

# SME Office NEWSLETTER

Information for SMEs on the EU regulatory environment for medicines.  
Published four times a year by the European Medicines Agency.

An agency of the European Union



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## Scientific guidelines for human medicines

### Multidisciplinary guidelines

A revised ICH guideline M7 on '*assessment and control of DNA reactive (mutagenic) impurities in pharmaceuticals to limit potential carcinogenic risk – addendum*' was released for public consultation ([EMA/CHMP/ICH/272147/2021](#)). The addendum was revised to include new monographs for acetaldehyde, dibromoethane, epichlorohydrin, ethyl bromide, formaldehyde, styrene, vinyl acetate.

### Quality guidelines

A revised ICH Q3C guideline on '*impurities: guideline for residual solvents*' was published ([EMA/CHMP/ICH/82260/2006](#)). The document was revised to add the permitted daily exposure for methyltetrahydrofuran, cyclopentyl methyl ether and tertiary-butyl alcohol.

A revised ICH Q9(R1) guideline on '*quality risk management*' was released for public consultation ([EMA/CHMP/ICH/24235/2006](#)). The revision aims to provide more scientific and robust applications of quality risk management principles with a view to improve quality manufacturing.

### Preclinical and clinical guidelines

A revised product-specific bioequivalence guidance was published for abiraterone acetate ([Link](#)).

New product-specific bioequivalence guidance

were released for public consultation for enzalutamide ([Link](#)), ibrutinib ([Link](#)), olaparib ([Link](#)), liposomal amphotericin B ([Link](#)) and ursodeoxycholic acid ([Link](#)).

An updated clinical pharmacology and pharmacokinetics Q&As ([Link](#)) was published on general bioequivalence.

An updated Q&A – Good clinical practice (GCP) ([Link](#)) was published on topics including investigational medicinal products (IMPs) in bioavailability and bioequivalence trials, GCP matters and study subject data records in clinical trials.

A revised guideline on the clinical investigation of human normal immunoglobulin for intravenous administration (IVIg) ([EMA/CHMP/BPWP/94033/2007 rev. 4](#)) was published to include measles exposure recommendations.

## Clinical trials (CTs)

In 2022, EMA will offer short talks for clinical trial sponsors focussed on the Clinical Trial Information System (CTIS) functionalities. Each talk includes a short demonstration of a CTIS functionality with practical guidance and provides time for sponsors to ask questions. The talks are broadcasted live on EMA website and no registration is required. SMEs are encouraged to check out the [EMA events page](#) and look at upcoming CTIS bitesize talks, CTIS walk-in clinics and other CTIS events.

To keep updated on CTIS, see also the [CTIS Highlights newsletters](#), [CTIS newsflash](#), [CTIS Sponsor Handbook](#) and [CTIS training materials](#).

A new guideline for the notification of serious breaches of Clinical Trial Regulation (CTR) (EU) No 536/2014 or of the clinical trial protocol came into force on 31 January 2022 ([EMA/698382/2021](#)). It elaborates on what is considered a serious breach and possible regulatory actions following a notification.

The following guidance documents have been updated:

- Guidance on the electronic submission of information on investigational medicinal products for human use in the Extended EudraVigilance medicinal product dictionary (XEVMPD) ([EMA/186412/2021](#)) revised on XEVPRM data element information for an unauthorised medicinal product.
- Guideline on the requirements for quality documentation concerning biological IMP in clinical trials ([EMA/CHMP/BWP/534898/2008 Rev. 2](#)) and the guideline on the requirements to the chemical and pharmaceutical quality documentation concerning IMP in clinical trials ([EMA/CHMP/QWP/545525/2017 Rev. 2](#)). Both documents have been updated in line with the provisions of the CTR regarding quality changes requiring submission of (non)-substantial modifications to the IMP dossier.

**T**he Accelerating Clinical Trials in the EU (ACT EU) – Delivering an EU clinical trials transformation initiative was launched on 13 January 2022. The aim is to further develop the EU as a focal point for clinical research, further promote the development of high quality, safe and effective medicines, and to better integrate clinical research in the European health system in light of the EU medicines agencies network strategy to 2025 and the EU Pharmaceutical Strategy. Additional information regarding objectives, governance, organisation, priority actions and resourcing can be found in the [news item](#) and [dedicated paper](#).

## Pharmacovigilance

**T**he XEVMPD training webpage on how to submit and retrieve medicinal product data using XEVMPD, also known as the 'Article 57 database', was updated including e-learning presentations ([Link](#)).

