

SME Office NEWSLETTER

Information for SMEs on the EU regulatory environment for medicines.
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Scientific guidelines for human medicines

Quality guidelines

A revised ICH Q3D guideline (R2) on 'Elemental Impurities' ([EMA/CHMP/ICH/353369/2013](#)) will come into effect on 24 September 2022. The document was revised to amend permitted daily exposure, monographs and add a section on limits for elemental impurities for cutaneous and transcutaneous formulations.

Revised ICH Q2(R2) on 'Validation of analytical procedures' ([EMA/CHMP/ICH/82072/2006](#)) and ICH Q14 on 'Analytical procedure development' ([EMA/CHMP/ICH/195040/2022](#)) guidelines were released for public consultation. The documents were revised to include recent analytical procedures, science and risk-based approaches for developing and maintaining analytical procedures suitable for quality assessment of active substances and finished products.

Multidisciplinary guidelines

Guidance on the 'Mandatory use of ISO ICSR/ICH E2B(R3) and EDQM terminology for Dosage Forms (DF) and Routes of Administration (RoA)' was published on 16 May 2022 ([EMA/580321/2021 Rev 1*](#)). The document was revised to include information on EDQM dosage form term selection and term description displayed in EudraVigilance.

Preclinical and Clinical guidelines

A new ICH E11A guideline on 'Paediatric Extrapolation' ([EMA/CHMP/ICH/205218/2022](#)) was released for public consultation until 6 August 2022. It provides recommendations for harmonised approaches for paediatric extrapolation to support the development and authorisation of paediatric medicines.

A reflection paper on 'Data required in confirmatory studies of medicinal products for the treatment of type 2 diabetes' ([EMA/240473/2022](#)) was released for public consultation until 31 August 2022. The document elaborates on data requirements and therapeutic indications claims to be considered in the final revision of the guideline on clinical investigation of medicinal products for the treatment or prevention of diabetes mellitus ([CPMP/EWP/1080/00 Rev. 2](#)).

Guidance on individual case safety reports (ICSRs) in the context of COVID-19 ([EMA/174312/2020](#)) was revised on topics including recording of vaccine dose schedule, lack of efficacy and vaccine name.

New product-specific bioequivalence guidance were released for public consultation for paracetamol ([Link](#)), tadalafil ([Link](#)), ibuprofen ([Link](#)), lanreotide acetate ([Link](#)), enzalutamide ([Link](#)), ibrutinib ([Link](#)), ursodeoxycholic acid ([Link](#)) and olaparib ([Link](#)).

Clinical trials

EMA released guidance ([Link](#)) on clinical trials impacted by the war in Ukraine. It covers actions that sponsors can take to ensure studies' integrity and trial participants safety.

EMA has launched a [pilot project](#) on the analysis of 'raw data' from clinical trials by regulatory authorities in the context of marketing authorisation applications (MAAs). Additional information for potential applicants is available on EMA's project [website](#).

EMA is offering in 2022 short talks on Clinical Trial Information System (CTIS) functionalities for clinical trial sponsors. Each talk includes a demonstration of a CTIS functionality with practical guidance followed by a Q&A. The talks are broadcasted live on EMA's website, and no registration is required. For further information consult the [EMA events page](#) for upcoming CTIS training events, and other sources of information ([CTIS Highlights newsletters](#), [CTIS newsflash](#), [CTIS Sponsor Handbook](#), [CTIS training materials](#)).

Regulatory guidance

The following guidance documents have been published or updated:

- Guidance for scientific advice and protocol assistance ([EMA/4260/2001 Rev. 13](#)) on e.g. procedural aspects.
- Pre-authorisation guidance ([EMA/821278/2015](#)) on topics including orphan designation, test methods transfer, procedural, good manufacturing practice (GMP) and good clinical practice (GCP) inspections.
- Guidance for applicants/MAHs involved in GMP and GCP inspections coordinated by EMA ([Link](#)) on e.g. extension of GMP certificates and time-limited manufacturing and import authorisations to year end 2022.
- Guidance on GCP inspection procedures ([Link](#)) on e.g. annexes setting out procedural details of GCP inspections requested by CHMP – Annex I (investigator site), II (clinical laboratories), IV (sponsor and contract research organisation), VI (record keeping and archiving document) and VII (bioanalytical part, pharmacokinetic and statistical analyses of bioequivalence trials).
- QRD templates Appendix II - MedDRA (Medical Dictionary for Regulatory Activities) terminology for section 4.8 'undesirable effects' of the summary of product characteristics ([Link](#)).
- Q&A on Irish language derogation ending on 1 January 2022 ([EMA/699123/2021/Rev. 2](#)).

