

European Medicines Agency A look at its activities and the way ahead

SUMMARY

The European Medicines Agency (EMA) is a decentralised agency of the EU. Its mission is to foster scientific excellence in the evaluation and supervision of medicines in the Member States of the EU and the European Economic Area.

The EMA began operating in London in 1995. In the context of the United Kingdom's withdrawal from the EU (Brexit), the EMA will have to move to another location that will be decided upon by common agreement among the remaining 27 Member States (EU-27). The criteria and the decision-making process for selecting the new location were announced on 22 June 2017. Interested Member States have until 31 July 2017 to submit their offers. A decision is expected to be taken in November 2017.

The EMA is governed by a management board and employs 897 staff (December 2016 figures). Its executive director is Guido Rasi. Around 89 % of the agency's budget comes from fees and charges levied for services rendered. Its scientific work is conducted in its scientific committees, working parties and other groups. Its main activities include: facilitating the development of and patient access to medicines; evaluating applications for marketing authorisations; monitoring the safety of medicines throughout their use in healthcare practice; and providing information to healthcare professionals, patients and the public.



In this briefing:

- Legal role and mission
- Funding and structure
- Main activities
- Relocation in the wake of Brexit
- Stakeholder views
- Main references

Glossary

Advanced-therapy medicinal product (ATMP): A medicine for human use that is based on genes or cells. ATMPs can be classified into four main groups: gene therapy medicines, somatic-cell therapy medicines, tissue-engineered medicines and combined ATMPs.

Orphan medicine: A medicine for the diagnosis, prevention or treatment of diseases that are rare (affecting not more than five in 10 000 people in the EU), or for which the medicine is unlikely to generate sufficient profit to justify research and development costs.

Pharmacovigilance: Activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problems. Also referred to as safety-monitoring of medicines.

Randomised controlled (clinical) trial: A study in which a number of similar people are randomly assigned to two or more groups to test a specific medicine, treatment or other intervention. One group (the 'experimental group') has the intervention being tested, the other (the 'comparison group' or 'control group') has an alternative intervention, a dummy intervention ('placebo') or no intervention at all. The groups are followed up to see how effective the experimental intervention was.

Real-world data: An umbrella term for data regarding the effects of health interventions (such as benefit, risk and resource use) that are collected from observations of routine clinical practice, for instance from patient registries, medical records and observational studies.

Source: Adaptsmart [glossary](#), the EMA [glossary](#) and the NICE [glossary](#).

Legal role and mission

The European Medicines Agency (EMA) is a decentralised agency of the EU. It was established on the basis of [Council Regulation \(EEC\) No 2309/93](#) and began operating in London in 1995 as the European Agency for the Evaluation of Medicinal Products (EMEA). [Regulation \(EC\) 726/2004](#) introduced the centralised authorisation procedure (see 'Background' box, below) and changed the name of the agency to 'European Medicines Agency'. The EMA's [mission](#) is 'to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health' in the Member States of the EU and the European Economic Area (EEA),¹ by ensuring that all medicines available on the European market are safe, effective and of high quality.² To fulfil its mission, the EMA works closely with the medicines regulatory authorities in the Member States (the 'national competent authorities') in a partnership known as the European medicines regulatory network.

EMA fees

The EMA charges fees for its services. This includes fees for processing applications for marketing authorisation and for scientific advice, as well as annual fees for authorised medicines. The applicable rules are laid down in the Fee Regulation ([Council Regulation \(EC\) No 297/95](#)) and the Pharmacovigilance Fee Regulation ([Regulation \(EU\) No 658/2014](#)). The national competent authorities in the EU Member States receive a share of the EMA's revenue for the work they carry out on behalf of the agency. In 2016, this share amounted to [€114.5 million](#).

Funding and structure

Management board and executive director

The EMA is governed by a management board that has a supervisory role with responsibility for budgetary and planning matters (including rule-making authority for implementation of certain parts of the Fee Regulation), the appointment of the executive director and the monitoring of the EMA's performance. The board is made up of [36 members](#): one representative of each of the 28 EU Member States; two representatives of the European Commission; two representatives of the European

Parliament; two representatives of patients' organisations; and one representative of doctors' and veterinarians' organisations, respectively. Moreover, the board has one observer each from Iceland, Liechtenstein and Norway. The executive director is the legal representative of the EMA in charge of operational matters, staffing issues and for drawing up the annual work programme (see the [2017 work programme](#)). The current director is Guido Rasi, who began his second five-year term on 16 November 2015.

