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# 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 documents to help companies prepare for Brexit have been published on EMA's website:

- An updated questions and answers document (Link) including additional information on how 'Brexit' will affect applications and authorisations for different types of medicinal products e.g. generic, hybrid and biosimilar medicines.
- Procedural guidance for companies applying for changes to their marketing authorisation for different types of medicinal products. (EMA/478309/2017).

In January EMA launched a targeted survey for those companies which need to introduce regulatory changes as a result of 'Brexit'. (Link).

Further details can be found in the dedicated pages on 'Brexit' (Link) and the 'Agency relocation to Amsterdam' (Link). SMEs can address questions relating to Brexit directly to SME@ema.europa.eu.

## GMP

### EU-US mutual recognition of inspections of medicines manufacturers

As part of the mutual recognition agreement (Link) between the European Union (EU) and the United States of America (USA), the recognition of inspections of manufacturing sites for human medicines came into operation on 1 November 2017. The US FDA can carry out GMP inspections at a level equivalent to the EU and the FDA confirmed the capability of eight EU Member States (Austria, Croatia, France, Italy, Malta, Spain, Sweden, and United Kingdom) to perform such inspections. Further information can be found in Link.

### Good manufacturing practices for advanced therapies medicinal products (ATMPs)

Guidelines on good manufacturing practices (GMP) for advanced therapies will enter into force on 22 May 2018 (Link). They adapt EU GMP requirements to the specific characteristics of ATMPs, address novel manufacturing scenarios and foster a risk-based approach to manufacturing and testing (see also EMA/European Commission joint action plan for the development of ATMPs Link).

# Pharmacovigilance

### Eudravigilance update

On 22 November 2017, EMA launched the new and improved version of EudraVigilance (Link) with enhanced features for reporting and analysing suspected adverse reactions. It includes a simplified reporting of individual case safety reports by marketing authorisation holders (MAHs), which no longer have to provide these reports to national competent authorities and can send them directly to EudraVigilance (see also EudraVigilance training and support webpage link).

EMA and the European Commission have agreed transitional arrangements to streamline the monitoring of EudraVigilance by marketing authorisation holders. During a pilot phase of a year, which will start on 22 February 2018, MAHs of active substances included in the 'List of medicinal products under additional monitoring' (Link) will have to monitor the substances in EudraVigilance and inform the Agency and National Competent Authorities of validated signals. More information on the phased implementation of these requirements can be found in Link.

### Good Pharmacovigilance Practice (GVP) update

An explanatory note on GVP module VII has been published (EMA/670256/2017). It sets out the changes planned in the next update to address challenges encountered during the two years of implementation of the Periodic Safety Update Report (PSUR) single assessment (PSUSA) procedure.

# Regulatory Guidance

### Fees payable to the Agency

The following changes to the fees payable to the Agency have been introduced:

- A 1-year fee reduction for notifications of parallel distribution to ensure wider access to centrally authorised products (EMA/275221/2017).
- An increase in pharmacovigilance fees to align with inflation (Link).

### Updates to eAFs

New versions of electronic Applications Forms for marketing authorisation applications, renewals and variations for human and veterinary medicines have been released. The main changes include the implementation of Organisations Management Service (OMS) and Referentials management service (RMS). These enable users to select information supplied directly by master data services when preparing their regulatory submissions. The new forms (eAF v.1.22) will replace the previous version (eAF v.1.21) on 15 February 2018. For ongoing procedures, the version of the form should not be changed.

### Product information

EMA has published an action plan (EMA/680018/2017) to improve the product information of EU medicines. One of the key actions is to explore how electronic or digital means can be used to improve accessibility to medicines' information.

### Pre-authorisation guidance (human medicines)

Pre-authorisation procedural advice (EMA/821278/2015) was updated to include changes to Good Pharmacovigilance Practices (GVP) and reflect marketing authorisation guidance '*HMA-EMA Best-practice guide on measures improving the predictability of submissions/responses* (EMA/488783/2017) and *Validation issues frequently seen with initial MAAs'* (EMA/454165/2015).

### Post-authorisation guidance (human medicines)

Post-authorisation guidance was updated (EMEA-H-19984/03 Rev. 75) on the following topics:

- Type-IA/IB variations on e.g. presenting Type IA/IAIN variations, triggering new EU-numbers and obtaining EU sub-numbers;
- Periodic safety update reports on e.g. submission after withdrawal of marketing authorisation;
- Post-authorisation measures on e.g. definition of a specific obligation;
- Pre-submission queries service;
- Risk management plan to reflect the latest version of GVP.

### Herbals

A revised guideline on the assessment of clinical safety and efficacy in the preparation of EU herbal monographs for well-established and traditional herbal medicinal products (EMA/HMPC/104613/2005 Rev. 1) came into effect on 28 November 2017.

A questions and answers document on herbal medicinal products was updated (Link) to include clarifications on the differences between a herbal monograph and a summary of product characteristics.

