



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")	1
Clinical data publication	1
Eu public consultation	1
Advanced Therapies Medicinal Products	2
Pharmacovigilance	2
Regulatory and administrative guidance	3
Scientific guidelines	3
Veterinary Medicines	4
Workshops, Meetings and Reports	5
Contact details	6

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

A dedicated webpage on 'Brexit' is available on the EMA website ([Link](#)). It includes information on EMA's operational preparedness and guidance to help pharmaceutical companies prepare for the UK's withdrawal from the EU including a Questions and Answers document related to establishment requirements within the EEA. Meetings with the industry stakeholders representing human and veterinary companies have also been held ([Meeting on Brexit and operation of the centralised procedure for human medicinal products, meeting for veterinary medicinal products](#)). SMEs can address questions relating to Brexit to SME@ema.europa.eu.



Clinical data publication

The website on clinical data published under the EMA policy on the publication of clinical data (Policy 70) celebrates its one-year anniversary ([Link](#)). As of 20 October 2017, clinical reports on 50 medicines, including orphan, biosimilar and generic medicines, as well as medicines for use in children, have been made publicly available. Facts and figures are available in a leaflet ([Link](#)) and an overview is provided in the dedicated press release ([Link](#)).

EU public consultation

As part of the Single Market Strategy adopted in October 2015, a public consultation on supplementary protection certificates (SPC) and patent research exemptions of SPC has been launched by the European Commission until 4 January 2018 ([Link](#)). SMEs and stakeholders are invited to provide feedback which will be used for the evaluation and impact assessment of any potential modification of the SPC and patent exemption framework in the EU.

Advanced Therapies Medicinal Products

The European Commission and the EMA have published a joint action plan to foster the development of ATMPs ([Link](#)). The plan was developed following the multi-stakeholder workshop that took place in May 2016 at the EMA ([Link](#)). The purpose of this document is to streamline procedures based on experience and to better address the specificities of ATMPs.

Pharmacovigilance

New Eudravigilance System

On 22 November 2017, a new version of EudraVigilance with enhanced features for the reporting and analysis of suspected adverse reactions will be released ([Link](#)). The release requires a downtime period from 8 to 21 November that affects a number of key EudraVigilance functionalities and other IT systems (e.g. [EVWEB](#) and [XEVMPD](#) unavailable). It does not affect the direct reporting of side effects by patients and healthcare professionals to national competent authorities or marketing authorisation holders, and the European database of suspected adverse drug reaction reports remain live ([Link](#)). Alternative reporting arrangements are described in the EudraVigilance go-live plan ([EMA/399493/2017](#)). More information can be found [here](#) and in the Questions and Answers from stakeholders ([EMA/629943/2017](#)).

Good Pharmacovigilance practices (GVP)

The following revised guidelines on good pharmacovigilance practices ([Link](#)) came into effect on 13 October 2017:

- Module VIII on post-authorisation safety studies ([EMA/813938/2011 Rev 3](#)), revised to be aligned with Module VI on Individual case safety report (ICSR) submission and management.
- GVP Module XV on safety communication ([EMA/118465/2012 Rev 1](#)), revised in light of experience and working practices at Member States' and EU level.

The following revised guidelines on good pharmacovigilance practices ([Link](#)) will come into effect on 22 November 2017:

- Module VI Addendum I on duplicate management of suspected adverse reaction reports ([EMA/405655/2016](#)) (e.g. on electronic reporting modalities of ICSRs and on the roles and responsibilities of parties in the operation of duplicate detection and management of reports of suspected adverse reactions).
- Module VI on collection, management and submission of reports of suspected adverse reactions to medicinal products ([EMA/873138/2011 Rev 2](#)) (e.g. on guidance on submission, validation and management of ICSRs; duplicate detection and data quality management; management of individual reports of off-label use and management of reports from post-authorisation efficacy studies).
- Module IX on signal management ([EMA/827661/2011 Rev 1](#)), which streamlines the signal management process in the light of experience gained with the 2010 pharmacovigilance legislation and to support the new EudraVigilance functionalities.
- Module IX Addendum I on the methods for signal management, including statistical methods ([EMA/209012/2015](#)), which updates some of information from the Guideline on the Use of Statistical Signal Detection Methods in the EudraVigilance Data Analysis System ([EMEA/106464/2006 rev. 1](#)).

