



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The European regulatory system for medicines

A consistent approach to medicines regulation across the European Union



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This booklet explains how the European regulatory system for medicines operates. It describes how medicines are authorised and monitored in the European Union (EU) and how the European medicines regulatory network – a partnership between the European Commission, the medicines regulatory authorities in EU Member States and the European Economic Area (EEA), and the European Medicines Agency (EMA) – works to ensure that patients in the EU have access to high-quality, effective and safe medicines.

The EU regulatory system for medicines



The European medicines regulatory system is based on a network of around 50 regulatory authorities from the 31 EEA countries (28 EU Member States plus Iceland, Liechtenstein and Norway), the European Commission and EMA. This network is what makes the EU regulatory system unique.

The network is supported by a pool of thousands of experts drawn from across Europe, allowing it to source the best possible scientific expertise for the regulation of medicines in the EU and to provide scientific advice of the highest quality.

EMA and the Member States cooperate and share expertise in the assessment of new medicines and of new safety information. They also rely on each other for exchange of information in the regulation of medicine, for example regarding the reporting of side effects of medicines, the oversight of clinical trials and the conduct of inspections of medicines' manufacturers and compliance with good clinical practice (GCP), good manufacturing practice (GMP), good distribution practice (GDP), and good pharmacovigilance practice (GVP). This works because EU legislation requires that each Member State operates to the same rules and requirements regarding the authorisation and monitoring of medicines.

IT systems which connect all parties in the network facilitate the exchange of information on aspects such as safety monitoring of medicines, authorisation and supervision of clinical trials or compliance with good manufacturing and distribution practices.

The diversity of experts involved in the regulation of medicines in the EU encourages the exchange of knowledge, ideas and best practice between scientists striving for the highest standards for medicines' regulation.

By working closely together, Member States reduce duplication, share the workload and ensure the efficient and effective regulation of medicines across the EU.

Marketing authorisations



To protect public health and ensure the availability of high quality, safe and effective medicines for European citizens, all medicines must be authorised before they can be placed on the market in the EU. The European system offers different routes for such an **authorisation**.

The **centralised procedure** allows the marketing of a medicine on the basis of a single EU-wide assessment and marketing authorisation which is valid throughout the EU. Pharmaceutical companies submit a single authorisation application to EMA. The Agency's Committee for Medicinal Products for Human Use (CHMP) or Committee for Medicinal Products for Veterinary Use (CVMP) then carries out a scientific assessment of the application and gives a recommendation to the European Commission on whether or not to grant a marketing authorisation. Once granted by the European Commission, the centralised marketing authorisation is valid in all EU Member States. The use of the centrally authorised procedure is compulsory for most innovative medicines, including medicines for rare diseases.

The majority of medicines authorised in the EU do not fall within the scope of the centralised procedure but are authorised by national competent authorities (NCAs) in the Member States.

When a company wants to authorise a medicine in several Member States, it can use one of the following procedures:

- the **decentralised procedure** where companies can apply for the simultaneous authorisation of a medicine in more than one EU Member State if it has not yet been authorised in any EU country and does not fall within the scope of the centralised procedure;
- the **mutual-recognition** procedure where companies that have a medicine authorised in one EU Member States can apply for this authorisation to be recognised in other EU countries. This process allows Member States to rely on each other's scientific assessments.

Rules and requirements applicable to pharmaceuticals in the EU are the same, irrespective of the authorisation route for a medicine.

Transparency about how the system works and how it reaches its decisions is an important feature of the EU regulatory system for medicines.

A European Public Assessment Report, or EPAR, is published for every human or veterinary medicine that has been granted or refused a marketing authorisation following an assessment by EMA. For a medicine that is authorised by a Member State, details on the assessment of the medicine are also available in a Public Assessment Report.

EMA enables one application, one assessment, one market authorisation for the whole of the EU.

Different authorisation routes: one set of common rules.

¹ The regulation of medical devices does not fall within the scope of the European regulatory system for medicines.

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Pricing and reimbursement



Once a marketing authorisation has been granted, decisions about price and reimbursement take place at the level of each Member State considering the potential role and use of the medicine in the context of the national health system of that country.

