EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Scientific advice and protocol assistance

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The European Medicines Agency (EMA) can provide medicine developers advice on the most appropriate way to generate robust evidence on a medicine's benefits and risks. EMA provides

scientific advice to support the timely and sound development of high-quality, effective and safe medicines, for the benefit of patients.

At any stage of a medicine's development, a developer can ask guidance and direction from EMA on the best methods and study designs to generate robust information on how well a medicine works and how safe it is, regardless of whether the medicine is eligible for the centralised authorisation procedure or not.

Scientific advice helps to ensure that developers perform the **appropriate tests and studies**, so that no major objections regarding the design of the tests are likely to be raised during the evaluation of the marketing authorisation application. This also helps avoid patients taking part in studies that will not produce useful evidence.

For human medicines, scientific advice and protocol assistance are given by the Committee for Medicinal Products for Human Use (CHMP) on the recommendation of the Scientific Advice Working Party (SAWP).

For information on how to request scientific advice from EMA, see Requesting scientific advice or protocol assistance from EMA.

EMA is currently experiencing some delays in processing scientific advice requests.

This is due to a higher than expected increase in demand for scientific advice, which is partly related to the COVID-19 pandemic.

EMA is putting in place measures to mitigate these delays and is liaising closely with the companies concerned.

Applicants can contact EMA for more information on expected timelines before submitting a request, by writing to scientificadvice@ema.europa.eu.

How scientific advice works

EMA gives scientific advice by **responding to specific questions** posed by the medicine developer on the development of a particular medicine.

The developer of a medicine presents the way it plans to develop its medicine and identifies questions and possible solutions. EMA then gives advice on the developer's proposals.

Scientific advice is prospective in nature. EMA **does not pre-evaluate** the results of the studies and in no way concludes on whether the benefits of the medicine outweigh the risks.

Scientific advice from EMA is not legally binding on EMA or on the medicine developer with regard to any future marketing authorisation applications for the medicine concerned.

When scientific advice is most useful

Scientific advice and protocol assistance are particularly useful to medicine developers when:

- they are developing an **innovative medicine** and there appears to be no or insufficient relevant detail in EU guidelines or guidance documents, or in Pharmacopoeia monographs, including draft documents or monographs released for consultation;
- they are developing new or repurposed medicines targeting (re)emerging pathogens for which there is an **unmet medical need** but insufficient or no guidance is available;
- the developer chooses to **deviate from scientific guidelines** in its development plan;
- the medicine developer has **limited knowledge** about medicine regulation, such as some academic groups or micro, small and medium sized enterprises (SMEs).

Medicine developers can request scientific advice or protocol assistance either during the **initial development** of a medicine before submission of a marketing authorisation application or later on, during the **post-authorisation phase**.

Types of questions addressed

Questions during scientific advice can relate to:

- quality aspects (manufacturing, chemical, pharmaceutical and biological testing of the medicine);
- non-clinical aspects (toxicological and pharmacological tests designed to show the activity of the medicine in the laboratory);
- clinical aspects (appropriateness of studies in patients or healthy volunteers, selection of endpoints, i.e. how best to measure effects in a study, post-authorisation activities including riskmanagement plans);
- methodological issues (statistical tests to use, data analysis, modelling and simulation).

Examples of questions

- Are the patients to be included in a study sufficiently representative of the population for whom the medicine is intended?
- Are the planned measures to assess the benefits of a medicine valid and relevant?
- Is the proposed plan to analyse results appropriate?
- Does the study last long enough and include enough patients to provide the necessary data for the benefit-risk assessment?
- Is the medicine being compared with an appropriate alternative?
- Are the plans to follow the long-term safety of the product appropriately designed?

Protocol assistance

Protocol assistance is the special form of scientific advice available for developers of designated orphan medicines for rare diseases.

In addition to scientific advice, developers of orphan medicines can receive answers to questions relating to the criteria for authorisation of an orphan medicine. These include:

- the demonstration of significant benefit within the scope of the designated orphan indication;
- similarity or clinical superiority over other medicines. This is relevant if other orphan medicinal products exist that might be similar to the product concerned and which have market exclusivity in the same indication.

Scientific advice on medicine repurposing

Through a pilot project, EMA and national competent authorities can offer tailored scientific advice to **not-for-profit organisations** and **academics** (institutions and individuals) on repurposing an authorised medicine for a new indication.

The aim is to help gather or generate enough evidence to support a new indication with **important public health benefits** for a medicine whose marketing authorisation holder is otherwise unlikely to undertake the necessary research and regulatory steps.

