



SME Office NEWSLETTER

Information for SMEs in the EU regulatory environment for medicines.
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Pharmaceutical development guidance

A guideline on the declaration of the quantitative composition / potency labelling of biological medicinal products will come into effect on 1 September 2014 ([EMA/CHMP/BWP/85290/2012](#)). It applies to medicinal products that include modified proteins as their active substance taking into account the product class, the clinically established declared value for the non-modified product, the method of assay and the relevance of the potency assay.

A revised guideline on stability testing for variation applications ([EMA/CHMP/CVMP/QWP/441071/2011- Rev.2](#)) will come into effect in August 2014. It provides guidance on stability testing for type IA and type IB variations and addresses the data requirements for common type II variations.

A guideline on the Quality Module of marketing authorisation applications for influenza vaccines will come into effect on 1 November 2014 ([EMA/CHMP/BWP/310834/2012](#)). All guidelines on influenza vaccines will be consolidated under a single guideline, developed according to a modular approach with distinct modules covering each relevant topic. The present module compiles the quality requirements for the different types of influenza vaccines and further guidelines will follow.

A guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance will come into effect on 1 December 2014 ([EMA/CHMP/BWP/247713/2012](#)). It addresses the requirements regarding the manufacturing processes, the quality comparability exercise considering e.g. the reference medicinal product, analytical methods and physicochemical characterisation.



A revised guideline on data requirements for the use of near infrared spectroscopy (NIRS) will come into effect in August 2014 ([EMA/CHMP/CVMP/QWP/17760/2009 Rev2; Addendum to the guideline](#)). NIRS is an analytical procedure used in the identification, qualification and assay of starting materials, intermediates and finished products and verification of physicochemical properties and one of the major techniques in Process Analytical Technology (PAT) and Real Time Release Testing (RTRT) strategy. The document provides guidance on the use of NIRS procedures including the development, calibration and validation, for qualitative and quantitative analysis and in PAT applications.

The Agency has published guidance on the Qualified Person's Declaration ([EMA/196292/2014](#)) template. All medicinal products have to be certified by a QP in accordance with the relevant requirements prior to their release. The objective of this document is to harmonise the format and to enhance the efficiency of regulatory submissions, their validation and review.



A draft guideline on process validation for the manufacture of biotechnology-derived active substances was released for public consultation until 31 October 2014 ([EMA/CHMP/BWP/187338/2014](#)). It covers process evaluation and verification studies for the upstream and downstream processes, in the context of a marketing authorisation application or a variation application.

The ICH guideline Q9 on quality risk management ([Link](#)) and Q10 on pharmaceutical quality system ([Link](#)) were updated to include workshop training materials and points to consider on questions raised during training workshop sessions. They cover topics relevant to the implementation of the ICH guidelines.

- ICH Q8/Q9/Q10 Training material ([Link](#))
- ICH Q8/Q9/Q10 Points to consider ([Link](#))

A questions and answers document related to the ICH guideline E2C (R2) on periodic benefit-risk evaluation report (PBRER) has been released in May 2014 ([EMA/CHMP/ICH/271908/2014](#)). It aims to clarify key issues linked to the evolution of the traditional PSUR from an interval safety report to cumulative benefit-risk report and with a change in focus from individual case reports to more aggregate data evaluation.

The following EMA questions and answers webpages were updated:

- Part 2 on Quality of medicines ([Link](#)): it now contains information on e.g. the acceptability of two different appearances (shape, dimensions, colour) for a single strength tablet in a single Marketing Authorisation.
- Good manufacturing practice ([Link](#)): it now includes information on voluntary inspections of an active-substance manufacturer.

Non-clinical and Clinical development guidance

A draft guideline on non-clinical local tolerance testing of medicinal products has been released for public consultation until 31 July 2014 ([EMA/CHMP/SWP/2145/2000 Rev.1](#)). This document provides guidance on the non-clinical strategies to be considered when developing a finished product (both active substance and excipients) that could come into contact with different sites of the body following normal clinical use, as well as after unintentional administration.

A questions and answers document on the withdrawal of the 'Guideline on pharmacokinetics and metabolic studies in the safety evaluation of new medicinal products in animals' was released ([EMA/CHMP/SWP/1991104/2014](#)). The aim of this Q&A document is to provide clarification on how to obtain information from other sources following the withdrawal of the guideline.

A revised draft guideline on non-clinical and clinical development of similar biological medicinal products containing recombinant human insulin and insulin analogues has been released for consultation until 31 July 2014 ([EMA/CHMP/BMWP/32775/2005 Rev. 02](#)).

A revised draft guideline on clinical investigation of medicinal products for the treatment of juvenile idiopathic arthritis was released for consultation until 15 November 2014 ([EMA/CHMP/239770/2014 Rev. 2](#)). This revision takes into account recent developments relating to study design and also validated disease activity evaluation tools to assess clinical and structural outcomes.

A draft guideline on the role of the Pathological Complete Response (pCR) as an endpoint in neoadjuvant breast cancer studies has been released for public consultation until 31 July 2014 ([EMA/CHMP/151853/2014](#)). Currently, disease-free

survival (DFS) is considered to be an appropriate endpoint for efficacy and as a surrogate endpoint for overall survival. pCR is now proposed as a surrogate endpoint for the evaluation of the efficacy of novel therapies for invasive breast cancer without distant metastases.

A draft reflection paper on the use of patient reported outcome (PRO) measures in oncology studies has been released for consultation until 30 November 2014. It focuses on the add-on value of these data from a regulatory perspective as well as emphasising their use to estimate patient perception of the side effects of therapy ([Link](#)).

A questions & answers document outlining positions on specific questions addressed to the pharmacokinetics working party was updated ([EMA/618604/2008 Rev. 9](#)).