- EMA medical terms simplifier ([EMA/329258/2022 Rev. 1](#)) on e.g. oncology clinical trials, seizure-related entries.
- Procedural advice for post-orphan medicinal product designation activities ([Link](#)) on maintenance review at the time of MAA and line extension.
- Guidance on EMA's companion diagnostics (CDx) consultation procedure by notified bodies ([EMA/198592/2022](#)) in line with Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR). As part of a CDx conformity assessment, notified bodies are required to seek a scientific opinion on the CDx suitability with a medicinal product, from competent authorities designated by Member States or EMA, before issuing an EU technical documentation assessment certificate, an EU type-examination certificate or a supplement for the CDx. For additional information, refer to the Q&A and EMA's Medical Devices webpage.
- Post-authorisation guidance ([EMA-H-19984/03 Rev. 99](#)) on topics including type II variations, extension, annual re-assessment of MAs under exceptional circumstances, renewal of conditional MAs and transfer of MA.
- eXtended EudraVigilance Medicinal Product Dictionary Data entry tool user manual ([Link](#)) with revised sections on EVWEB, XEVPRM, EV post functionality use, exporting query.
- [Q&A](#) on parallel distribution on topics including notification requirements, grounds for invalidation/negative outcome, inspections, quality defects, safety and annual updates.
- IRIS guide for applicants ([Link](#)) updated with a new section on supply and availability MAH i-SPOC registration (industry single point of contact).
- [Q&A](#) on technical and procedural guidance on the removal/replacement of titanium dioxide in medicinal products.
- Procedural variation guidance for variant strain(s) update to vaccines intended for human coronavirus ([EMA/175959/2021 Rev.2](#)).

The European Commission published on 14 July 2022 a draft regulation to improve standards of quality and safety for substances of human origin (SoHOs) intended for human application ([Link](#)). SoHOs include blood, tissues, cells and any other substances of human origin, directly intended for human application, used in preparations or in manufactured products. Activities that fall within the scope of the regulation include donor recruitment, processing, distribution, import and export and human applications. The draft regulation will be discussed by the Council and the European Parliament, and once adopted its provisions take effect after a transition period.

Veterinary medicines

EMA and the Heads of Medicines Agencies (HMA) have adopted a [Veterinary Big Data strategy to 2027](#) outlining plans for fostering data-driven, digital innovations in the veterinary medicines' field in the European Union (EU). As part of the implementation of the veterinary legislation, the EU Network has made significant investments to implement new IT systems that generate and centrally collect increased amounts of data. The strategy sets up a framework for managing and using data to support key regulatory activities to provide accurate and reliable information to promote public and animal health.

Guidelines

The following documents were published:

- Guideline on preclinical and clinical data requirements for veterinary medicinal products intended to reduce the risk of transmission of vector-borne pathogens in dogs and cats' ([EMA/CVMP/EWP/278031/2015](#)). It will come into effect on 1 January 2023.
- Guideline on 'Requirements for the production and control of immunological veterinary medicinal products' ([EMA/CVMP/IWP/206555/2010-Rev.2](#)). It was revised to take into account the revision of Annex II to Regulation (EU) 2019/6 on veterinary medicinal products, and new or updated Ph. Eur. requirements for the management of extraneous agents. It will come into effect on 16 December 2022.
- Guideline on the evaluation of medicinal products indicated for the treatment of bacterial infections ([CPMP/EWP/558/95 Rev 3](#)), and Addendum ([EMA/CVMP/678496/2021-rev](#)). It provides revised recommendations on primary endpoints, primary analysis populations and non-inferiority margins in trials to support certain infection site-specific indications. It will come into effect on 1 December 2022.
- Draft VICH GL7 guideline on 'Efficacy of anthelmintics: general requirements' ([EMA/CVMP/VICH/832/1999](#)). It provides recommendations on standardisation and simplification of methods used for the evaluation of anthelmintics in domesticated animals. It is released for public consultation until 1 November 2022.
- [Q&A](#) on CVMP guideline on environmental impact assessment for veterinary medicines in support of VICH guidelines GL6 (Phase I) and GL38 (Phase II) on e.g. scientific data, information, parameters, test conditions and default values to be used in the assessment of persistent, bio-accumulative and toxic or very persistent and very bio-accumulative veterinary medicinal products.
- [Q&A](#) on CVMP guideline on data requirements for multi-strain dossiers for inactivated veterinary vaccines ([EMA/CVMP/IWP/105506/2007-Rev.2](#)) on topics such as variable antigen and adjuvant contents, target species, dose-volumes, need for efficacy data for target species and new strain, fixed combination products, data extrapolation.
- [Q&A](#) on Maximum residue limits (MRL) with updated information on e.g. definition, scope, procedural aspects, fees, legal status of excipients/preservatives/adjuvants, withdrawal periods, biocidal evaluation, reference points of action.
- Draft report on the 'development of a harmonised approach to exposure assessment methodologies for residues from veterinary medicinal products, feed additives and pesticides in food of animal origin' ([EMA/CVMP/499555/2021](#)). The document compares models of consumer exposure and provides harmonised EMA and European Food Safety Authority (EFSA) recommendations for the assessment of exposure to residues of veterinary medicines, feed additives and pesticides in food of animal origin. It is released for public consultation until 31 August 2022.