The role of the European Commission



The European Commission plays an important role in the regulation of medicines in the EU. On the basis of scientific assessments carried out by EMA, it grants or refuses, changes or suspends marketing authorisations for medicines that have been submitted via the centralised procedure. It can also take EU-wide action when a safety issue has been identified for a nationally authorised product and when harmonised regulatory measures in all MSs are considered necessary following assessment by EMA's PRAC. The European Commission can also take action concerning other aspects of medicine regulation:

- **Right of initiative** – it can propose new or amended legislation for the pharmaceutical sector;
- **Implementation** – it can adopt implementing measures as well as oversee the correct application of EU law on pharmaceuticals;
- **Global outreach** – it ensures appropriate collaboration with relevant international partners and promotes the EU regulatory system globally.

The role of EMA



EMA is responsible for the scientific evaluation, primarily of innovative and high-technology medicines developed by pharmaceutical companies for use in the EU. EMA was established in 1995 to ensure the best use of scientific resources across Europe for the evaluation, supervision and pharmacovigilance of medicines.

Experts participate in the work of EMA as members of its scientific committees, working parties, scientific advisory groups and other ad hoc advisory groups, or as members of the national assessment teams that evaluate medicines. The experts are chosen on the basis of their scientific expertise and many of them are made available to EMA by the NCAs in Member States. Increasingly, patients and healthcare professionals are involved in the work of the Agency including in the evaluation of medicines.

EMA's scientific committees

The EMA has seven scientific committees that carry out its scientific assessments:

- Committee for Medicinal Products for Human Use (CHMP)
- Pharmacovigilance Risk Assessment Committee (PRAC)
- Committee for Medicinal Products for Veterinary Use (CMVP)
- Committee for Orphan Medicinal Products (COMP)
- Committee on Herbal Medicinal Products (HMPC)
- Committee for Advanced Therapies (CAT)
- Paediatric Committee (PDCO)

National Competent Authorities

The national competent authorities (NCAs), responsible for the regulation of human and veterinary medicines in the EU, coordinate their work in a forum called **Heads of Medicines Agencies (HMA)**. The heads of the NCAs work closely with EMA and the European Commission to maximise cooperation and ensure the European medicines regulatory network functions efficiently. The HMA meets four times per year to address key strategic issues for the network, such as the exchange of information, IT developments and sharing of best practices, and to streamline mutual recognition and decentralised procedures.

Guidelines and scientific advice



EMA prepares **scientific guidelines** in cooperation with experts from its scientific committees and working groups. These guidelines reflect the latest thinking on developments in biomedical science. They are available to guide the development programmes of all medicine developers who wish to submit an application for a marketing authorisation in the EU, and to ensure that medicines are developed consistently and to the highest quality.

EMA also gives product-specific scientific advice to companies for the development of medicines. This is an important tool to help develop and make available high-quality, effective and safe medicines, for the benefit of patients. Scientific advice can also be given by NCAs.

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Authorisation and supervision of manufacturers



Manufacturers, importers and distributors of medicines in the EU must be licensed before they can carry out those activities. The regulatory authorities of each Member State are responsible for granting licences for such activities taking place within their respective territories. All manufacturing and importing licenses are entered into EudraGMDP, the publicly-available European database operated by EMA.

Manufacturers listed in the application of a medicine to be marketed in the EU are inspected by an EU competent authority. This includes manufacturers located outside the EU unless a mutual recognition agreement (MRA) is in place between the European Union and the country of manufacture. Inspection outcomes can be accessed by all Member States and are made publicly available across the EU through EudraGMDP.

Equivalence between Member States' inspectorates is ensured and maintained in a variety of ways, including common legislation, common good manufacturing practice (GMP), common procedures for inspectorates, technical support, meetings, trainings, and internal and external audits.

In order to be imported into the EU, an active pharmaceutical ingredient needs to be accompanied by a Written Confirmation issued by the competent authority of the country where it is produced, confirming that the good manufacturing practice (GMP) applied is at least equivalent to the recognised EU GMP standards. A waiver applies for some countries which have applied to have their regulatory systems for the supervision of manufacturers of active pharmaceutical ingredients assessed by the EU and have been found to be equivalent to the EU.

Every batch of medicines must be certified as having been manufactured and tested in accordance with GMP and in conformance with the marketing authorisation before it can be released onto the market in the EU. If the product is manufactured outside the EU and has been imported, it needs to undergo full analytical testing in the EU, unless a mutual recognition agreement (MRA) is in place between the EU and the exporting country.

Safety monitoring of medicines



The European regulatory system for medicines monitors the safety of all medicines that are available on the European market throughout their life span.