The following documents were also published:

- Revised Eudravigilance registration manual ([EMA/13454/2020, Rev. 11](#)).
- EudraVigilance - EVWEB User Manual ([EMA/501718/2018](#)).

From 30 June 2022, EudraVigilance users will need to report individual cases of suspected side effects using the ISO ICSR/ICH E2B(R3) format and related ISO standard terminology for pharmaceutical form and route of administration. New and revised guidance together with additional information are available on the dedicated [webpage](#).

A new guideline on good pharmacovigilance practices (GVP), Module XVI Addendum III – Pregnancy prevention programme and other pregnancy-specific risk minimisation measures was released for public consultation until 31/05/2022 ([EMA/608947/2021](#); [EMA/95595/2022](#)).

## European Medicines Regulatory Network Data Standardisation Strategy

**T**he strategy published on 16 December 2021 ([EMA/447502/2021](#)) outlines actions to enable and support harmonisation of data to reduce the administrative efforts currently required to receive, process, make available and reuse scientific data throughout the EU as well as in the global life science industry.

## PRIME: priority medicines

**E**MA published a 5-year report ([Link](#)) on the PRIME scheme providing a detailed analysis and review of the Agency's experience since the scheme was launched. It also gives recommendations and calls for further improvements including consideration to the best timepoint for applicants to enter the scheme and be better prepared for the marketing authorisation application (MAA) phase (see also [dedicated webpage](#) and [fact-sheet highlights](#)).

A new guidance is available for developers of medicines supported by EMA's PRIME scheme on the tools they can use to generate robust quality data packages for their MAA ([EMA/CHMP/BWP/QWP/IWG/694114/2019](#)). The document aims to address common challenges with meeting quality and manufacturing development data requirements for medicines containing chemical, biological or biotechnologically derived substances and advanced therapies. For additional information, see [dedicated webpage](#).

## Regulatory guidance

The following guidance documents have been updated:

- Procedural advice on classification of advanced therapy medicinal products in accordance with article 17 of regulation (EC) no 1394/2007 ([EMA/CAT/99623/2009 Rev.2](#)) revised on preparation of classification reports and coordinators appointments.
- Pre-authorisation guidance ([EMA/821278/2015](#)) on topics including SME support, legal basis, proposed (invented) name, transfer of test methods and MAA procedure.
- Post-authorisation guidance ([EMA-H-19984/03 Rev. 98](#)) on topics including type IA/IAIN-IB-II variations, extension of MA, worksharing of variations, pre-submission queries service and marketing status updates.
- EMA service desk is now available to raise pre-submission queries about various post-authorisation procedures ([Link](#)).
- Guide on access to unpublished documents ([EMA/304162/2014 Rev.5](#)) revised on Covid-19 documents and definition of 'document'.
- Guideline on core SmPC for human normal immunoglobulin for intravenous administration (IVIg) ([EMA/CHMP/BPWP/94038/2007 Rev. 6](#)); revised on measles exposure prophylaxis information.
- EMA Medical Terms Simplifier ([EMA/158473/2021](#)).
- Guidance for Applicants seeking scientific advice and protocol assistance ([EMA/4260/2001 Rev. 12](#)) revised on submission process.
- Guidance on parallel EMA/EUnetHTA 21 Joint Scientific Consultation ([EMA/410962/2017 Rev.5](#)) revised on organisational structure and process.
- Updated version of human electronic application forms ([v1.26.0.0](#)).

The following guidance on product information (PI) and quality review document (QRD) annexes were updated to reflect the inclusion of the Irish language:

- Terms/abbreviations for 'batch number' and 'expiry date' to be used on the labelling of human medicinal products ([EMA/286379/2019 rev. 14](#)).
- MedDRA terminology to be used in Section 4.8 "Undesirable effects" of SmPC ([EMA/295934/2018 v.3](#)).
- Tables of non-standard abbreviations ([EMA/27236/2003 rev. 14](#)).
- Names of EU-EEA countries ([EMA/123695/2004 rev.1](#)).
- Declaration of storage conditions ([EMA/29277/03 v.5](#)).

A revised guideline on the acceptability of names for human medicinal products processed through the centralised procedure was released for public consultation ([EMA/CHMP/287710/2014, Revision 7](#)). It elaborates on criteria applied to address safety and public health concerns, international non-proprietary names issues, product-specific aspects, conditional acceptability of names and bilateral negotiations between companies, and planned changes to the duration of the validity of an (invented) name and the review process.