Pharmacovigilance

A list of VeDDRA (veterinary dictionary for drug regulatory activities) low level terms and codes for reporting suspected adverse reactions in animals and humans to veterinary medicinal products that have become 'non-current' was published on 24 June 2022 ([Link](#)). It should be read in conjunction with guidance on the use of VeDDRA terminology ([EMA/CVMP/PhVWP/288284/2007-Rev.14](#)).

A revised combined VeDDRA list of list of clinical terms for reporting suspected adverse reactions in animals and humans to veterinary medicinal products was published on 24 June 2022 ([Link](#)). It should be read in conjunction with the list of changes to combined VeDDRA list of clinical terms ([Link](#)) and the VeDDRA 'dataload friendly file including deprecated terms' ([Link](#)).

A revised document including standard term lists mapping from the data elements guideline standard to VICH standard ([Link](#)) was published on 13 June 2022. For more information, refer to the EudraVigilance Veterinary [webpage](#) and the VICH [webpage](#).

Procedural guidance

The following documents were published:

- Pre-authorisation guidance ([Link](#)) with updated information on e.g. support to SMEs, centralised procedure eligibility, rapporteurs appointment, animal/human origin materials in product or manufacturing, and active substance master file.
- Procedural advice for veterinary vaccine antigen master files (VAMFs) ([EMA/CVMP/127488/2021](#)) on submission, evaluation, certification and use of a VAMF.
- Manual on reporting of antimicrobial sales and use in animals at EU level ([Link](#)) with information on standards for quantifying antimicrobial consumption in animals in the context of veterinary medicines Regulation (EU) 2019/6 (VMR) (see also European Surveillance of Veterinary Antimicrobial Consumption-ESVAC dedicated [webpage](#)).

Fees

Explanatory notes on general fees payable to EMA has been updated on 1 April 2022 ([Link](#)). Changes include clarifications on fees for cancellation of inspections and scientific service fees for VAMFs and vaccine platform technology master files for veterinary medicines.

New EMA Mandate under Regulation (EU) 2022/123

Regulation (EU) 2022/123 provides EMA with a framework to monitor and mitigate shortages of centrally and nationally authorised medicinal products for human use considered as critical to address a public health emergency or major event. EMA established in March 2022 the Executive Steering Group on Shortages and Safety of Medicinal Products ([MSSG](#)) to provide leadership for coordinated action to prevent and mitigate medicine supply disruptions. The group adopted on 7 June 2022 a list of [critical medicines for COVID-19](#), which supply and demand will be closely monitored to identify and manage potential or actual shortages. For additional information refer to EMA's [webpage](#).

