

SME Office NEWSLETTER

Information for SMEs on the EU regulatory environment for medicines.
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SME office report

A [report](#) highlighting EMA's support for micro, small and medium-sized enterprises (SMEs) between 2016 and 2020 was published. It provides key facts and figures of companies registered as SMEs with EMA and services provided. The publication of the report marks the 15-year anniversary of the adoption of the [SME Regulation](#), which promotes innovation and the development of new medicines for human and veterinary use. For additional information, see reports of the [EMA roundtable with stakeholders on the 15-year anniversary of the SME Regulation](#), the [SME Office's 2020 survey](#), [SME office webpage](#) and [EMA News announcement](#).

SME Veterinary Info Day

An Info day for EMA registered SMEs is planned on 28 October 2021 ([Link](#)) to raise awareness of EMA initiatives supporting SMEs and service providers operating in the veterinary medicines sector. It will highlight platforms for early dialogue with EMA, the range of support that companies can access to optimise their development plans and the experience with marketing authorisation applications. The event will also focus on the impact on SMEs of the implementation of the [Veterinary Medicinal Products Regulation \(EU\) 2019/6](#), which will become applicable on 28 January 2022. The registration for this event is by invitation only and opens in September 2021.

EMA annual report

EMA has published its [2020 annual report](#) provides an overview of the Agency's major achievements and contributions to public health in Europe and outlines the most important highlights of the evaluation and monitoring of human and veterinary medicines, the European medicines regulatory network's rapid response to COVID-19, and an overview of key figures. Please also see [Link](#).

Medical Devices Regulation (MDR)

The Medical Device Regulation (MDR, [Regulation \(EU\) 2017/745](#)) became applicable on 26 May 2021 and replaces the existing Directives for medical devices ([93/42/EEC](#) and [90/385/EEC](#)). It changes the European legal framework for medical devices and introduces new roles for EMA and for national competent authorities in the assessment of certain categories of products. The MDR introduces new or revised responsibilities for EMA for medicines with an integral device, medical devices containing an ancillary medicinal substance, medical devices made from substances that are absorbed by the human body to achieve their intended purpose and borderline products for which there is an uncertainty over which regulatory framework applies (see also [Link](#)). To support the implementation of the MDR, an [updated Q&A](#) was published including new sections on consultation procedure for ancillary medicinal substances and co-packaged medicinal products and devices. The Regulation on in vitro diagnostic medical devices, which will replace Directive [98/79/EC](#), will become applicable from 26 May 2022.

EMA engagement with academia

EMA has published an academia collaboration matrix action plan ([EMA/159144/2021](#)) which sets out EMA's objectives to enhance collaboration with Academia and researchers over 2021-2023. It lists actions in five areas: regulatory science and partnerships, innovation and support to academia, communication, events strategy and training.

EU Innovation Network

The EU Innovation Network ([EU-IN](#)) was set up in 2015 by EMA and the Heads of Medicines Agencies (HMA) to strengthen collaboration between national competent authorities (NCAs) and EMA on regulatory matters relating to emerging therapies and technologies. In order to pursue its objectives, the following initiatives have been developed:

- The STARS project which aims to engage with innovators in academia, address the regulatory knowledge gap and enhance the dialogue between academia and regulatory authorities. An overview of the project has recently been published ([Link](#)). See also the STARS website for further details ([Link](#)).
- A pilot for Simultaneous National Scientific Advice (SNSA) from NCAs to enable innovators to access scientific advice simultaneously in different EU Member States. This has been extended to the end of 2021 ([Link](#)). See also the corresponding guidance [here](#).

Clinical Trials

Clinical Trial Information System (CTIS)

On 21 April 2021, EMA's Management Board confirmed that the Clinical Trial Information System ([CTIS](#)) will go live on 31 January 2022 following recommendations of an independent audit confirming that it meets agreed requirements ([Link](#)). Online training modules and training material are available on EMA's website ([Link](#)). A catalogue of training activities is also available [here](#).

