (EMA/412376/2016 version 2);
- Organisation Management Services (OMS) operating model (EMA/459105/2016 version 4).

More information on SPOR can be found here and on the new SPOR registration webpage (Link).

Scientific guidelines

Clinical and non-clinical guidelines

- A revised guideline on the clinical evaluation of vaccines (EMEA/CHMP/VWP/164653/05 Rev. 1) is open for public consultation until 30 October 2018. It addresses the clinical evaluation of vaccines intended for the prevention of infectious diseases and includes specific considerations for special populations such as pregnant women and the elderly.

- An update of the EU recommendations for the influenza virus strains that should be included in vaccines for the prevention of seasonal influenza from autumn 2018 has been published (Link).

- A revised ICH S9 guideline on the non-clinical evaluation for anticancer pharmaceuticals (CHMP/ICH/646107/08) - questions and answers will come into effect on 16 November 2018. It is intended to facilitate the implementation of ICH S9 Guideline and to continue progress in the 3Rs of Reduction, Refinement, and Replacement in use of animals.

Quality guidelines

- An ICH guideline Q3D (R1) on elemental impurities - Step 2b (EMA/CHMP/ICH/353369/2013) is open for public consultation until 16 August 2018. It sets out a process to assess and control elemental impurities in the finished product using the principles of risk management as described in ICH Q9.

The following questions & answers (Q&A) have been released:

- Questions and answers on the implementation of risk-based prevention of cross contamination in production and the 'Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities' (EMA/CHMP/CVMP/SWP/169430/2012);

- Updated guidance on good manufacturing practice and good distribution practice (link) on e.g. GDP requirements, QP batch certification.

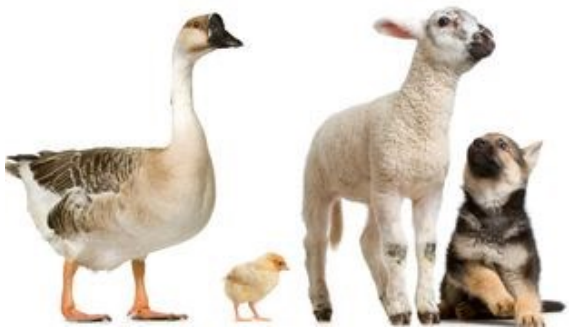
Veterinary medicines

Maximum Residue Limits (MRLs)

Commission Regulation 2018/782 (Link) establishing the methodological principles for the risk assessment and risk management recommendations referred to in Regulation (EC) No 470/2009 (the MRL regulation) was published in May 2018. It describes the methodology to be used in the scientific risk assessments that underpin MRL recommendations. It replaces the existing guidance on MRLs in Volume 8 of "The rules governing medicinal products in the European Union"; see also updated webpage (Link).

Pharmacovigilance

A revised recommendation for the surveillance of veterinary medicines in EudraVigilance Veterinary (EVVet) (EMA/CVMP/PhVWP/171122/2016) came into effect on 1 June 2018. It aims to improve the overall pharmacovigilance surveillance process by integrating periodic safety update report (PSUR) evaluation and signal detection processes based on EVVet data and risk-based principles.



Guidelines

A guideline on user safety of topically administered veterinary medicinal products (EMA/CVMP/SWP/721059/2014) will come into effect on 1 November 2018. It provides advice on methods to assess of the risk to users for topically administered products that remain on an animal's body after use.

The following draft guidelines are open for public consultation:

- A draft guideline on the summary of product characteristics for veterinary medicinal products containing antimicrobial substances (EMA/CVMP/383441/2005); until 30 September 2018;
- A draft guideline on the manufacture of veterinary finished dosage forms - Revision 1 (EMEA/CVMP/126/95) updated to reflect the legal requirements and current manufacturing practices in terms of complex supply chains and worldwide manufacture; until 22 October 2018;
- A draft guideline on the use of adjuvanted veterinary vaccines (EMA/CVMP/IWP/315887/2017); until 15 January 2019.

Reports, presentations and videos

Reports of interest:

- First report on the implementation of the EMA policy on the publication of clinical data (Policy 0070) (Link).
- 2017 Annual Report of the European Medicines Agency (Link)
- Report from the CAT expert meeting on scientific and regulatory considerations for adeno-associated viral vector (AAV)-based gene therapy (Link)

Presentations, reports and videos of the following events have been published:

- CAR-T cell therapy registries workshop – 09 February 2018 (Link)
- Multi-stakeholder workshop to further improve the implementation of the Paediatric Regulation- 20 March 2018 (Link)
- EMA veterinary medicines innovation day- 19 April 2018 (Link)
- Third industry stakeholder platform on research and development support- 18 May 2018 (Link)
- Rare Disease (RD)-ACTION/EMA/DG SANTE workshop: how European Reference Networks can add value to clinical research- 29-30 May 2018 (Link)
- Annual workshop of the European Network of Paediatric Research at the European Medicines Agency (Enpr-EMA) - 7 June 2018 (Link)

FUTURE EVENT—SME info day

The next SME info day entitled "Regulatory toolbox for medicines and combined devices developers" will take place on Friday, **26 October 2018** at the European Medicines Agency's offices in London. The agenda is available at the following Link.

Registered SMEs

Currently, 1790 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 Applying for SME status 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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