The following GVP annexes were also updated:

- Annex I on Definitions ([EMA/876333/2011 Rev 4](#));
- Annex II on Templates for Direct Healthcare Professional Communication (DHCPs) ([EMA/36988/2013 Rev 1](#)) and a new Template for DHPC Communication Plans ([EMA/334164/2015](#));
- Annex V on Abbreviations ([EMA/135814/2013 Rev 1](#)).



Regulatory and Administrative Guidance

Excipients' labelling

The annex to the European Commission guideline on excipients' labelling describes the excipients that must be declared in the labelling and package leaflet of medicines for human use and their agreed safety warnings ([Link](#)). It has been revised to include five new excipients and new safety warnings for ten existing excipients and applies to both centrally and nationally authorised products.

Facilitating submission of post-approval data

A [form](#) to submit data generated to meet post-authorisation measures ([PAMs](#)) for centrally authorised products has become mandatory since 1 September 2017.

The following guidance documents have been updated:

- Guidance for sponsors on post-orphan medicinal product designation procedures (on e.g. market exclusivity period and Brexit) ([EMA/62801/2015 Rev. 7](#));
- Guidance for applicants seeking scientific advice and protocol assistance (on e.g. change of functional mailbox for receipt of submissions) ([EMA/4260/2001 Rev. 9](#));
- Guideline on the linguistic review process of product information in the centralised procedure (revised Annex 6 "Submission of Day +25/235 final product information annexes") ([EMA/5542/02/Rev 5.1](#));
- Pre-authorisation procedural advice for users of centralised procedure ([EMA/821278/2015](#)) (on e.g. combination packs, medical devices, submission of MAA);
- Post-authorisation procedural advice for users of centralised procedure ([EMA-H-19984/03 Rev. 74](#)) (on e.g. extension of MAA, annual re-assessment of MAA, renewal application, annual renewal of conditional marketing authorisations, post-authorisation measures, extensions of marketing authorisations, classification of changes, changes for medical devices and PSURs assessment);
- Procedural advice on medicinal products intended exclusively for markets outside the Community under Article 58 of Regulation (EC) No 726/2004 in the context

of cooperation with the World Health Organization ([EMA/534107/2008 Rev.1](#)) (minor clarifications were introduced to the guidance and corresponding application form ([Link](#)) was aligned with current version of corresponding application forms for the centralised procedure);

- Guidance on the implementation of the EMA policy on the publication of clinical data for medicinal products for human use has been updated ([EMA/90915/2016](#); see also Questions and Answers document ([EMA/14227/2017 Rev. 1](#)) and summary of the changes [here](#)).

Scientific Guidelines

Multidisciplinary guideline

A revised ICH guideline M7 on the assessment and control of DNA reactive (mutagenic) impurities in pharmaceuticals to limit potential carcinogenic risk ([EMA/CHMP/ICH/83812/2013](#)) will come into effect on 1 February 2018. It provides a practical framework that is applicable to the identification, categorization, qualification, and control of mutagenic impurities to limit potential carcinogenic risk. It complements ICH Q3A(R2), Q3B(R2) (Note 1), and ICH M3(R2): Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorizations for Pharmaceuticals.



Clinical guidelines

A revised guideline on 'First-in-human and early clinical trials outlining strategies to identify and mitigate risks for trial participants' will enter into force on 1 February 2018 ([EMA/CHMP/SWP/28367/07 Rev. 1](#)). It addresses the increased complexity of protocols of first-in-human clinical trials, which combine several steps of the clinical development within a single clinical trial protocol.

The following scientific guidelines on the clinical investigation of medicines in cardiovascular diseases will come into effect on 1 March 2018:

- Revised guideline on the clinical investigation of products in the treatment of chronic heart failure ([CPMP/EWP/235/95, Rev.2](#)). It has been updated to

provide details on the different types of heart failure, the inclusion of clinically stable patients after hospitalisation, the need for morbidity and mortality trials and ways to measure worsening of heart failure.

- Guideline on the clinical investigation of products for the treatment of acute coronary syndrome ([EMA/CHMP/760125/2016](#)). It has been updated on a series of points including guidance and definitions of ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), unstable angina (UA), risk stratification using different scoring systems, and endpoints.

The following ICH guidelines will come into effect on 28 February 2018:

- ICH guideline E18 on harmonised principles of genomic sampling and management of genomic data in clinical studies ([EMA/CHMP/ICH/11623/2016](#)).
- ICH guideline E11 on clinical investigation of medicinal products in the paediatric population ([EMA/CPMP/ICH/2711/1999](#)), which was revised to harmonise approaches in global developments of paediatric medicines.