A webinar organised on 29 July 2021 helps sponsors prepare for CTIS ([Link](#)). Recordings of a dedicated SME and academia webinar on CTIS held on 22 February 2021 and 4 March 2021 are now also available ([Day 1](#), [Day 2](#)).

To stay up to date with CTIS, please refer to [CTIS Highlights Newsletters](#) (to subscribe write to CT.communication@ema.europa.eu).

Clinical trial applications

Two draft guidelines on quality documentation requirements in EU clinical trial applications have been released for consultation until 31 August 2021:

- Chemical and pharmaceutical quality documentation for investigational medicinal products in clinical trials ([EMA/CHMP/QWP/31884/2021](#)); see also [here](#).
- Quality documentation for biological investigational medicinal products in clinical trials ([EMA/CHMP/BWP/534898/2008 rev. 2 corrigendum](#)); see also [here](#).

Medicines for children and rare diseases

The European Commission (EC) has launched an initiative to explore options to address shortcomings identified in the evaluation of EU Regulations on medicines for children and rare diseases, in view of the pharmaceutical legislation review. The public consultation, open until 31 July 2021, invites stakeholders to share their views and experience on the main obstacles they are facing with medicines for rare diseases and children and ways to overcome these obstacles ([Link](#)).



COVID-19

EMA and the European Centre for Disease Prevention and Control (ECDC) have launched a new initiative aimed at strengthening post-marketing monitoring of safety, effectiveness and impact of COVID-19 vaccines in the European Union/European economic area (EU/EEA). More information can be found in a dedicated press release ([Link](#)).

Medicines regulators from around the world discussed global collaboration and information sharing on real-world evidence to facilitate regulatory decision-making on COVID-19 treatments and vaccines. The findings of the meeting convened by the International Coalition of Medicines Regulatory Authorities (ICMRA) and co-chaired by Health Canada and EMA, are summarised [here](#). See also the press release ([Link](#)).

The following guidance documents have also been published:

- A new procedural guidance on variation applications for updates of vaccine composition for centrally authorised vaccines against COVID-19 disease. ([EMA/175959/2021](#));
- A new document on core requirements for PSURs of COVID-19 vaccines ([EMA/362988/2021](#));
- An updated document on core requirements for Risk Management Plans of COVID-19 vaccines ([EMA/PRAC/234052/2021](#));
- An updated Q&A on labelling flexibilities for COVID-19 vaccines ([EMA/343077/2021 rev.21](#)).

Scientific guidelines for human medicines

Multidisciplinary

An ICH reflection paper identifying key areas where incorporation of the patient's perspective could improve the quality, relevance, safety and efficiency of drug development and inform regulatory decision making was released for information ([EMA/CHMP/ICH/338534/202](#)). It also highlights opportunities for the development of new ICH guidelines to provide a globally harmonized approach to include the patient's perspective in a way that is methodologically sound and fit-for purpose for industry and authorities.

Quality

An EU reflection paper on recommendations to support forecasting of demand for human medicinal products across the EU in exceptional situations like the COVID-19 pandemic ([EMA/162549/2021](#)) has been published. It was developed based on experience gained during the pandemic and sets out a common methodology to predict the demand of medicines for use in intensive care units. More information can also be found in a dedicated press release ([Link](#)).

A Q&A document for marketing authorisation holders/applicants on the CHMP opinion for the Article 5(3) of Regulation (EC) No 726/2004 referral on nitrosamine impurities in human medicinal products has been updated on e.g. report to competent authorities, nitrosamines limits in medicinal products ([EMA/409815/2020 Rev.4](#)).

EU recommendations for the seasonal influenza vaccine composition for 2021-2022 have been published on 24 June 2021 ([EMA/CHMP/BWP/80561/2021](#)).

A revised ICH guideline Q3C (R6) on residual solvents ([EMA/CHMP/ICH/82260/2006](#)) has been updated to add Permissible Daily Exposure for 2-Methyltetrahydrofuran (2-MTHF), Cyclopentyl Methyl Ether (CPME), and Tertiary Butyl Alcohol (TBA)); it will enter into force on 20 November 2021.

