



# SME Office NEWSLETTER

Information for SMEs on the EU regulatory environment for medicines.  
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## Veterinary Medicines

A guideline on efficacy studies for **intramammary products** for use in cattle will come into effect on 1 August 2017. It provides guidance on the design, conduct and reporting of pre-clinical and clinical studies to support applications and variations of products intended for intramammary use in dairy cattle ([EMA/CVMP/344/1999-Rev.2](#)).

A draft revised recommendation for **Eudravigilance Veterinary data** for centrally authorised products has been released for consultation until 31 August 2017 ([EMA/CVMP/PhVWP/171122/2016](#)). It aims to improve pharmacovigilance by integrating periodic safety update reports evaluation and signal detection processes using a risk-based approach.

A draft guideline on the assessment and **control of mutagenic impurities** in veterinary medicines was released for consultation until 31 August 2017. It provides a risk assessment framework for identifying and controlling levels of mutagenic impurities ([EMA/CVMP/SWP/377245/2016](#)).

A draft guidance on **antimicrobial use data by animal species** from national data collection systems has been released for consultation until 24 September 2017

([EMA/489035/2016](#); Q&A document [EMA/716249/2016](#)). It defines standards for the collection, analysis and reporting of data on antimicrobial use in animal species in the EU.

A CVMP document on risk management strategy for minimising the potential presence of **replication competent endogenous retrovirus RD114** in starting materials and final products of feline and canine vaccines has been published in February 2017 ([EMA/CVMP/IWP/592652/2014](#)).



The following guidance, documents and questions and answers were updated/released:

- Type-IA variations Q&A ([Link](#)), updated on dossier format and non-significant in-process control or specification parameters.
- Revised product information templates (see [EMA](#) and [CMDv](#) websites).
- Q&A on the product information guidance on section 5.1 'pharmacodynamic properties' of the summary of product characteristics ([EMA/CVMP/757903/2016](#)).

## Quality Guidance

**A** draft reflection paper on '*Statistical methodology for the comparative assessment of quality attributes in drug development*' has been released for consultation until 31 March 2018 ([EMA/CHMP/138502/2017](#)). It provides statistical and methodological perspectives on the comparative assessment of quality attributes in pre- and post-manufacturing changes, biosimilar and generic developments and discusses sampling strategies, sources of variability, options for statistical inference and acceptance ranges.

## Clinical Guidance

**A** revised guideline on the **clinical development of fixed combination medicinal products** will come into effect on 1 October 2017. It applies to products containing active substances in a single pharmaceutical form, which may be authorised or unauthorised substances in the EU ([EMA/CHMP/158268/2017](#)).

A draft guideline on **multiplicity issues in clinical trials** has been released for consultation until 30 June 2017 ([EMA/CHMP/44762/2017](#)). It discusses aspects relating to demonstrating efficacy in confirmatory trials, and includes details on multiplicity adjustment, significance with respect to multiple secondary endpoints, composite endpoints and regulatory claims, and confirmatory evidence in subgroup analyses.

A concept paper on the revision of the '*Guideline on the requirements for clinical documentation for **orally inhaled products** including the requirements for demonstration of therapeutic equivalence between two inhaled products for use in the treatment of asthma and chronic obstructive pulmonary disease in adults and for the treatment of asthma in children and adolescents*' has been released for consultation until 30 June 2017 ([EMA/CHMP/267194/2016 22/06/2017](#)). Comments are invited on the proposal to revise the guideline to address advances in inhaler technology, relevance of pharmacokinetic studies in demonstrating therapeutic equivalence and paediatric requirements.

## Pharmacovigilance

The following good pharmacovigilance practices (GVP) were released:

Module II – **Pharmacovigilance system master file** ([EMA/816573/2011 Rev 2\\*](#)). It includes minor updates and clarifications without changes to the content.

Module V – **Risk management systems** ([EMA/838713/2011 Rev 2\\*](#)). It includes major revisions relating to e.g. 'important identified or important potential risk and missing information', requirements for different types of initial marketing authorisation applications and expected changes during the product life cycle (see also updated RMP template [EMA/PRAC/613102/2015 Rev.2](#); Q&A [EMA/156738/2014 Rev. 1](#)).

**Risk management plans** (RMP) submitted in initial marketing authorisation applications and Day 121 responses applying GVP Module V Rev 1 will be accepted for a further 6 months. All other RMP submissions (including Day 91 responses for an initial application under accelerated assessment) will be accepted until 31 March 2018.



