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SME Office NEWSLETTER

Information for SMEs on the EU regulatory environment for medicines.
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Scientific guidelines for human medicines

Quality guidelines

A revised ICH guideline on elemental impurities in finished products came into force on 29 March 2019. It outlines a process to assess and control elemental impurities using the principles of risk management described in ICH Q9 (ICH Q3D (R1); EMA/CHMP/ICH/353369/2013).

A guideline on sterilisation of active substances, excipients, medicinal products and primary containers will come into force on 1 October 2019 (EMA/CHMP/CVMP/QWP/850374/2015). It provides guidance on the acceptance of terminal sterilisation processes (e.g. sterilising filtration or aseptic processing) as alternatives to terminal sterilisation using a reference condition of the European Pharmacopoeia. It replaces the decision trees for the selection of sterilisation methods, which are annexed to the guidance documents on development pharmaceutics CPMP/QWP/155/96 and EMEA/CVMP/315/98.

A draft ICH guideline on bioanalytical method validation was released for consultation until 1 September 2019 (ICH M10; EMA/CHMP/ICH/172948/2019). It will provide recommendations for the validation of bioanalytical assays for chemical and biological product quantification and their application in the analysis of study samples.

EMA's quality of medicines questions and answers (Q&As) were updated on the use of peptones in the manufacture of active substance (Link).

Recommendations for marketing authorisation holders and manufacturers of sartan medicines to review manufacturing processes in relation to nitrosamine impurities have been released on 1 August 2019 (Press release).

A draft guideline on quality requirements for medical devices was released for consultation until 31 August 2019 (EMA/CHMP/QWP/BWP/259165/2019). It addresses the new requirements of Regulation (EU) 2017/745 on medical devices, in particular Article 117 provisions for marketing authorisation applications to include a CE (Conformité Européenne) certificate, declaration of device conformity or a notified body opinion. More information can be found in a press release and webpage.

Non-clinical and clinical guidelines

A guideline on subgroups analyses in confirmatory clinical trials included in marketing authorisation applications came into effect on 1 August 2019 (EMA/CHMP/539146/2013). It focuses on the exploratory evaluation of subgroups as part of the assessment of the treatment effect in the patient population (e.g. consistency in risk-benefit across subgroups, subgroup analyses in cases of inconclusive primary data analysis).

A Q&As document on adjustments for patients cross-over in estimating effects in oncology trials has been published (EMA/845963/2018).

A guideline on equivalence studies to demonstrate therapeutic equivalence of locally applied, locally acting products in the gastrointestinal tract came into effect on 1 May 2019 (CPMP/EWP/239/95 Rev. 1, Corr.1*). It is an addendum to the *'Note for guidance on the clinical requirements for locally applied, locally acting products containing known constituents'* (CPMP/EWP/239/95) and defines requirements to waive clinical trials with clinical or pharmacodynamic endpoints.

A draft ICH guideline on *'General considerations for clinical studies'* was released for consultation until 30 September 2019 (E8 (R1); EMA/CHMP/ICH/544570/1998). It provides guidance on quality aspects to consider when designing and conducting clinical studies in order to facilitate their acceptance by regulatory authorities.

A draft ICH guideline on optimisation of safety data collection was released for consultation until 29 September 2019 (ICH E19; EMA/CHMP/ICH/173706/2019). It sets out an optimised approach to safety data collection in late-stage pre-approval or post-approval studies when the safety profile of a product is sufficiently characterised. Its key objective is to improve the efficiency of clinical studies and reduce the burden to study participants e.g. patient visits or laboratory tests.

EMA's Q&As on clinical pharmacology and pharmacokinetics were updated on topics relating to bioequivalence studies with crushed tablets for generic applications and pharmacokinetic characteristics of iron salts (Link).

Pharmacovigilance

Updated EudraVigilance guidance ('Release notes') was published on 30 July 2019. The changes relate to a new MedDRA version implemented in EudraVigilance and a EVWEB interface search function (Link).