A Q&A on good manufacturing practice and good distribution practice has been revised on manufacturing of starting materials of biological origin used to transfer genetic material for the manufacturing of ATMPs ([EMA/246400/2021](#)).



Nonclinical

An ICH guideline S12 on the design and conduct of biodistribution studies for gene therapy products was released for consultation until 24 October 2021 ([EMA/CHMP/ICH/318372/2021](#)).

Clinical

EMA holds regular meetings with non-EU regulators in so-called 'clusters' focusing on special topics and therapeutic areas requiring an intensified exchange of information and collaboration. EMA/FDA's Paediatric Medicinal products Cluster has provided an opportunity to engage in discussions of paediatric development plans and regulatory alignment considered critical in international clinical trials in rare diseases such as childhood cancer. A [document](#) describing key issues commonly requested by EMA and FDA and discussed with sponsors has been published.

A draft ICH guideline E6 on Good Clinical Practice (GCP) was released for information on 24 June 2021 ([EMA/CHMP/ICH/337843/2021](#)). It includes draft updated principles that are currently under development for a framework for clinical trial conduct. Public consultation will be initiated together with its draft Annex on interventional clinical trials.

A draft guideline on computerised systems (including instruments, software and services) used in clinical trials in the creation/capture of electronic clinical data and the control of other processes in the conduct of a clinical trial of investigational medicinal products has been released for consultation until 17 December 2021 ([EMA/226170/2021](#)). This guideline will replace the 'Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials' ([EMA/INS/GCP/454280/2010](#)).

Pharmacovigilance

Big data

EMA is currently developing a coordination centre called Data Analysis and Real-World Interrogation Network ([DARWIN EU](#)). It aims to provide timely and reliable evidence on the use, safety and effectiveness of medicines for human use, including vaccines, from real world healthcare databases across the EU. DARWIN EU is one of the recommendations set out in [EMA-HMA Big Data Steering Group workplan](#) and the [European medicines agencies network strategy to 2025](#).

Eudravigilance

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. Revised guidance on technical requirements and processes for transmitting individual case safety reports (ICSRs) is available [here](#) to help pharmaceutical companies, sponsors of clinical trials and medicines regulatory authorities prepare for using the new ICSR standard. The revised guidance also includes updates on e.g. registration process, business rules, data protection and changes to the reporting requirements for clinical trials that will apply after go-live of the Clinical Trials Information System (CTIS). For more information, see also EMA management board announcement ([EMA/561671/2019](#)).

The following documents were also published:

- Change of qualified person for pharmacovigilance/responsible person for EudraVigilance (QPPV/RP) ([EMA/503895/2018](#))
- Revised template of Eudravigilance user declaration for qualified person for pharmacovigilance/responsible person for Eudravigilance ([EMA/204890/2017](#))
- EudraVigilance registration ([EMA/503894/2018](#))
- Revised Eudravigilance registration manual ([EMA/13454/2020, Rev. 9](#))
- Revised guidance on monitoring of medical literature and the entry of relevant information into the EudraVigilance database by EMA ([EMA/517840/2015 Rev 3*](#)) (Covid-19 related amendments)

Regulatory guidance

Medicines for use outside the EU

In addition to the EU-M4all procedure exclusively intended for third countries, EMA is now offering the option to run evaluations of centralised and EU-M4all applications in parallel, to obtain an EU-M4all Scientific Opinion and a Centralised Marketing Authorisation at the same time. Guidance on applying for the two procedures in parallel is now available ([EMA/104275/2021](#)).

Orphan guidance

Guidance for sponsors for orphan products designations was updated to include advice to SME sponsors on translations. SME applicants are not required to submit translations at the time of submission of an application for orphan medicinal product if they have received EMA SME status. More information can be found in the document ([EMA/420706/2018 Rev 10](#)). The corresponding template on translations required with the submission of an application for orphan medicinal product designation was updated ([Link](#)).