Guidance for veterinary medicines

A guidance document for companies requesting classification of products for minor use or minor species (MUMS) or for limited market was updated ([EMA/CVMP/370663/2009](#)). It provides an overview of the procedure to obtain classification and gives guidance to applicants in preparing their request. The update reflects new developments and includes accumulated experience.

A reflection paper on anthelmintic resistance was released for consultation until 31 July 2014 ([EMA/CVMP/EWP/573536/2013](#)). It discusses how documented evidence on anthelmintic resistance should be worded in the summary of product characteristics.



A questions and answers document on the CVMP guideline on pharmaceutical fixed combination products was released ([EMA/CVMP/EWP/325284/2011-Rev.1](#)).

It provides additional explanations on Section 4 of the guideline 'Justification of the combination for a fixed combination'.

Guidance on pharmacovigilance for human medicines

A revised guideline on good pharmacovigilance practices (GVP) - Module V – Risk management systems came into effect on 28 April 2014 ([EMA/838713/2011 Rev 1](#)). Revisions include amendments to the definitions of 'Missing information' and 'Safety concern' and amendments of other terms throughout the Module.

Updated EMA webpages are available under:

- Good pharmacovigilance practices ([Link](#))
- Risk-management plans ([Link](#))



A draft implementation guide on individual case safety reports (ICSR) was released for consultation until 30 June 2014 ([EMA/51938/2013](#)). The guide describes the additional EU specific requirements to generate a valid ICSR and Message Acknowledgment.

A draft guide on the monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the EMA was released for consultation until 27 July 2014 ([EMA/161530/2014](#)).

Launch of Adaptive Licensing pilot

A framework for Adaptive Licensing (AL) was released in March 2014. Adaptive Licensing is a prospectively planned, flexible approach to regulation of medicines and biologics. Through a 'staggered approval' or 'progressive licensing', Adaptive Licensing seeks to maximize the positive impact of new drugs on public health by balancing timely access for patients with the need to assess and to provide adequate evolving information on benefits and harms.

The AL pilot project is launched to help develop an understanding of how future Adaptive Licensing pathways might be designed for different types of products and indications. Further information is available on the dedicated webpage ([Link](#)). SMEs interested in participating in the pilot are advised to contact the [SME Office](#).

Regulatory and procedural guidance

A best practice guidance for pilot parallel scientific advice procedures involving the EMA and health-technology-assessment bodies (HTAs) has been released for consultation until 14 July 2014 ([Link](#)).

The EMA Q&A webpage on Periodic safety update reports was updated on e.g. timelines of EURD list enforcement, submitting a RMP update within a PSUR/PSUSA procedure ([Link](#)).

Updates on the following EMA Q&A webpages were published: [Pre-submission guidance](#), [Post-authorisation guidance](#), [Type-IB variations](#), [Article-61\(3\) notifications](#), [Type-II Variations](#), , [Transfer of marketing authorisation](#). They provide the most up to date information on issues that marketing authorisation holders may have when preparing such applications.

The Agency has announced that fees payable to EMA by applicants and marketing-authorisation holders will increase by 1.5% on 1 April 2014 to account for inflation ([Link](#)). At the same time, new fee incentives for SMEs for post-authorisation activities are being introduced ([Link](#)).

EudraCT Information

The posting of clinical trial summary results in the European Clinical Trials Database (EudraCT) will become mandatory for sponsors as of 21 July 2014. Sponsors will be obliged to post results for any interventional trials registered in EudraCT and that have ended within a certain period of time. More information on this including the implications on public access to information on clinical trial results can be found [here](#).

EU news

The European Commission has adopted a delegated act specifying the situations where a post-authorisation efficacy study (PAES) can be required by regulatory authorities. The act was published on 10 April 2014 in the Official Journal of the European Union (EU) and will enter into force on 30 April 2014 ([Link](#)).

Meetings

The following upcoming meetings and workshops have recently been announced:

- **11 September:** Committee for Advanced Therapies (CAT) and the German Society for Transfusion Medicine and Immunohaematology (DGTI) workshop on advanced-therapy medicinal products: How to bring cell-based medicinal products successfully to the market ([Link](#));
- **7 November:** European Medicines Agency workshop on the investigation of subgroups in confirmatory clinical trials ([Link](#));
- **24-25 November:** EMA workshop on the clinical investigation of medicines for the treatment of Alzheimer's disease ([Link](#));

The reports and videos of the following meetings have recently been released:

- **10 January:** Joint European Medicines Agency (EMA), US Food and Drug Administration (FDA), and Japanese Ministry of Health, Labour and Welfare (MHLW) and Pharmaceuticals and Medical Devices Agency (PMDA) orphan medicinal product workshop ([Link](#));
- **26 February:** Workshop report on regulatory and methodological standards to improve benefit-risk evaluation of medicines ([Link](#)).
- **28 February:** Consultation meeting with stakeholders: Request from the European Commission for advice on the impact on public and animal health of the use of antibiotics in animals ([Link](#));
- **4 April:** SME workshop for micro, small and medium-sized enterprises: Focus on quality for medicines containing chemical entities ([Link](#));
- **28 April:** Pharmacovigilance in the paediatric population workshop ([Link](#));

Registered SMEs

Currently, 1163 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 [How to apply](#) section of the SME Office pages on the Agency's website for information on how to do this.



The European Medicines Agency is moving

Please note that from 1 August 2014 our new address will be:
30 Churchill Place | Canary Wharf | London E14 5EU | United Kingdom

Contacting the SME office from 1 August via telephone:

Tel.: +44 (0)20 3660 8787

Important: Please use the current address and contact details for any correspondence with the EMA and the SME office until 1 August 2014.

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 regulatory strategy;
- organising workshops 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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