This provides a way of making new treatment options available to patients if it leads to the authorisation of the new indication.

Scientific advice **fees are waived** automatically for eligible academic sponsors repurposing a medicine for an orphan condition. Fees will also be waived for a subset of other applicants based on the expected public health benefits and strength of the evidence in their application.

The deadline to apply was 28 February 2022

More information including **eligibility criteria** is available in the documents below.

Question and Answers on repurposing pilot project on proposal for framework to support not-for-profit

organisations and academia in repurposing authorised medicines (PDF/333.43 KB)

First published: 28/10/2021
Last updated: 04/02/2022

Submission form - Repurposing pilot project for authorised medicines (DOCX/137.24 KB)

First published: 28/10/2021
Last updated: 20/01/2022

Scientific advice on post-authorisation safety studies (PASS)

EMA encourages medicine developers to seek scientific advice for PASS protocols. This voluntary, optional procedure will help to improve the design of studies meant to collect further information on a medicine's safety once it is on the market.

EMA ran a 12-month pilot for this procedure between July 2015-2016.

For more information, see:

- Question on 'Scientific advice for safety studies' on our page Post-authorisation safety studies: questions and answers.

Parallel scientific advice with the United States

The Agency provides scientific advice and protocol assistance in parallel with the United States Food and Drug Administration (FDA).

General principles: European Medicines Agency-Food and Drug Administration parallel scientific advice (PDF/150.31 KB)

First published: 22/07/2009
Last updated: 18/08/2021

Timeline: European Medicines Agency-FDA parallel scientific advice (PDF/73.96 KB)

First published: 19/05/2017
Last updated: 19/05/2017

EMA and FDA launched a pilot programme in September 2021 to provide parallel scientific advice to marketing authorisation applicants for **hybrid** or **complex generic** products. More information is available in the documents below:

Pilot programme: European Medicines Agency-Food and Drug Administration parallel scientific advice for hybrid/complex generic products - General principles (PDF/865.41 KB)

First published: 15/09/2021

For more information on EMA's cooperation with FDA:

- United States

Parallel consultations from regulators and HTA bodies

EMA offers consultations in parallel with European Network for Health Technology Assessment (EUnetHTA) as of July 2017. This aims to allow medicine developers to obtain feedback from regulators and HTA bodies on their evidence-generation plans to support decision-making on marketing authorisation and reimbursement of new medicines at the same time.

The procedure is a **single gateway for parallel consultations** with EMA, EUnetHTA and HTA bodies on their evidence-generation plans.

Consultations can take place before or after the product is made available on the market. The objective is to help generate **optimal and robust evidence** that satisfies the needs of both regulators and HTA bodies.

This initiative **replaces the parallel scientific advice procedure** by EMA and HTA bodies which required medicine developers to contact Member States' HTA bodies individually.

For more information, see Parallel consultation with regulators and health technology assessment bodies.

Scientific advice on biosimilars

EMA offers tailored scientific advice on development programmes of new **biosimiliar medicines**.

The tailored procedure advises developers on the studies they should conduct, based on a **review of the quality, analytical and functional data** they already have available.

The tailored scientific advice procedure is open to **all types of biosimilars** and companies are encouraged to request a pre-submission meeting to review the suitability of the data package. Applicants should note that the SAWP will need an extra month in addition to normal scientific advice timelines to review applications.

EMA first introduced the tailored procedure as a pilot project in 2017. A report on the pilot phase is available below.

Tailored Scientific advice to support step-by-step development of new biosimilars (PDF/103.56 KB)

First published: 16/12/2016
Last updated: 14/10/2021
EMA/289230/2021

Tailored Scientific Advice for biosimilar development: report on the experience from the pilot (2017-2020) (PDF/168.38 KB)

First published: 14/10/2021
EMA/297462/2021

Fees and fee reductions

EMA charges a fee for scientific advice, which varies depending on the scope of the advice.

Reductions apply for certain types of medicines and applicants, including a 75% fee reduction for medicines for **orphan medicines** and a 90% fee reduction for **SMEs**.

A **full waiver** applies by default to scientific advice applications on clinical trials and clinical trials protocols for medicines intended to treat, prevent or diagnose a declared **public health emergency**.

Applicants from the academic sector are eligible to receive free protocol assistance for developing orphan medicines as of 19 June 2020. For more information see Academia and Fees payable to the European Medicines Agency.

For more information on fees for scientific advice and protocol assistance, see Fees payable to the European Medicines Agency.

