EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The European regulatory system for medicines and the European Medicines Agency

A consistent approach to medicines regulation across the European Union

An agency of the European Union

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This booklet is intended to explain how the European regulatory system for medicines operates. It describes how medicines[1] 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 the 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 safe and efficacious medicines.

The EU regulatory system for medicines

The European medicines regulatory system is based on a network of medicines regulatory authorities from the 31 EEA Member States, the European Commission and the European Medicines Agency (EMA). This network is what makes the EU regulatory system unique.

The network is supported by a pool of many thousands of experts drawn from right 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.

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In a number of aspects in the regulation of medicines, Member States rely on each other for exchange of information, for example the reporting of side effects of medicines in their territories, 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 of medicines and keeping medicines safe.

Relying on the competence of other Member States also reduces duplication of efforts, shares the workload and ensures the efficient and effective regulation of medicines across the EU. A number of IT systems are in place to facilitate the exchange of information.

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

Marketing authorisations

To guarantee the protection of public health and to ensure the availability of high quality, safe and efficacious 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 authorising medicines.

Under the **centralised** procedure, pharmaceutical companies submit a single marketing-authorisation application to the EMA. The EMA's Committee for Medicinal Products for Human Use (CHMP) or Committee for Medicinal Products for Veterinary Use (CVMP) carries out a scientific assessment of the application and gives a recommendation 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.

This allows the marketing-authorisation holder to market the medicine and make it available to patients and healthcare professionals throughout the EU on the basis of a single marketing authorisation. The use of the centralised procedure is compulsory for certain medicines and most innovative medicines go through this procedure.

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

Different authorisation routes: one set of common rules.

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 it does not fall within the mandatory scope of the centralised procedure;

or the **mutual-recognition procedure** where companies that have a medicine authorised in one EU Member State 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.

[1] The regulation of medical devices does not fall within the scope of the European 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 the EMA. For a medicine that is authorised by a Member State, details on the assessment of the medicine are available in a public assessment report.

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 Medicines Agency

The EMA is responsible for the scientific evaluation, primarily of innovative and high technology medicines developed by pharmaceutical companies for use in the EU. The EMA was set up to ensure the best use of scientific resources across Europe.

Experts participate in the work of the EMA as members of its scientific committees, working parties, scientific advisory groups and other ad hoc advisory groups, or as members of the assessment teams carrying out the evaluation of medicines. Experts are chosen on the basis of their scientific expertise and are mostly made available to the EMA by the medicines regulatory authorities in Member States. Increasingly, patients and healthcare professionals are involved in the work of the EMA.

The EMA's scientific committees

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

- Committee for Medicinal Products for Human Use
- Pharmacovigilance Risk Assessment Committee
- Committee for Medicinal Products for Veterinary Use
- Committee for Orphan Medicinal Products
- Committee on Herbal Medicinal Products
- Committee for Advanced Therapies
- Paediatric Committee

Heads of Medicines Agencies

The Heads of Medicines Agencies (HMA) is a forum of the heads of the NCAs, the agencies responsible for the regulation of medicines for human and veterinary use in the EEA. The HMA co-operates with the EMA and the European Commission in order to ensure the efficient and effective operation of the European Medicines Regulatory network. The HMA meets four times a year to address key strategic issues for the network, such as the exchange of information, IT developments and sharing of best practices, and to ensure the efficient operation of the mutual recognition and decentralised procedures.

Guidelines and scientific advice

The EMA prepares scientific guidelines in cooperation with experts from its scientific committees and working groups. These guidelines reflect the latest thinking on scientific developments. They are available to all medicines developers globally who wish to submit an application for a marketing authorisation in the EU to guide them in their development programs and to ensure that medicines development is conducted consistently and to the highest quality across the EU.

The EMA also gives scientific advice to companies involved in the development of medicines. Scientific advice is an important tool used by the EMA to facilitate the development and availability of high-quality, effective and safe medicines, for the benefit of patients. Scientific advice can also be given by NCAs.

Authorisation and supervision of manufacturers

Manufacturers, importers and distributors of medicines in the EU must be licensed before they can carry out this activity. The regulatory authorities of each Member State are responsible for granting a license within their respective territories. This includes medicines produced solely for export. All manufacturing and importing licenses are entered into EudraGMDP, the publicly-available European database operated by the EMA.

All manufacturers listed in the application dossier of a medicine authorised for market in the EU are regularly inspected by an EU competent authority, irrespective of whether they are located in the EU or in a country outside the EU. Inspection outcomes are available to all Member States and are made publicly available across the EU through EudraGMDP.

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 GMP is at least equivalent to the recognised EU standards.

All batches of medicines released onto the market in the EU must be certified both for quality and GMP compliance. If the product is manufactured outside the EU and has been imported, in order to be certified it needs to undergo a full re-test in the EU, unless a mutual recognition agreement is in place. Once the batch is certified it can move freely within the entire EU territory.

Equivalence between inspectorates is ensured and maintained in a variety of ways, including common legislation, common GMP, common procedures for inspectorates, technical support, meetings, trainings, internal and external audits.

Safety monitoring of medicines

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

The 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 the total number of individual suspected-side-effect reports submitted to EudraVigilance.