## Medical devices

A new guideline on procedural aspects for the consultation of EMA by a notified body on companion diagnostics was released for consultation ([EMA/747623/2021](#)). The document should be read in conjunction with the related Q&A ([EMA/708170/2021](#)). Additional information can be found on the [dedicated webpage](#) under the section companion diagnostics ('in-vitro diagnostics').



## Veterinary medicines

### Antimicrobials

A draft reflection paper on the prophylactic use of antimicrobials in animals in the context of Article 107(3) of Regulation (EU) 2019/6 (VMR) was released for public consultation until 29 April 2022 ([Link](#)). It aims to define the term 'prophylaxis' as provided in the regulation and intends to develop principles to guide the implementation of restrictions on the prophylactic use of antimicrobials in animals.

EMA published advice on the designation of antimicrobials or groups of antimicrobials to be reserved for human use only.- The recommendations were developed in relation to implementing measures under Article 37(5) of the VMR ([EMA/CVMP/678496/2021](#)).





### New veterinary medicines regulation (EU) 2019/6 (VMR)

An updated scientific guideline on summary of product characteristics for antiparasitic veterinary medicinal products ([EMA/CVMP/EWP/170208/2005-Rev.1](#)) will come into effect on 1 July 2022. The revision takes into account the evolution of antiparasitic resistance in the EU and the scientific knowledge on factors that influence resistance development.

The following scientific guidelines came into effect on 28 January 2022 to address the VMR requirements:

- Guideline on data requirements for multi-strain dossiers for inactivated veterinary vaccines ([EMA/CVMP/IWP/105506/2007 Rev. 2](#)) replacing the guideline on data requirements for multi-strain dossiers for inactivated vaccines against avian influenza (AI), Bluetongue (BT) and Foot-and-Mouth disease (FMD) (EMA/CVMP/IWP/105506/2007-Rev1).
- Guideline on data requirements for vaccine platform technology master files (vPTMF) ([EMA/CVMP/IWP/286631/2021](#)).
- Guideline on data requirements for vaccine antigen master files (VAMF) ([EMA/CVMP/IWP/258755/2021](#)).
- Guideline on clinical trials with immunological veterinary medicinal products ([EMA/CVMP/IWP/260956/2021](#)) replacing the Note for guidance field trials with veterinary vaccines (EMA/CVMP/852/99-Final).
- Guideline on data requirements for authorisation of immunological veterinary medicinal products in exceptional circumstances ([EMA/CVMP/IWP/251947/2021](#)) replacing guidelines on requirements for an authorisation under exceptional circumstances for vaccines for emergency use against bluetongue (EMA/CVMP/IWP/37267/2008) and on requirements for an authorisation under exceptional circumstances for vaccines for use in birds against avian influenza (EMA/CVMP/IWP/222624/2006).

For information and updates on the VMR consult the Veterinary Medicines Regulation highlights newsletters ([Link](#)).

### Scientific guidelines

The following draft guidance documents were released for public consultation:

- Concept paper on the revision of annex 4 of on good manufacturing practice guidelines – manufacture of veterinary medicinal products other than immunologicals ([EMA/628488/2021](#)), revised to facilitate (v)ICH guidelines implementation and cover new technologies, methods and products. It replaces 'Eudralex Volume 4: manufacture of veterinary medicinal products other than immunologicals' and PIC/S participating authorities 'PE 009-14: annex 4 - manufacture of veterinary medicinal products other than immunologicals'.
- Concept paper on the revision of annex 5 of the guidelines on good manufacturing practice for medicinal products – manufacture of immunological veterinary medicinal products ([EMA/628491/2021](#)), revised to facilitate (v)ICH guidelines implementation and cover new technologies, methods and products. It replaces 'Eudralex Volume 4: manufacture of immunological veterinary medicinal products' and for PIC/S participating authorities 'PE 009-14: annex 5 - manufacture of immunological veterinary medicinal products'.
- Procedural advice for veterinary vaccine antigen master file (VAMF) certification ([EMA/127488/2021](#)).
- Concept paper on the revision of CVMP recommendation on the evaluation of the benefit-risk balance of veterinary medicinal products ([EMA/CVMP/299406/2021](#)), aligned with VMR. It replaces the Recommendation on the evaluation of the benefit-risk balance of veterinary medicinal products (EMA/CVMP/248499/2007).
- Guideline on determination of the need for an MRL evaluation for biological substances ([EMA/CVMP/SWP/591282/2021](#)); on MRL requirements for biological non-immunological substances used in products intended for food-producing species.
- Guideline on requirements for the production and control of immunological veterinary medicinal products ([EMA/CVMP/IWP/206555/2010-Rev.2](#)) superseding the guideline on requirements for the production and control of immunological veterinary medicinal products (EMA/CVMP/IWP/206555/2010 Rev. 1).
- Concept paper on the development and data requirements of potency tests for cell-based therapy products and the relation to clinical efficacy ([EMA/CVMP/NTWP/470741/2021](#)); on additional guidance to Regulation (EU) 2019/6, European Pharmacopoeia, in particular Ph. Eur. 0062 Vaccines for veterinary use, and relevant VICH guidelines and requirements not covered in VMR annex I and II.
- Concept paper on quality, safety and efficacy of bacteriophages as veterinary medicines ([EMA/CVMP/NTWP/438290/2021](#)).