The following ICH guidance have been revised and released for consultation until 28 February 2018:

- Draft addendum to the guideline on statistical principles for clinical trials ([ICH E9](#)) elaborating on the choice of estimand and sensitivity analysis in clinical trials and providing a framework to align its planning, design, conduct, analysis and interpretation ([EMA/CHMP/ICH/436221/2017](#));
- Draft ICH S5 guideline on reproductive toxicology providing key considerations for developing a testing strategy to identify hazard and characterize reproductive risk for human pharmaceuticals ([EMA/CHMP/ICH/544278/1998](#)).

A reflection paper on how medicine developers can better address the needs of older people taking medicines has been released for consultation until 31 January 2018 ([EMA/CHMP/QWP/292439/2017](#)). It describes aspects such as the selection of appropriate routes of administration and dosage forms, dosing frequency,

excipients, container closure systems, devices and technologies, and user instructions in the product information. Further information can be found in the dedicated press release ([Link](#)).

Quality guidelines

A revised guideline on the manufacture of the finished dosage form will come into effect in February 2018 ([EMA/CHMP/QWP/245074/2015](#)). It has been updated to follow the format and content of the Common Technical Document Module 3 dossier and address current manufacturing practices in terms of complex supply chains and worldwide manufacture.

A revised guideline on influenza vaccines–quality module will come into effect on 1 February 2018 ([EMA/CHMP/BWP/310834/2012_Rev.1](#)). The minor changes to the document include a review of the naming of pandemic/pre-pandemic vaccines.

The following documents have also been updated:

- Questions and answers on quality ([Link](#)) (e.g. Part 1 : Calculation of thresholds for impurities, potency for veterinary drug products / Part 2 : new section on needle safety system added);
- Questions and answers on good manufacturing practice ([Link](#)) (on GMP non-compliance statement);
- Questions and answers on ICH Q11 on development and manufacture of drug substances ([EMA/CHMP/ICH/809509/2016](#)).

Veterinary Medicines

Guidance on the classification of veterinary medicinal products for Minor Use Minor Species/limited market has been revised to align it with the revised guidelines on data requirements for products intended for MUMS/limited market ([EMA/CVMP/388694/2014-Rev.1](#)).

A draft revised guideline on data requirements for multi-strain dossiers for inactivated vaccines against avian influenza, bluetongue and foot-and-mouth disease has been released for consultation until 31 March 2018 ([EMA/CVMP/IWP/105506/2007-Rev.1](#)). Minor changes were introduced

following comments raised by stakeholders and their experience with the guideline. See also the corresponding Questions and Answers document ([EMA/CVMP/IWP/105506/2007-Rev.1](#)).



The EMA has launched a public consultation on a reflection paper on off-label use of antimicrobials in the European Union ([EMA/CVMP/AWP/237294/2017](#)). The document aims to define off-label use and to better understand the underlying reasons for the practice in relation to the use of antimicrobials. The deadline to submit comments is 31 January 2018.

The following Q&A documents were updated:

- Q&A on transfer (e.g. change of the name of the medicinal product as part of a transfer application) ([Link](#))
- Q&A on classification as minor uses minor species (MUMS) / limited markets ([EMA/CVMP/370663/2009-Rev.3](#))

Reports, Presentations and/or Videos of the following meetings have been published:

June 2017

- Cystic fibrosis workshop - Registries initiative ([Link](#))
- First European Medicines Agency-EuropaBio annual bilateral meeting ([Link](#))
- Workshop on generation and use of Health Based Exposure Limits ([Link](#))

July 2017

- Second EMA-EFPIA annual bilateral meeting ([Link](#))
- Multiple sclerosis workshop - Registries initiative ([Link](#))

September 2017

- Info session on antimicrobial resistance ([Link](#))
- Eleventh stakeholder forum on the pharmacovigilance legislation ([Link](#))
- Public hearing on valproate-containing medicines ([Link](#))

Selection of Upcoming Events

November 2017

- EMA info day on measuring the impact of pharmacovigilance activities – 14/11/2017 ([Link](#))
- SME info day "Supporting innovative medicines' development and early access – 17/11/2017 ([Link](#))

December 2017

- EMA/DIA statistics forum: The role of observational data in assessing the benefits and risks of medicines – 01/12/2017 ([Link](#))
- Opportunities and challenges for a common data model in Europe -11 & 12/12/2017 ([Link](#))

Registered SMEs

Currently, 1848 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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