Guidance for sponsors for post-orphan medicinal product designation activities was updated to include information on a COMP negative trend vote during review of the orphan medicinal product designation criteria ([EMA/469917/2018](#), Rev 11).

The EC Q&A document providing guidance on the assessment of similarity for Advanced Therapy Medicinal Products (ATMPs) in the context of the orphan legislation has been updated to reflect recent experience and developments in this field ([Link](#)). It addresses questions raised by developers regarding the application of the concept of 'similar active substance' ([Link](#)).

Other guidance

The following guidance documents have also been updated:

- IRIS guide for parallel distribution applicants ([Link](#))
- IRIS guide to registration ([Link](#))
- EMA pre-authorisation guidance ([EMA/821278/2015](#)) (on e.g. change of contact person, information regarding transfer of test methods for biological medicinal products, risk management plans, EMA fees)
- EMA post-authorisation guidance ([EMA-H-19984/03 Rev. 93](#)) (on e.g. notifying a change of marketing status, EMA fees, submission of revised product information, presentation of variations, changes triggering new EU numbers)
- Validation checklist for Type II quality variations ([Link](#))
- Validation checklist for Type II (non)clinical variations ([Link](#))
- Template on Mutual-recognition decentralised referral product information ([Link](#))
- Frequently asked questions about parallel distribution ([Link](#))

- Checklist for annual updates for parallel distribution ([EMA/405782/2020 Rev. 1](#))
- Checklist for initial notifications for parallel distribution ([EMA/267299/2020 Rev. 1](#))
- Member states contact points for translation review ([EMA/102302/2005 v. 6.18](#))

Fees

The explanatory note on general fees payable to EMA has been updated on 1 April 2021 ([Link](#)). Changes include the removal of a maximum period for fee incentives applying to certain post-authorisation activities for pandemic post-authorisation applications. Fee incentives for post-authorisation applications were also introduced for certain human vaccines authorised under exceptional circumstances for preparedness against biological agents that might be used as weapons of bioterrorism.

IT and digitalisation

Electronic product information (ePI)

EMA held workshops on 5 July 2021 and 8 July 2021 ([link](#) to events) to launch a public consultation on the draft EU common standard for electronic product information (ePI) developed as part of the ePI set-up project started by EMA, national competent authorities and the EC. The document has been published for consultation until 31 July 2021 ([Link](#)).

IRIS

EMA's [IRIS](#) platform will now be used to notify EMA of the placing on the market and the temporary or permanent marketing cessation of centrally authorised medicinal products (CAPs). Marketing authorisation holders must use IRIS to report a marketing status change for any product not previously marketed in the EU or EEA, and have until 31 January 2022 to enter marketing status details of products already on the market in IRIS ([Link](#)).

From 10 October 2021, a Research Product Identifier (RPI) will be required for paediatric procedures, and will be a mandatory field in the electronic application form for paediatric investigation plans (PIPs), modifications of agreed PIPs, and requests for waivers. Until then, the RPI can be entered in the appropriate field in the e-Submission Gateway/Web Client. Consult the [IRIS guide to registration](#) for more information.

Mandatory registration in OMS for new sites and organisations

As part of the development of the Substance, Product, Organisation and Referential (SPOR) data management services, registration in [Organisation Management Service \(OMS\)](#) will become mandatory from the 30 September 2021 for new sites and organisations to be registered as part of any regulatory procedure submitted to EMA. This includes pre-submission phase activities (e.g. eligibility requests, pre-submission meeting requests, change in contact person requests), marketing authorisation applications, line extensions and variations. This is applicable to both human and veterinary medicinal products.



Certificates of Medicinal products

Since March 2020, EMA is only issuing certificates for human and veterinary medicines that are signed and authenticated electronically. EMA's electronic system for issuing certificates now permanently replaces the previous paper-based system, as part of EMA's digitalisation activities. An online verification system is available for stakeholders and partners to check the authenticity of an electronic certificate issued by EMA ([Link](#)).

