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SME Office NEWSLETTER

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Scientific guidelines for human medicines

Quality guidelines

Information on nitrosamines for marketing authorisation holders has been updated (see dedicated webpage, questions & answers (Q&A) document and press release). The guidance sets out the steps and actions that companies should take in relation to nitrosamine impurities in medicines manufacturing.

Non-clinical and clinical guidelines

A guideline on the clinical investigation of medicinal products intended for the treatment of gout has been published on 14 November 2019 (EMA/CHMP/774470/2018). It provides guidance on study design, inclusion criteria, primary endpoints and trial duration for the development of new urate-lowering and anti-inflammatory medicines (Link).

Product-specific bioequivalence guidance (Link) were released on 15 October 2019 for:

- Apixaban
- Colchicine
- Palbociclib
- Alectinib
- Cabozantinib
- Ezetimibe
- Gefitinib

Advanced Therapy Medicinal Products (ATMPs)

Q&A documents on exemption from batch controls for ATMPs imported in the EU from third countries (EMA/354272/2019) and on the use of out-of-specification batches of authorised cell/tissue-based ATMPs (EMA/CAT/224381/2019) were released on 21 August 2019.

A Q&A document on comparability aspects of ATMPs was released on 13 December 2019 (EMA/CAT/499821/2019). It discusses how to demonstrate comparability for gene and cell-based medicinal products following a manufacturing change or with addition of a manufacturing site.

Updated guidance on Genetically Modified Organisms (GMOs) requirements for investigational products has been released by the European Commission (EC) (Link). It includes a Q&A document, a repository of national regulatory requirements for clinical trials with medicinal products that contain or consist of GMOs, and good practice documents and application forms for GMO-related aspects in the context of clinical trials with viral vectors, adeno-associated virus vectors, and genetically modified cells.

Clinical trials

An updated EC Q&A document on Clinical Trials Regulation (EU) No 536/2014 was released in November 2019 (Link). It provides details on a series of topics including: trials authorised subject to conditions, responsibilities for trials with multiple sponsors, request for information during the review of trial applications, publication of assessment reports, sponsors' responsibilities for changes which are not substantial modifications but relevant for trial supervision, types of trials falling within the scope of the regulation.

An updated Enpr-EMA document on informed consent for paediatric clinical trials in Europe was released on 23 October 2019 (Link).

EMA has published a final qualification opinion on the use of eSource Direct Data Capture (DCC) in the conduct of clinical trials in the European Union (EU) (EMA/CHMP/SAWP/483349/2019). eSource DDC refers to an electronic application or device that allows capture of clinical study source data electronically by investigator site staff at the point of care. The document sets out regulatory expectations for the use of an eSource DDC in clinical trials conducted to support an MA application.

Pharmacovigilance

A revised EudraVigilance access policy was published in August 2019 (EMA/759287/2009 Revision 4). It was updated to include references to Regulation (EU) 2016/679, the General Data Protection Regulation (GDPR) and Regulation (EU) 2018/1725, the EU Data Protection legislation.

A revised list of Important Medical Event (IME) terms was published on 18 September 2019 (MedDRA version 22.1). The list aims to facilitate the classification of suspected adverse reactions for pharmacovigilance activities in the EU. It was revised to consider the latest version of MedDRA, the ICH definition of seriousness and important medical event (EMA/494099/2019).

A draft 'Guideline on good pharmacovigilance practices (GVP); Product- or population-specific considerations III: pregnant and breastfeeding women' was released for consultation until 28 February 2020 (EMA/653036/2019; EU-GVP webpage Link).

The EU electronic Register of Post-Authorisation Studies (EU PAS Register) is the publicly available register of non-interventional post-authorisation studies (PAS) maintained by EMA. The latest upgrade includes the option to delay protocol publication until the end of the study and other new functionalities to further increase transparency on non-interventional research for medicines authorised in the European Union (e.g. date of first registration, search by country); See Link.

New or updated guidance and release notes have been published:

- Guidance for notifications of a first user qualified person for pharmacovigilance/responsible person (QPPV/RP) of a new organisation, or a change of QPPV/RP (EMA/503895/2018).
- EudraVigilance Release Notes (EMA/571561/2019); revised following the latest MedDRA upgrade (version 22.1).
- EudraVigilance registration documents for production (EMA/503894/2018).
- Electronic registration process in EudraVigilance XCOMP - registration phases I, II and III (EMA/101243/2016) and EudraVigilance XCOMP - organisation and user registration documents (EMA/583210/2019) - providing guidance for connecting to XCOMP for testing a company's own software/IT system interoperability with EudraVigilance.