# Scientific Guidelines (human medicines)

## Clinical Guidelines

A new guideline on the clinical development of medicinal products for the treatment of Autism Spectrum Disorder (EMA/CHMP/598082/2013) will come into effect on 1 June 2018. It provides guidance on patient selection, study design and clinical safety.

A revised guideline on the clinical investigation of products intended for axial spondyloarthritis (EMA/CPMP/EWP/4891/03 Rev.1) will come into effect on 1 May 2018. It takes into account advances in clinical practice and definitions of patient populations and includes details on e.g. new outcome measures for the treatment and design of confirmatory trials.

A revised guideline on the clinical investigation of products intended for rheumatoid arthritis (CPMP/EWP/556/95 Rev. 2) will come into effect on 1 July 2018. It revises the previous points to consider document and takes into account advances in treatment strategies and new classification criteria to updated recommendations on endpoints, patients populations, prevention of structural bone damage and clinical safety assessment from trials and registries.

A revised guideline on the evaluation of anticancer medicinal products in man will come into effect on 1 April 2018 (EMA/CHMP/205/95 Rev.5). It addresses changes relating to the collection and reporting of safety data ito inform benefit-risk evaluation.

An ICH guideline E17 on multi-regional clinical trials (EMA/CHMP/ICH/453276/2016) will come into effect on 14 June 2018. It sets out principles for the planning and design of such trials with the objective of increasing their acceptability in global regulatory submissions.

A draft guideline (EMA/CHMP/257022/2017) on the clinical evaluation of products intended for prophylaxis or treatment of respiratory syncytial virus (RSV) disease was released for consultation until 30 April 2018. It sets out safety and efficacy requirements in populations most likely to develop RSV lower respiratory tract infections and severe RSV diseases. It also includes details on non-clinical investigations of efficacy and risk of vaccine-associated enhanced disease to support clinical trials.

## Quality Guidelines

Guidance on investigational medicinal products (IMP) in clinical trials will come into effect on 14 March 2018. The following documents were revised to take into account Regulation (EU) No. 536/2014:

- Guideline on the quality documentation (EMA/CHMP/QWP/545525/2017). It replaces the "Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials" (CHMP/QWP/185401/2004 final).
- Guideline on quality requirements for biologicals (EMA/CHMP/BWP/534898/2008 rev. 1).

An ICH guideline on pharmaceutical product lifecycle management (EMA/CHMP/ICH/804273/2017) has been released for consultation until 31 December 2018. It complements the existing ICH Q8 to Q11 guidelines and provides guidance to manage post-approval chemistry, manufacturing and controls (CMC) changes more efficiently.

## Questions and answers

The following questions and answers documents have been updated:

- Questions and answers on ICH Guideline S3A: Note for guidance on toxicokinetics: the assessment of systemic exposure in toxicity studies – (EMA/CHMP/ICH/320985/2016)
- Questions and answers on quality of medicines – part 2 on e.g. design of in-use shelf-life for solid oral dosage forms in multi-dose containers (Link)

# Veterinary medicines

A guidance document on monoclonal antibodies for veterinary use was released on 11 December 2017 (EMA/CVMP/ADVENT/307606/2017). It provides guidance on topics including quality control for potential contaminants, stability testing and reproductive safety.

Recommendations on the need for field efficacy trials in the development of veterinary vaccines were published on 9 November 2017 (EMA/548726/2017).

New and updated guidance documents have been published:

- Article 13 referral procedures (EMA/503274/2017);
- Article 33(4) referral procedures (EMA/503275/2017);
- Article 35 referral procedures (EMA/503277/2017);
- Type II variations (link) updated on e.g. changes to product information and introduction of a new manufacturing site;
- Type-IB variations (link) updated on e.g. applying for a new pack size;
- Guidance for applicants requesting scientific advice (EMEA/CVMP/SAWP/172329/2004 Rev. 5);
- QRD guidance on the use of approved pictograms (EMA/776723/2017);

# Reports, presentations and/or videos

- EC and EP Report on the 10 year of implementation of the paediatric regulation (Regulation (EC) No 1901/2006) (link).
- Report of meeting on field efficacy trials in the context of an EU authorisation for veterinary vaccines - 6 June 2017 (Link)
- European network of paediatric research/European Medicines Agency (Enpr-EMA) meeting - 25 November 2017 (Link)
- Second industry stakeholder platform on research and development support - 15 November 2017 (Link)
- Joint Biologics Working Party/Quality Working Party workshop with stakeholders in relation to 'prior knowledge' and its use in regulatory applications – 23 November 2017 (Link)

# Other news

### Horizon 2020

In order to support applicants to H2020 research funding, including SMEs and academia, EMA has published a dedicated **page** with practical advice on EMA procedures to consider when planning for EU funding.

### Public consultation on EU Funds

A consultation aimed at collecting the views of stakeholders for the future of EU funding in the areas of investment, research & innovation, SMEs and single market is open for consultation until 8 March 2018. SMEs can provide their comments in **link.**

# Registered SMEs

Currently, 1635 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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