Resources

In 2016, the EMA's [budget](#) was €308.4 million. In 2017, total appropriations amount to €322.1 million. Approximately 89 % of the budget comes from fees and charges (see EMA fees box) levied on companies for services rendered, 5 % from the EU contribution for public health and 7 % from other sources. EMA staff (see the [organisation chart](#)) support the executive director in administrative and procedural aspects related to the evaluation and pharmacovigilance of medicines. As at December 2016, there were [897](#) staff.

Scientific committees and the European medicines regulatory network

The EMA's scientific work is conducted in its [scientific committees](#), working parties and other groups. There are seven scientific committees: (1) the Committee for Medicinal Products for Human Use (CHMP), responsible for medicines for human use ('human medicines'); (2) the Pharmacovigilance Risk Assessment Committee (PRAC), for assessing and monitoring the safety of human medicines; (3) the Committee for Medicinal Products for Veterinary Use (CVMP); (4) the Committee for Orphan Medicinal Products (COMP), for applications for the designation of orphan medicines; (5) the Committee on Herbal Medicinal Products (HMPC), for compiling and assessing scientific data on herbal substances, preparations and combinations; (6) the Committee for Advanced Therapies (CAT), for assessing ATMPs and following scientific developments in the field; and (7) the Paediatric Committee (PDCO), for medicines for children ('paediatric medicines').

In addition, there are 34 working parties and other groups that the scientific committees can consult. Together, they form a pool of over 4 500 [European experts](#) made available by the 50 national competent authorities of the EU/EEA Member States as part of their collaboration with the EMA and the Commission in the European medicines regulatory network. The EMA requires these experts to sign a declaration of interests each year, to ensure that they do not have financial or other interests in the pharmaceutical industry that could affect their impartiality.

Patients, healthcare professionals and academia

Patients and healthcare professionals are increasingly participating in the EMA's activities. A two-year [pilot project](#) on involving patients in the assessment of the benefits and risks of medicines has found this to be positive for both patients and regulators. In March 2017, the EMA adopted a [framework](#) and an [action plan](#) to reinforce collaboration with the academic community, which have received broad support.

Heads of Medicines Agencies

The Heads of Medicines Agencies ([HMA](#)) is a network of the heads of the national competent authorities in the EU/EEA, which is supported by working groups and a permanent secretariat. The HMA cooperates with the EMA and the Commission in the European medicines regulatory network and address [strategic issues](#) for the network, such as the exchange of information, IT developments and best practices, as well as the streamlining of the mutual recognition and decentralised procedures (see 'Background' box).

Main activities

Facilitating the development of and patient access to medicines

The EMA uses the regulatory mechanisms offered by the [EU pharmaceutical legislation](#) to facilitate the medicines development process from an [early stage](#) and to provide patients with timely access to new medicines. To do so, it makes use of tools, such as: **accelerated assessment**, which reduces the time for reviewing applications for marketing authorisation with regard to medicines of major public health interest; **conditional marketing authorisation**, which involves the early approval of a medicine based on less complete clinical data than are normally required; and **compassionate use**, which allows the use of an unauthorised medicine for patients with unmet medical needs (health conditions that are not adequately addressed by existing treatments).

Moreover, the EMA provides scientific advice and protocol assistance to pharmaceutical companies on the appropriate tests and studies required in the development of a medicine. The EMA considers 'early dialogue' as one of its key instruments for supporting the development of high-quality, effective and safe medicines that meet patients' needs.³ In consultation with the national competent authorities, the EMA also prepares [scientific guidelines](#) to help companies prepare applications for marketing authorisation. Besides, the EMA fosters pharmaceutical research and innovation and provides regulatory, financial and administrative assistance to micro, small and medium-sized enterprises (SMEs) through its SME office (see the 2017 [SME Office annual report](#) and [action plan](#)).

Evaluating applications for marketing authorisation

The EMA's scientific committees carry out assessments of applications for marketing authorisation to determine whether a medicine meets the necessary quality, safety and efficacy requirements and has a positive benefit-risk balance (that is, whether the benefits outweigh the risks). The assessments result in recommendations that form the basis of the Commission's decision on a marketing authorisation throughout the EU/EEA.