Module XVI – **Risk minimisation measures**: selection of tools and effectiveness indicators ([EMA/204715/2012 Rev 2\\*](#)). It includes amendments to increase clarity and consistency with other GVP Modules.

Explanatory note to GVP Module VII – **Periodic Safety Update Report (PSUR)**. It identifies areas for further guidance in light of experience gained with the implementation of the PSUR Single Assessment (PSUSA) process ([EMA/102307/2017](#)).

As of 10 April 2017, for new non-pharmacovigilance referral procedures under Article 31 of Directive 2001/83/EC, the EudraVigilance registration system contact point will be used as the contact point for the products concerned by a referral. Marketing authorisation holders are advised to keep the EudraVigilance registration system contact point up to date ([EMA/398931/2016](#), questions and answers: [EMA/457344/2016 Rev. 1](#))

## Inspections

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**A** guideline on 'Good clinical practice compliance for trial master file (TMF) (paper and/or electronic) for content, management, archiving, audit and inspection of clinical trials' has been released for consultation until 11 July 2017 ([EMA/15975/2016](#)). It describes the requirements of the new Clinical Trials Regulation (EU) No 536/2014 and ICH-GCP E6, and includes topics relating to archiving and retention times in case of 'digitisation' of paper records.

An EU and US mutual recognition agreement on good manufacturing practice inspections will enter into force on 1 November 2017. The agreement encourages international harmonisation, makes better use of inspection capacity and reduces duplication. Further information is available on EMA website ([Link](#)).

## Regulatory & Procedural Advice

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The following guidance, webpages and questions and answers were updated/released:

- Questions and answers on quality of medicines ([Part 1](#); [Part 2](#)) updated to include details on heavy metals specifications and product information of orally inhaled products.
- A document on applications for medicinal products intended for markets outside the EU ('Article 58') which sets out early support mechanisms available for such applications ([Link](#)).
- Research & Development webpages updated to provide guidance on opportunities for early dialogue and interaction in the development phase of a medicinal product ([Link](#)).
- Explanatory note on general fees payable to the EMA ([Link](#)) highlighting the revised EMA fees applicable from 1 April 2017.

SMEs planning the submission of a scientific advice or marketing authorisation application are advised to check that their SME status is valid in order to benefit from the SME fee incentives. The SME office can be directly contacted to discuss SME status and incentives.

## Clinical Data Publication and Access to Documents

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**A** revised guidance on the implementation of clinical data publication (Policy 0070) was released on 12 April 2017 ([EMA/90915/2016](#); see also Q&A document for topics relating to '**commercially confidential information**' and '**anonymisation**' [EMA/14227/2017](#)). It was updated in light of experience gained with the policy and feedback received from stakeholder organisations ([Industry associations webinar](#)).

A revised draft policy on access to documents has been released for consultation until 16 May 2017. The revisions extend the scope of the policy to include corporate documents and take into account the Agency's proactive approach to transparency ([Link](#)).

## New EMA & EU Initiatives

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**A framework of collaboration between EMA and academia** ([Link](#)) and related action plan ([Link](#)) were adopted in March 2017. The framework and action plan include initiatives for education and training, staff exchange programs, a strategic research agenda for regulatory science and the creation of an EMA entry point for academia ([Link](#)).



A '**Startup and Scale up initiative**' was launched by the European Commission in November 2016. It aims at improving the conditions for start-ups to scale-up, create more jobs and enhance Europe's competitiveness. It brings together a range of existing and new actions to create a more coherent framework to allow start-ups to grow and do business across Europe ([Link](#)).

## Reports, Workshops and Meetings

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### November 2016

- Report from a workshop on big data in medicines development and regulatory science – 14 & 15 November 2016 ([Link](#))

### December 2016

- Report from a workshop on adaptive pathways on 8 December 2016 ([Link](#)).

### February 2017

- Industry stakeholder platform on the operation of EU pharmacovigilance legislation on 3 February 2017 ([Link](#))



### March 2017

- SME info day on the new clinical trial regulation ([Link](#))
- EMA veterinary medicines info day ([Link](#))
- Seventh Framework Program (FP7) small-population research methods projects and regulatory application workshop ([Link](#))
- Annual Report MUMS/limited market for veterinary medicines ([Link](#))
- 2016 Annual Report on EudraVigilance for the European Parliament, the Council and the Commission - ([Link](#))

### May 2017

- 'First anniversary of PRIME (PRIority Medicines scheme): experience so far' – 19 May ([Link](#)).
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## Registered SMEs

Currently, 1712 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 \(veterinary medicines\)](#)

### Contact the SME Office

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