Regulatory guidance

The following guidance documents have been updated:

- Pre– and post-procedural guidance for orphan medicinal product designation (EMA/420706/2018 Rev 5; EMA/469917/2018) on topics including IRIS and orphan designation removal.
- Pre-authorisation guidance (EMA/821278/2015) on topics including orphan designation, conditional marketing authorisation and accelerated assessment.
- Post-authorisation guidance (EMEA-H-19984/03 Rev. 83) on topics including IA/IA_{IN}-II variations, orphan designation, extension of indication, renewal application, grouping and work-sharing of variations, post-authorisation safety studies, risk management plan update, periodic safety update reports, periodic safety updated report single assessment procedure, withdrawn products notification.
- Parallel distribution frequently asked questions (FAQ) on braille text labelling requirements (Link).
- Procedural guidance on biosimilar medicines and generic/hybrid medicinal products on topics including centralised procedure eligibility and pre-authorisation good clinical practices (GCP) inspection.

Product information (PI)

As of 28 June 2019, any new centralised marketing authorisation (MA) application needs to comply with revised PI templates (v10.1) (Link). Holders of existing MA(s) are encouraged to use the first upcoming regulatory procedure impacting product information annexes to comply with the revised templates.

A revised annex to the EC guideline on excipients in the labelling and package leaflet of medicinal products for human use came into effect on 22 November 2019 (Link). Specific information on the use of ethanol as an excipient is provided in Link. Holders of MA(s) are encouraged to use upcoming procedures to implement the revised guidance.

A guide on the wording of therapeutic indications for new active substances or new indications was published on 21 October 2019. It aims to support a consistent approach in defining therapeutic indications during the assessment of centralised MAs (EMA/CHMP/483022/2019).

Medical devices regulation

A revised Q&A document on the implementation of the Medical Devices Regulation (MDR)/(EU) 2017/745, and In Vitro Diagnostic Regulation (IVDR)/(EU) 2017/746) (EMA/37991/2019 and EMA/37991/2019 – tracked changes version) was published on 22 October 2019. It was updated in relation to requirements of the MDR Regulation for medicinal products with an integral or co-packaged medical device.

IRIS (regulatory and scientific information management platform)

In November 2019, IRIS was extended to EMA's Innovation Task Force (ITF) activities and applicants for a briefing meeting with EMA's Innovation Task Force (ITF) are advised to use IRIS (see IRIS guide for applicants - scientific applications for industry and individual applicants - Link, and IRIS registration guide - Link).

Veterinary medicines

A new webpage on the new Veterinary Medicines Regulation (Regulation (EU) 2019/6) has been published. It includes updates on the implementation of the regulation and information on EMA's scientific and technical recommendations to EC that will feed into delegated acts of the legislation.

Scientific guidelines for veterinary scientific

A draft reflection paper on *'Promoting the authorisation of alternatives to antimicrobials in the EU'* was released for consultation until 30 April 2020 (EMA/CVMP/461776/2017). It was developed to identify additional measures that could be implemented to promote the authorisation of alternatives to antimicrobials in the EU.

A draft VICH GL59 guideline on the *'harmonisation of criteria to waive laboratory animal batch safety testing for vaccines for veterinary use'* was released for consultation until 10 April 2020 (EMA/CVMP/VICH/677723/2016). Guidance on target animal batch safety test for inactivated and live veterinary vaccines are respectively addressed in VICH GL50 and VICH GL55 (R).

A VICH GL58 guideline on *'stability testing of new veterinary drug substances and medicinal products in climatic zones III and IV'* will come into effect on 1 November 2020 (EMA/CVMP/VICH/335918/2016). It is an annex to the VICH parent stability guideline *'stability testing of new veterinary drug substances and medicinal products'* (VICH GL3 (R)).

Regulatory guidance

A revised procedural advice on appointment and responsibilities of CVMP (co-)rapporteurs was published on 20 September 2019 (EMA/CVMP/468877/2009 - Rev. 2). It was updated to take into account procedural changes, multinational assessment teams and appointments for referral procedures.

Other news

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

- 'From Lab to Patient' interactive map and booklet. The tools describes the journey of a medicine for human use authorised by EMA, from initial research to patient access and explains how EMA supports a medicine's development through scientific advice, assesses benefits and risks, and monitors safety.
- Additional reports on big data in the context of medicines development and regulation in the EU from the HMA/EMA joint Task Force on Big Data (Link).
- EMA and EU healthcare payer community meeting on cooperation to improve timely and affordable access of patients to new medicinal products (Link).
- Multi-stakeholder workshop on 'Regulatory Science to 2025' strategy (human medicines Link – 18-19/11/2019; veterinary medicines Link – 5-6/12/2019).

EMA's new contact details

Since January 2020, EMA is located in its permanent building in the Zuidas district of Amsterdam (Link). The Agency has published an orientation guide for industry, which includes details on how to get to the building, facilities, and arrangements for companies attending meetings (Link).

Registered SMEs

1 951 companies had SME status assigned by the Agency at year end 2019.

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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