For more information and guidance, the following documents are available:

- Updated guidance on the format and validity features of electronic certificates for medicines issued by EMA ([EMA/206719/2020 Rev 1](#)).
- Updated guidance on information package for certificates of medicinal products issued by EMA ([EMA/119843/2013 Rev 16*](#)).
- Handling times for requests for EMA certificates through standard procedure ([EMA/579807/2018 Rev 1](#))
- Notification on authenticity of EMA certificates ([EMA/296924/2011 Rev 1](#))
- Updated application form to request certificates ([Link](#)) and guidance on how to complete the form ([EMA/193330/2014 Rev 14*](#)).

Veterinary medicines



Guidance on product information

A revised product information template (supporting the requirements of the Veterinary Medicinal Products Regulation ([Regulation \(EU\) 2019/6](#)) will apply for initial marketing authorisation applications validated on or after 28 January 2022 ([Link](#)). The available version is in English and other language versions will be released in October 2021.

A revised product information guidance for medicines containing antimicrobial substances will come into effect on 28 January 2022 ([EMA/CVMP/383441/2005-Rev.1](#)).

An updated Quality Review of Documents (QRD) guidance on the use of approved pictograms on the packaging of veterinary medicinal products authorised via the centralised, mutual recognition and decentralised procedures was published on 28 May 2021 ([EMA/776723/2017 rev. 2**](#)).

Post-authorisation procedural guidance

A guidance for marketing authorisation holders whose marketing authorisations' five-year validity period expires on or after 28 January 2022 is available in a [notice published by the European Commission](#). It explains the practical steps to take to implement the relevant provisions of the Veterinary Medicinal Products Regulation. EMA procedural guidance for centrally authorised veterinary medicinal products based on the European Commission notice is available [here](#).

Pharmacovigilance

The Veterinary Medicinal Products Regulation ([Link](#)) contains new pharmacovigilance provisions focusing on

continuous signal management based on adverse event data in the 'Union Pharmacovigilance Database', pharmacovigilance inspections and pharmacovigilance master files. To support companies in complying with pharmacovigilance obligations, EMA has released for consultation until 5 September 2021 a draft guideline on Veterinary Good Pharmacovigilance Practices (VGVP), composed of six modules, which will be applicable from 28 January 2022 ([Link](#)).

EMA will also launch on 28 January 2022 an enhanced EudraVigilance Veterinary system ([EVVet](#)). The system will use the pharmacovigilance reporting standards developed by the Veterinary International Conference on Harmonization (VICH). A draft implementation guide on reporting adverse events in the VICH format is available for public consultation until 4 August 2021 ([EMA/186368/2021](#)). Corresponding annexes and more information about Eudravigilance for veterinary products can be found in a dedicated EMA webpage ([Link](#)).

Scientific guidelines

A revised draft guideline on data requirements for multi-strain dossiers for inactivated veterinary vaccines was released for consultation until 30 September 2021 ([EMA/CVMP/IWP/105506/2007 Rev. 2](#)). Its aim is to address the use of a multi-strain dossier for inactivated vaccines against antigenically variable viruses or bacteria and to provide information on criteria for eligibility to use the multi-strain approach, and on the data to be included in a multi-strain dossier.

A draft guideline on scientific data requirements for vaccine antigen master files (VAMF) submission, evaluation and certification has been released for consultation until 30 September 2021 ([EMA/CVMP/IWP/258755/2021](#)).

Union Product Database

The Union Product Database ([UPD](#)) is a system mandated by the new Veterinary Medicines Regulation ([Regulation \(EU\) 2019/6](#)) which will provide information on all authorised veterinary medicines and their availability in the EU. A guide for companies and national competent authorities on data submission to the UPD, including details on formats, terminologies, requirements and processes is now available ([Link](#)).

Consult the Veterinary medicines Regulation Newsletter ([Link](#)) for information and updates on the Veterinary Medicinal Products Regulation.

Registered SMEs

Currently, 1634 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, and benefit from the [EMA SME incentives](#), 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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