## Pharmacovigilance

New scientific guidelines on veterinary good pharmacovigilance practices (VGVP) (see [dedicated webpage](#)) came into effect on 28 January 2022 on:

- Signal management ([EMA/522332/2020](#)).
- Pharmacovigilance systems, their quality management systems and pharmacovigilance system master files ([EMA/595115/2021](#)).
- Controls and pharmacovigilance inspections ([EMA/328998/2021](#)).
- Veterinary pharmacovigilance communication ([EMA/63454/2021](#)).
- Collection and recording of suspected adverse events for veterinary medicinal products ([EMA/306663/2021](#)).
- Glossary ([EMA/118227/2021](#)).

Manuals and guidance documents on EudraVigilance Veterinary ([EVVet](#)) and the Union Pharmacovigilance Database have also been published ([Link](#)).

## Regulatory guidance

New or updated guidance have been published:

- Implementation guide chapters, registration guide, guidance documents and video tutorials on veterinary medicines product data in the union product database (UPD) ([Link](#); [FAQ UPD](#)).
- Procedural advice to applicants/marketing authorisation holders on re-examination of CVMP opinions ([EMA/CVMP/321528/2017 – Rev.2](#)).
- Procedural advice on appointment and responsibilities of CVMP rapporteur, co-rapporteur and peer reviewer ([EMA/CVMP/468877/2009 – Rev. 3](#)).
- Variations requiring assessment ([Link](#)).
- Variations not requiring assessment ([Link](#)).
- Q&A document on requirements for pre-clinical studies submitted in support of a marketing authorisation application for a veterinary medicinal product ([EMA/CVMP/565615/2021-Rev.1](#)).
- Mock-ups checklist - Guidance for checking mock-ups ([EMA/102667/2014-Rev.2](#)); see also checking process [document](#) and [dedicated webpage](#).
- Guidance on good manufacturing practice and good distribution practice: Q&As ([Link](#)) on requirements for active substances used as starting materials in veterinary medicinal products.
- Changing the (invented) name of a veterinary medicine ([Link](#)).
- Updated version of veterinary electronic application forms ([v1.26.0.0](#)).

- Pre-authorisation guidance under VMR ([Link](#)) on topics including steps prior to submission, product name, PI and prescription status, genetically modified organisms, submission, validation, fees, MAA procedure and inspections.



## COVID-19

EMA published new and updated guidance documents on:

- Q&A on labelling flexibilities for COVID-19 vaccines ([EMA/747041/2021 rev.3](#)).
- Procedural guidance for variant strain(s) update to vaccines intended for protection against human coronavirus ([EMA/175959/2021 Rev.1](#)).
- Consideration on core requirements for risk management plans of COVID-19 vaccines ([EMA/PRAC/73244/2022](#)).
- Reflections on the regulatory experience of remote approaches to GCP and GMP regulatory oversight during the COVID-19 Pandemic. See [reflection paper](#) and [news item](#).

Guidance for companies (e.g. on research and development, assessment, marketing authorisation, pharmacovigilance), information on treatments and vaccines, medicines availability and public-health advice are regularly updated on EMA's dedicated webpage ([Link](#)).