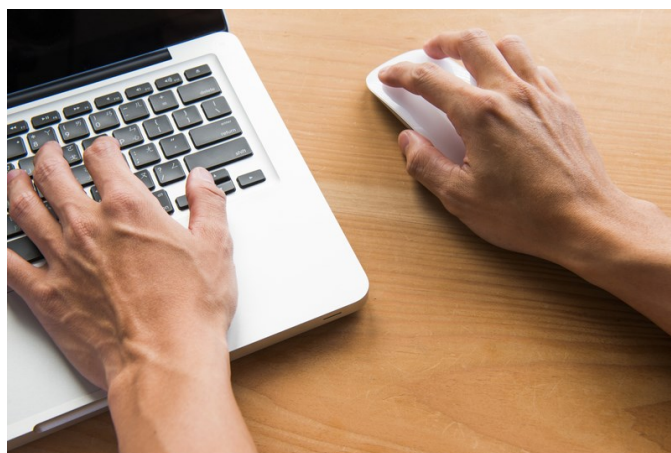
Pharmaceutical companies with a centrally or nationally authorised medicinal product in the EU are required to register by 2 September 2022 a single point of contact (i-SPOC). i-SPOCs will facilitate communication between EMA and companies to detect, report, and prevent or manage supply and availability issues of medicines included in a list of critical medicines for a public health emergency or a major event. For more information on how to register i-SPOCs in EMA's IRIS platform refer to [webpage](#).



Events

Upcoming events

- Multi-stakeholder workshop: Patient experience data in medicines development and regulatory decision-making ([Link](#)) (21 September 2022).
- EudraVigilance training ([Link](#)) (12-16 September 2022, 10-14 October 2022, 24-28 October 2022, 21-25 November 2022, 5-9 December 2022).
- Training for clinical trials sponsors using EudraVigilance system ([Link](#)) (5-7 October 2022 and 30 November–2 December 2022).
- Union Product Database: webinar on variations not requiring assessment for marketing authorisation holders ([Link](#)) (8 September 2022).
- Organisation Management System (OMS) Trouble Shooting Sessions for CTIS users ([Link](#)) (22 September 2022, 19 October 2022, 24 November 2022).
- Extended EudraVigilance medicinal product dictionary (XEVMPPD) training ([Link](#)) (26-28 September 2022, 26-28 October 2022, 16-18 November 2022).
- Extended EudraVigilance medicinal product dictionary (XEVMPPD) training for clinical trial sponsors ([Link](#)) (29-30 September 2022, 24-25 October 2022, 14-15 November 2022).
- Second Veterinary Big Data stakeholder forum ([Link](#)) (23 November 2022).
- ACT EU Multi-stakeholder meeting on decentralised clinical trials ([Link](#)) (4 October 2022).
- Training for patients, consumers and healthcare professionals involved in medicine regulatory activities ([Link](#)) (17-20 October 2022).
- Digital Application Dataset Integration (DADI) pdf electronic application forms (eAF) training webinar ([Link](#)) (2 September 2022).
- EMA/EATRIS joint webinar on scientific advice for advanced therapy medicinal products: what & when to ask – 10 June 2022 ([Video recording](#); [Link](#)).
- EMA workshop on thrombosis with thrombocytopenia syndrome – 27 June 2022 ([Presentations](#)).
- Digital application dataset integration (DADI) Q&A webinar - variations form for human medicinal products – 12 July 2022 ([Presentations](#)).
- Eight industry stakeholder platform on research and development support – 11 July 2022 ([Link](#)).
- Digital application dataset integration (DADI) and Product Management Service (PMS) webinar - Variations form for human medicinal products - What will happen at go-live – 16 May 2022 ([Video recording](#); [Presentations](#)).



Reports and workplans

- Clinical Trials Information System (CTIS) webinar: Six months of CTIS and looking forward – 1 July 2021 ([Presentations](#)).
- Multi-stakeholder workshop on EMA's extended mandate – 1 April 2022 ([Video recording](#)).
- Data quality framework for medicines regulation – 7 April 2022 ([Presentations](#)).
- EMA Patients' and Consumers' (PCWP) and Healthcare Professionals' (HCPWP) Working Parties joint meeting – 01-02 June 2022 ([Presentations](#)).
- Webinar on submissions of parallel distribution notifications for centrally authorised products (CAPs) – 9 June 2022 ([Presentations](#)).
- EMA annual report 2021 ([Link](#); [Webpage](#)).
- SME office annual report 2021 ([Link](#)).
- Stakeholder engagement Biennial Report (2020-2021) ([Link](#)).
- European Medicines Agency's interaction with industry stakeholders Biennial report 2020–2021 ([Link](#)).
- EMA/HMA Big Data Steering Group workplan 2022-25 ([Link](#), [press release](#), [Big Data Highlights](#)).
- EMA/European Network for Health Technology Assessment (EUnetHTA) consortium joint work plan until 2023—12 April 2022 ([Link](#); [press release](#)).

Registered SMEs

Currently, 1820 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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