The 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, patients and healthcare professionals in all Member States are given the same guidance by the committee and the same regulatory action is taken across the EU.

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 post-marketing benefit-risk assessment for medicines.

Clinical trials

The authorisation and oversight of a clinical trial is the responsibility of the Member State where the trial is taking place. Each trial must be approved by the Member State where the protocol was submitted. 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 protocol- and results-related information on clinical trials. A subset of this information is publicly available in the EU clinical trials register.

International cooperation

The European Commission and the 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 EMA works with the World Health Organization (WHO) on a range of issues, including medicines intended for markets outside the European Union ('Article 58' medicines), the quality of medicines and the development of international non-proprietary names.

One of the EU's main forums for multilateral international cooperation is the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) which brings together the drug regulatory authorities and pharmaceutical industry of Europe, Japan and the United States. ICH is dedicated to harmonisation in safety, quality and efficacy as the main criteria for approving and authorising new medicines. The International Conference on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) is the equivalent forum for veterinary medicines.

Regulatory cooperation and exchange of information with international regulators is assured through the International Pharmaceutical Regulators Forum.

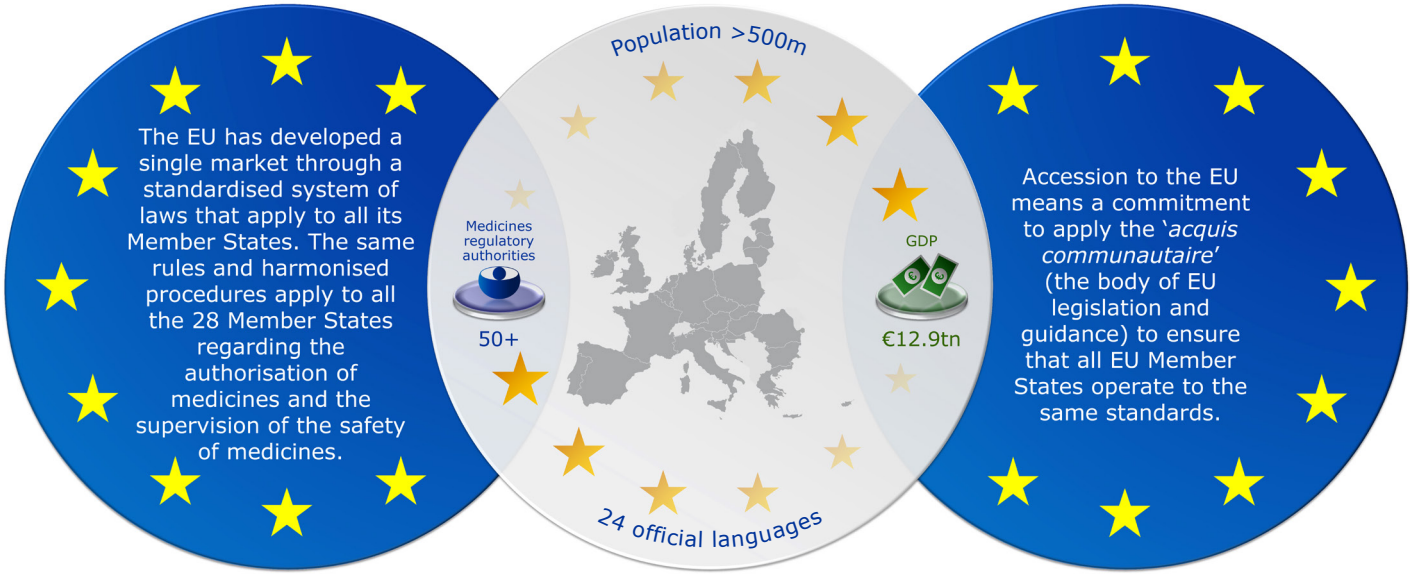
There are also bilateral confidentiality agreements in place that facilitate the exchange of important information on medicines between regulators inside and outside the EU.

Supporting regulators outside the EU - the Article 58 procedure

The CHMP can carry out scientific assessments and give opinions, in co-operation with the WHO, on medicines for human use that are intended exclusively for use outside the EU. When assessing these medicines, the CHMP applies the same rigorous standards as for medicines intended for patients in the EU. Medicines eligible for this procedure, which is derived from Article 58 of the Agency's founding regulation, are used to prevent or treat diseases of major public health interest. 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.

The European Union – key facts

The European Union (EU) operates through a system of supranational independent institutions and intergovernmental negotiated decisions by EU Member States. The EU is a legal entity and can negotiate international agreements on behalf of the Member States.



EU Member States: 28

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

Useful web addresses

European Commission – Health and Consumers Directorate General: http://ec.europa.eu/dgs/health_consumer/index_en.htm

European Medicines Agency: www.ema.europa.eu

Heads of Medicines Agencies: http://www.hma.eu/

European database of suspected drug reaction reports: www.adrreports.eu

EudraCT: https://eudract.ema.europa.eu/

EudraGMDP: http://eudragmdp.ema.europa.eu

EU Clinical Trials: http://ec.europa.eu/health/human-use/clinical-trials/index_en.htm

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