Background: Regulatory routes for the authorisation of medicines in the EU/EEA

Under the **centralised procedure** run by the EMA, a pharmaceutical company submits a single application to the EMA to request marketing authorisation for their product. The EMA's competent scientific committee (for human medicines, this is the CHMP) assesses the application and subsequently gives a recommendation (an 'opinion') on whether the medicine should be authorised. This opinion is forwarded to the Commission, which is responsible for issuing the decision on granting marketing authorisation. The centralised procedure is **compulsory** for medicines containing a new active substance to treat the human immunodeficiency virus (HIV) or the acquired immune-deficiency syndrome (AIDS); cancer; diabetes; neurodegenerative diseases; auto-immune and other immune dysfunctions; viral diseases; medicines derived from biotechnology processes, such as genetic engineering; ATMPs; and orphan medicines. It is **optional** for other medicines that contain new active substances for indications other than those mentioned above; that constitute a significant therapeutic, scientific or technical innovation; and the authorisation of which would be in the interest of public health at European level. The majority of **new, innovative medicines** pass through the centralised procedure. The **decentralised** and the **mutual-recognition procedures** are run by the Heads of Medicines Agencies. If a company wishes to request marketing authorisation in several Member States for a medicine that is outside the scope of the centralised procedure, it may use the **decentralised procedure**, with which a medicine that has not yet been authorised in the EU/EEA can be authorised in several Member States simultaneously, or the **mutual-recognition procedure**, whereby a marketing authorisation granted in one Member State can be recognised in others. These procedures are used for the majority of **established products** and **for generics**.

Monitoring the safety of medicines throughout their use in healthcare practice

EU legislation requires marketing authorisation holders, national competent authorities and the EMA to operate a [pharmacovigilance system](#) for authorised medicines. The EMA's main responsibilities in relation to pharmacovigilance include coordinating the European pharmacovigilance system, informing the public on the safe and effective use of medicines, and maintaining [EudraVigilance](#), a repository for reports of suspected adverse reactions to medicines that have been authorised (or are being studied in clinical trials) in the EU/EEA.

Providing information to healthcare professionals, patients and the public

The minimum level of transparency on how the EMA works is set by EU legislation. The agency points out that in many areas, it has decided to go beyond what is required so as to provide as much information to the public as possible. The main types of information published [at various stages](#) of the marketing-authorisation process comprise a summary of the opinion issued by the CHMP at the end of the evaluation process and a European public assessment report (EPAR) ([searchable](#)), once the Commission has issued a decision on the granting (or refusal) of a marketing authorisation. The EPAR is a set of documents consisting of an easy-to-read summary for the public, the CHMP assessment report and the approved product information. The latter contains the summary of product characteristics (that is, a document that describes the properties and the approved conditions of use of a medicine), the labelling for the medicine's outer packaging and the text of the package leaflet. After authorisation, the EPAR for each medicine on the market is updated.

Information on suspected side effects is provided in the [European database of suspected adverse drug reaction reports](#), in which the EMA publishes data from EudraVigilance. Information on clinical trials is accessible in the [EU Clinical Trials Register](#), which allows the public to search information held in the European Clinical Trials Database ([EudraCT](#)), the application used by national competent authorities to enter clinical trial data. Moreover, the EMA has started publishing the clinical-trial data submitted by pharmaceutical companies in support of their applications for marketing authorisation on the [clinical data website](#). According to the agency, this initiative will, inter alia, provide regulators with a more robust evidence base for decision-making.

Initiatives affording patients early access to medicines

Adaptive pathways is a scientific concept of medicines development and data generation for medicines that address patients' unmet medical needs. Under this iterative approach, a medicine will initially be authorised in a small group of patients likely to benefit the most. Then, as additional evidence (real-world data rather than data from randomised clinical trials) is gathered on a product, its use is expanded to a wider patient population. Between 2014 and 2016, the EMA conducted a pilot project on adaptive pathways, for which it received 62 applications. These covered a wide range of therapeutic areas, with medicines for treating cancer accounting for a third of submissions. The [final report](#) found that adaptive pathways can support medicines development in areas of high unmet medical need, and could foster innovation where research is lagging, as in the case of Alzheimer's disease and rare cancers. It is still a concept in development to be fine-tuned.