Regulatory guidance

Procedural Q&As were updated (pre-authorisation; post-authorisation; paediatric medicines; generic/hybrid applications) on topics including paediatric investigation plans, legal establishment of marketing authorisation applicants in the EU, risk management plan, classification of post-authorisation changes, post-authorisation measures and extensions of marketing authorisations.
Revised recommendations for exemptions to the labelling and package-leaflet obligations for centralised procedures have been released (EMA/135540/2019 rev.4*).

ITF

EMA's Innovation Task Force provides a forum for early dialogue with applicants on innovative medicines developments. The Task Force is inviting developers working on medicines for life-threatening microbial infections to enter into early dialogue with the Agency (Link).

Fees

General non-pharmacovigilance fees payable to EMA by applicants and marketing authorisation holders increased by 1.7% on 1 April 2019 (Link).

IRIS (regulatory and scientific information management platform)

Updated guidance for sponsors submitting orphan designation procedures have been published (Guidance for sponsors submitting an application via IRIS secure online portal; Post-orphan medicinal product designation procedures). For information about the launch of IRIS for parallel distribution notifications, see IRIS guide to the platform for parallel distribution industry users).

Medicines shortages and availability

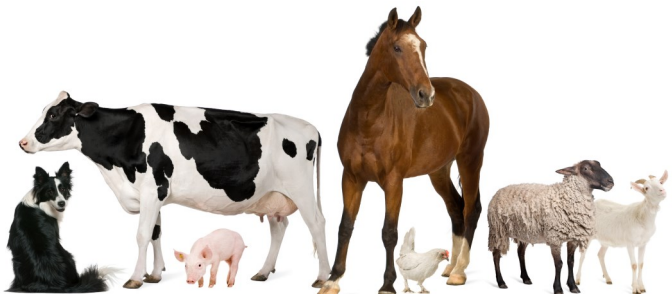
EMA and Heads of Medicines Agencies' Task Force on the availability of human and veterinary medicines has published two documents setting out an improved approach for the reporting and communication on medicines' shortages and availability:
Guidance for marketing authorisation holders (EMA/674304/2018) on the detection and notification of shortages to competent authorities. Guidance for competent authorities on good communication practices to patients and healthcare professionals (EMA/632473/2018).

Mutual recognition agreements (MRA)

FDA confirmed the capability of all 28 EU Good Manufacturing Practices (GMP) inspectorates for human medicines to carry out inspections at a level equivalent to the US. EU and US authorities are now able to rely on each other's inspection results. Batch testing waiver now also applies with EU qualified persons no longer having to carry out quality controls for products manufactured in and imported from the US, when controls have already been carried out in the US (Link; Q&A on MRA; Q&A EU-US MRA on marketing authorisation applications and variations).

Scientific guidelines for veterinary medicines

A revised VICH guideline on *'Studies to evaluate the safety of residues of veterinary drugs in human food: general approach to establish a microbiological ADI'* came into effect in August 2019 (GL36(R2); EMA/CVMP/VICH/467/2003).



A VICH guideline on *'Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing species: marker residue depletion studies to establish product withdrawal periods in aquatic species'* will come into effect in February 2020 (GL57; EMA/CVMP/VICH/517152/2013). It complements the general parent residues guidance VICH GL48 with species-specific recommendations.

Post-authorisation procedural Q&As were updated on topics including transfers, renewals, post-authorisation measures, invented name change, IA-IB-II variations, extension applications, grouping and work-sharing of variations, mock-ups, transparency and sunset clause (Link).

Other news

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

- Stakeholder workshop on support to quality development in early access approaches, such as PRIME and Breakthrough Therapies; European Medicines Agency; 26 November 2018 (Link).
- Stakeholder meeting on the development of medicinal products for chronic non-infectious liver diseases; European Medicines Agency; 3 December 2018 (Link).
- EMA's SME 2018 Office annual report (Link)
- EMA's 2018 annual report (Link)

Registered SMEs

Currently, 1868 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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