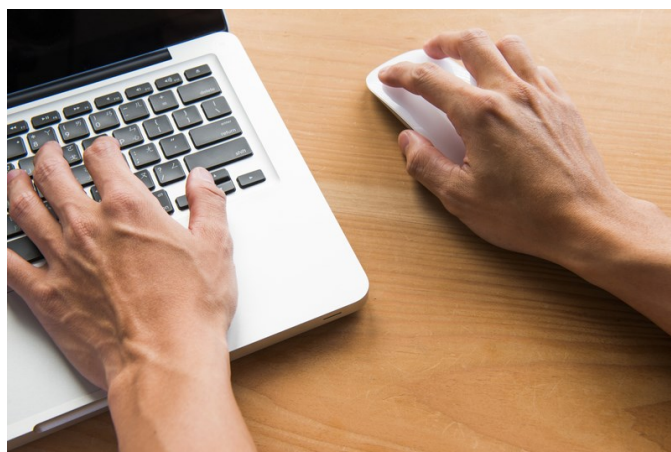
The following documents have also been published:

- International Coalition of Medicines Regulatory Authorities (ICMRA) statement on the need for continued focus on COVID-19 therapeutics ([Link](#) and [news item](#)).
- ICMRA and world health organisation (WHO) report on flexibilities used by regulators to respond to the COVID-19 pandemic ([Link](#)).

## Events of interest

**P**resentations, reports and/or videos of the following events have been published:

- EMA and Nuclear Medicines Europe bilateral meeting – 23/09/2021 ([Link](#)).
- Q&As – Webinar for MAHs on integration of EudraGMDP and OMS – 11/11/2021 ([Link](#)).
- Union Pharmacovigilance Database: webinar on adverse event collection and recording – 10/11/2021 ([Link](#)).
- 16th industry stakeholder platform - operation of EU pharmacovigilance – 17/11/2021 ([Link](#)).
- Seventh industry stakeholder platform on research and development support – 23/11/2021 ([Link](#)).
- Union Pharmacovigilance Database: webinar on signal detection and analysis – 23 and 24/11/2021 ([Link](#)).
- Annual Patients and Consumers Working Party (PCWP) and Healthcare Professionals Working Party (HCPWP) meeting with eligible organisations – 24/11/2021 ([Link](#)).
- EMA and Federation of Veterinarians of Europe (FVE) webinar on data collection on sales and use of antimicrobials – 24/11/2021 ([Link](#)).
- Public stakeholder meeting on COVID-19 vaccines and therapeutics in the EU – 25/11/2021 ([Link](#)).
- EMA/EATRIS joint webinar: navigating the regulatory requirements for ATMPs – 29/11/2021 ([Link](#); [video recording](#)).
- EMA veterinary medicines info day – 30/11/2021 ([Link](#)).
- Learnings initiative webinar for optimal use of big data for regulatory purpose – 30/11/2021 ([Link](#)).
- Seventh meeting of the industry stakeholder platform on the operation of the centralised procedure for human medicines – 01/12/2021 ([Link](#)).
- EU Big Data Stakeholder Forum 2021 – 07/12/2021 ([Report](#)).
- Webinar on veterinary pharmacovigilance (PhV) inspections and systems, their quality management systems and PhV system master files: Introduction and principles – 08/12/2021 ([Link](#)).
- Nitrosamine Implementation Oversight Group (NIOG) - second meeting with pharmaceutical industry – 08/12/2021 ([Link](#)).
- Regulatory science research needs launch event – 18/01/2022 ([Link](#)).
- Webinar on the digital application dataset integration (DADI) network project to replace electronic application forms – 18/01/2022 ([Link](#)).
- Union Pharmacovigilance Database: follow up webinar on collection and recording of suspected adverse events for veterinary medicinal products – 19/01/2022 ([Link](#)).
- Union Pharmacovigilance Database: follow up webinar on signal detection, evaluation and yearly reporting – 19/01/2022 ([Link](#)).
- Clinical Trials Information System (CTIS) demonstration for stakeholders – 20/01/2022 ([Link](#)).
- UPD: follow up webinar for marketing authorisation holders – 25/01/2022 ([Link](#)).
- Digital application dataset integration (DADI) webinar - common factors in the Fast Healthcare Interoperability Resources (FHIR) data standard for Article 57(2) and electronic application forms (eAF) – 25/01/2022 ([Link](#)).
- DARWIN EU: multi-stakeholder information webinar – 24/02/2022 ([Link](#)).
- CTIS bitesize talk: User access and role management – 24/02/2022 ([Link](#)).
- Annual report from the European Surveillance of Veterinary Antimicrobial Consumption project (ESVAC) ([Link](#)).



## Other News

**T**he following documents have been published:

- Regulatory science research needs initiative ([news item](#)).
- EMA framework of interaction with healthcare professionals: 10 years of implementation ([EMA/698996/2021](#)).
- Human medicines highlights 2021 ([Link](#)).
- Veterinary medicines highlights 2021 ([Link](#)).
- Big data highlights ([Link](#)).
- Big Data Steering Group (BDSG): 2021 report ([EMA/40400/2022](#)).



## Registered SMEs

Currently, 1768 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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