PRIME (PRiority MEDicines) is a voluntary scheme, [launched in May 2016](#), to reinforce early dialogue and regulatory support to medicine developers both in the pharmaceutical industry and the academic sector. It aims to stimulate innovation, optimise development and enable accelerated assessment of medicines that target unmet medical needs and have the potential to bring a major therapeutic advantage to patients ('promising medicines'). Between April 2016 and April 2017, 96 requests were processed, of which 20 were granted (12 of them for ATMPs). PRIME mainly targets medicines for treating cancer and blood disorders.

Implementing EU Telematics

The EMA is also responsible for the implementation of the [EU Telematics](#) programme, a joint endeavour of the EU regulatory network that aims to maintain common information-technology (IT) services in the context of European pharmaceutical policy and legislation. EU Telematics is made up of systems such as EudraCT; [EudraGMDP](#), which supports the exchange of information on good manufacturing compliance and on manufacturing and import authorisations; EudraLink, a secure file-transfer system for exchanging regulatory information; EudraNet, a network linking the members of the European medicines network and the EMA; the database of authorised medicines [EudraPharm](#),⁴ which includes the EU Clinical Trials Register; and EudraVigilance.

Relocation in the wake of Brexit

In the context of the United Kingdom's withdrawal from the EU (Brexit), the EMA will have to move its headquarters. The future location will be decided by common agreement among the remaining 27 Member States (EU-27).

Applicable criteria and decision regarding the relocation

European Council President, Donald Tusk, and Commission President, Jean-Claude Juncker, have suggested a specific procedure for deciding on the relocation of the EMA.⁵ The procedural arrangement was discussed on the margins of the General Affairs Council ([Article 50](#)) and endorsed by the EU-27 Heads of State and Government on the margins of the European Council (Article 50) on 22 June 2017. As outlined in the [European Council document](#), the resulting procedure consists of a call for offers from the EU-27, based on 'specified objective criteria'. Member States have until **31 July 2017** to submit their bids for hosting the EMA. The Commission will then examine the offers on the basis of the 'stipulated unweighted criteria' and convey its assessment to the Secretary-General of the Council of the EU by **30 September 2017**. This assessment will inform political discussions in the autumn. The decision on the relocation will be taken by the EU-27 leaders by vote, following a specific process. The vote is expected to be held on the margins of the General Affairs Council (Article 50) meeting of 15 November 2017.

Figure 1 – 4-step procedure with timeline for the decision on relocating the EMA



Source: [Council](#) of the European Union, General Secretariat, 2017.

According to the European Council document, the criteria for the EMA's relocation are based by analogy on those set out in point 6 of the [Joint Statement and Common Approach on Decentralised Agencies](#), with special regard to the fact that the agency

already exists and that its business continuity 'is vital and must be ensured'. The six applicable criteria laid down are: (1) the assurance that the agency can be set up on-site and take up its functions at the date of the UK's withdrawal from the EU; (2) the accessibility of the location, including flight connections; (3) the existence of adequate education facilities for the staff's children (648 children aged up to 18 were schooled as of September 2016); (4) appropriate access to the labour market, social security and medical care for both children and spouses; (5) business continuity; and (6) geographical spread.

EMA preparedness

In its assessment of the [potential risks](#) associated with Brexit, the EMA has identified two specific issues, among others: the loss of existing staff since some may not be willing to relocate, as well as the inability to recruit new staff; and the loss of UK expertise in the scientific work, given that UK experts constitute 15 % of the agency's expert base and conduct around 20 % of scientific work. To mitigate this gap, the EMA has established a [working group](#) tasked with exploring options for a (re-)distribution of workload, including broadening the concept of [multinational assessment teams](#). Discussions between the EMA and the heads of the national competent authorities on 28 April 2017 resulted in the establishment of [principles for workload distribution](#), which include: ensuring business continuity; maintaining the quality and robustness of the scientific assessment; continuing to comply with legal timelines; ensuring knowledge retention; and assuring easy implementation and medium- and long-term sustainability. On 31 May 2017, the EMA published jointly with the Commission a list of [Questions and Answers](#) for pharmaceutical companies to help them prepare for Brexit. It follows the publication of a [notice](#) on 2 May 2017 and is to be further complemented in the near future.