EMA has a committee dedicated to the safety of medicines for human use – the Pharmacovigilance Risk Assessment Committee, or PRAC. If there is a safety issue with a medicine that is authorised in more than one Member State, the same regulatory action is taken across the EU and patients and healthcare professionals in all Member States are provided with the same guidance.

All suspected side effects that are reported by patients and healthcare professionals must be entered into EudraVigilance, the EU web-based information system operated by EMA that collects, manages and analyses reports of suspected side effects of medicines. These data are continuously monitored by EMA and the Member States in order to identify any new safety information.

EMA provides public access to reports of suspected side effects for centrally-authorised medicines in the European **database** of suspected drug-reaction reports. This website allows users to view all suspected side effect reports submitted to EudraVigilance

The PRAC has a broad remit covering all aspects of pharmacovigilance. In addition to its role in risk assessment, the committee provides advice and recommendations to the European medicines regulatory network on risk management planning and benefit-risk assessment for medicines after marketing.

Public hearings

In addition, the EU's **pharmacovigilance legislation** enables the PRAC to hold **public hearings** during safety reviews of medicines if deemed useful. Public hearings are intended to support the committee's decision-making by providing perspectives, knowledge and insights into the way medicines are used in clinical practice.

Clinical trials



The authorisation and oversight of a clinical trial is the responsibility of the Member State in which the trial is taking place. The **European Clinical Trials Database** (EudraCT) tracks which clinical trials have been authorised in the EU. It is used by NCAs and clinical-trial sponsors to enter information protocols and results of clinical trials. A subset of this information is made publicly available by EMA via the EU clinical trials register.

International cooperation



The European Commission and EMA, in close cooperation with Member States, work to forge close ties with partner organisations around the world. These activities aim to foster the timely exchange of regulatory and scientific expertise and the development of best practices in the regulatory field across the world.

The European Commission and EMA work with the World Health Organization (WHO) on a range of issues, including medicines intended for markets outside the EU (medicines reviewed under EMA's so-called 'Article 58 procedure'), the quality of medicines and the development of international non-proprietary names.

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Supporting regulatory science outside the EU – the Article 58 procedure

The CHMP can carry out scientific assessments and give opinions, in cooperation with WHO, on medicines for use exclusively outside the EU. When assessing these medicines, the CHMP applies the same rigorous standards as for medicines intended for use inside the EU. Medicines eligible for this procedure, which is derived from Article 58 of the regulation founding the Agency, are used to prevent or treat diseases that impact global public health. This includes vaccines used in the WHO Expanded Programme on Immunization, or for protection against a public health priority disease, as well as medicines for WHO target diseases such as HIV/AIDS, malaria or tuberculosis.

For the EU, one of the main forums for multilateral international cooperation is the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), which brings together medicines regulatory authorities and pharmaceutical industry from around the world. ICH is

dedicated to harmonisation in safety, quality and efficacy as the main criteria for approving and authorising new medicines. The Veterinary International Conference on Harmonisation (VICH) is the equivalent forum for veterinary medicines.

EMA and many NCAs are also involved in the Pharmaceutical Inspection Convention and the Pharmaceutical Inspection Co-operation Scheme (jointly referred to as PIC/S), a close international cooperation between pharmaceutical inspection authorities in the field of GMP.

Regulatory cooperation and exchange of information with international regulators is also assured through the International Pharmaceutical Regulators' Forum (IPRF).

A strategic forum at the level of global agencies has recently been established – the International Coalition of Medicines Regulatory Authorities (ICMRA). ICMRA is a voluntary, executive level entity of medicines regulatory authorities worldwide providing strategic coordination, advocacy and leadership.

There are also a number of bilateral cooperation agreements in place that facilitate the exchange of important information on medicines between regulators inside and outside the EU.

The European Union – key facts

>500m
Population

€ 12.9tn
GDP

24 official languages

Medicines regulatory authorities 50+

*The EU has developed a single market through a standardised system of laws that apply to all its Member States. The same rules and harmonised procedures apply to all the **28 Member States** regarding the authorisation of medicines and the supervision of the safety medicines.*

*Accession to the EU means a commitment to apply the "**acquis communautaire**" (the body of EU legislation and guidance) to ensure that all EU Member States operate to the same standards.*

EU Member States: 28



The European Economic Area (EEA) is formed of the 28 EU Member States plus:





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