Stakeholder views

The debate will be illustrated by two topics that have recently attracted attention: **adaptive pathways and PRIME** (approaches to facilitating early patient access). Some stakeholders have expressed concerns about the impact **adaptive pathways** may have on the standards of evidence for the approval of medicines in the EU/EEA. In its [position paper](#), the European Consumer Organisation (BEUC) [reiterated its concerns](#) on what it refers to as 'sidestepping the standard benefit-risk assessment for licensing a medicine'. [Healthcare payers](#) have expressed the need for further scrutiny of the scope and necessity of schemes such as adaptive pathways, which in their view put high demands on their community. A December 2016 EMA stakeholder [workshop](#) on the issue found that there remains confusion as to what the concept is and how it is to be applied in practice. There is also discussion on the need for a clear definition of 'unmet medical needs'. Some stakeholders support the concept for its potential to improve patients' access to new medicines. As a [health commentator](#) put it, advocates would argue that 'a confident regulatory system should be able to understand that early access implies no automatic lowering of evidentiary standards'. The pharmaceutical industry has been broadly supportive of the concept, although it reportedly wants more details on real-world data standards. **PRIME** has also been [generally well received](#) by the industry. A Federation of Pharmaceutical Industries and Associations (EFPIA) commentator called it 'a [welcome step](#) towards connecting healthcare decision-makers to expedite patient access to new medicines'. Another is said to have argued that PRIME would [meet its objectives more successfully](#), provided its scientific advice covered both clinical development and topics relating to production processes. [Comments](#) from a public consultation highlighted, inter alia, the need for greater transparency of the oversight of the scheme.

On **relocation**, the Pharmaceutical Industry Heads of Research and EFPIA pleaded in an [open letter](#) for 'world class connectivity' as a fundamental requirement for the new location, as well as for the focus to be put on retaining highly competent staff so that the system continues to function with the same level of efficiency. For EFPIA, [regulatory continuity](#) across Europe is essential. Referring to the outcome of the European Council meeting of 22 June 2017, EFPIA has also expressed [concern at the postponement](#) of the relocation decision until November, stating that priority be given to 'ending the uncertainty' over the location. In an [open letter](#), BEUC, the European Patients' Forum (EPF) and EURORDIS-Rare Diseases Europe have stressed that the decision on the future relocation is critical and should be taken as soon as possible to ensure minimal disruption and no delays that would have negative consequences for the lives of EU citizens and patients. From their perspective, prerequisites for the EMA's future location include a focus on flights, ground transportation and accessible hotel accommodation.

European Parliament's view on adaptive pathways and relocation

In its [decision](#) of 27 April 2017 to grant discharge as regards the implementation of the EMA's budget for 2015, Parliament indicated that the adaptive pathways pilot 'raises numerous public health concerns and undermines the core mission of the Agency' of ensuring safety of medicines. Regarding relocation, it noted that the EMA's rental contract until 2039 does not include an early-termination clause and that the rental cost from 2017 to 2039 would be €347.6 million.⁶

Main references

EMA, [About us](#), February 2017.

EMA, [Annual Report 2016](#).

Endnotes

- ¹ Iceland, Liechtenstein and Norway.
- ² This briefing focuses only on the EMA's activities in relation to medicines for human use.
- ³ The EMA has started to routinely offer 'parallel scientific advice' together with health technology assessment (HTA) bodies. Parallel scientific advice means that companies receive feedback from regulators and HTA bodies simultaneously. According to the EMA, this fosters a more rational approach that will ultimately improve patient access to new medicines. (See also an [EPRS briefing](#) on HTA.)
- ⁴ The EMA [envisions](#) a larger European medicines web portal providing free access to multilingual, reliable and unbiased information on all medicines authorised in the EU. It would replace EudraPharm and also incorporate the EU Clinical Trials Register and the European database of suspected adverse drug reaction reports, as well as the new clinical data website.
- ⁵ This also applies to the European Banking Authority (EBA) – the other agency currently situated in London.
- ⁶ In a [written question](#) of 2 June 2017, the Commission was asked to specify, inter alia, the expected relocation costs.

Disclaimer and Copyright

The content of this document is the sole responsibility of the author and any opinions expressed therein do not necessarily represent the official position of the European Parliament. It is addressed to the Members and staff of the EP for their parliamentary work. Reproduction and translation for non-commercial purposes are authorised, provided the source is acknowledged and the European Parliament is given prior notice and sent a copy.

© European Union, 2017.

Photo credits: © Lydie / Fotolia.

eprs@ep.europa.eu

<http://www.eprs.ep.parl.union.eu> (intranet)

<http://www.europarl.europa.eu/thinktank> (internet)

<http://epthinktank.eu> (blog)