Medicines intended for a disease causing public health emergency (new)

EMA has a dedicated Emergency Task Force (ETF) to support its Committee for Medicinal Products for Human Use (CHMP) in providing scientific advice for **new** or **repurposed human medicines** that are intended to treat, prevent or diagnose a disease causing a declared **public health emergency**.

On a case-by-case basis, the ETF also provides advice on medicines targeting selected **pathogens** that can potentially cause a public health emergency.

EMA encourages developers of such medicines to contact the Agency early if they are interested in the following procedures:

- Early guidance on medicine development plan (when the plan is not yet suitable for formal scientific advice)
- Requesting scientific advice
- Applying for a marketing authorisation

They can contact EMA by writing to pheearlyinteractions@ema.europa.eu.

Early contact is particularly important during a declared public health emergency.

When submitting a request for scientific advice, developers should indicate in their application form in which Member State(s) they intend to run clinical trials. The ETF requires this information because it involves clinical trial experts from these Member State(s) in preparing the scientific advice, in order to facilitate approval of the trial later in the process.

Scientific advice on the clinical aspects of medicine development or on clinical trials protocols is **free of charge** for medicines intended for a disease causing public health emergency.

The procedure generally follows an **accelerated timetable.**

This includes COVID-19 medicines, which follow the same rules. For more information, see Free rapid scientific advice for COVID-19 treatments or vaccines.

For queries on technical aspects related to the scientific advice procedure, applicants should write to scientificadvice@ema.europa.eu.

For information on facilitating clinical trials, see COVID-19 guidance: Research and development: Clinical trials for COVID-19 medicines.

Free rapid scientific advice for COVID-19 treatments or vaccines

Since 2020, EMA has applied a **rapid scientific advice procedure** for potential COVID-19 treatments and vaccines, which is **free of charge** and **accelerated where possible**.

The rapid procedure reduces review time to a **maximum of 20 days** (from 40-70 days), with **no pre-specified submission deadlines.** The scientific advice is provided by the CHMP based on the recommendation of the Emergency Task Force (ETF).

In addition, **flexibility** can be agreed on a case-by-case basis on the type and extent of the briefing dossier.

These aspects are in line with the Regulation on EMA's Reinforced Role (Regulation (EU) 2022/123) .

EMA encourages developers interested in requesting rapid scientific advice to **contact EMA as soon as possible,** to discuss their strategy for evidence-generation.

They should email their proposals to pheearlyinteractions@ema.europa.eu or 2019-ncov@ema.europa.eu.

EMA and the ETF can provide **early guidance** to developers whose development plan is not yet suitable for formal rapid scientific advice.

The ETF can also support clinical trial **sponsors** with certain aspects of running a clinical trial.

For this type of support please contact EMA via the phesupportCT@ema.europa.eu.

More information:

- Scientific advice and protocol assistance: Medicines intended for a disease causing public health emergency
- Guidance for medicine developers and companies on COVID-19: Accelerated procedures for COVID-19 treatments and vaccines
- EMA initiatives for acceleration of development support and evaluation procedures for COVID-19 treatments and vaccines
- Decision of the Executive Director on fee reductions for scientific advice requests on products for the prevention and/or treatment of COVID-19

Why following scientific advice does not guarantee marketing authorisation

Scientific advice and the assessment of the benefits and risks of a medicine are different by nature.

Scientific advice looks at **how a medicine should be tested** in studies to generate robust evidence, while the assessment at the time of marketing authorisation looks at the evidence generated to determine **whether the medicine's benefits outweigh its risks**, regardless of any advice previously given.

Scientific advice can make the evaluation of a medicine easier and quicker because the evidence is likely to be more robust, appropriate and complete, but it **does not affect the stringent assessment of safety and efficacy**.

Complying with scientific advice therefore increases the chances of receiving marketing authorisation but it does not guarantee it.

What EMA publishes on outcomes of scientific advice

During the development and assessment phases, the detailed advice given to a medicine developer is not made public. This is because disclosing information at this stage may undermine research and development efforts and discourage research in new medicines.

However, information is made available after a medicine obtains marketing authorisation. All medicines whose assessment report was finalised after 1 January 2019 include a **summary of the developer's questions** and key elements of EMA's advice and whether or not the developer complied with this advice within the assessment report.

During a declared public health emergency, EMA publishes a list of medicines that have received informal or formal advice from the CHMP and the ETF.

In addition, the full advice can be made available upon request. For more information, see Access to documents.

Scientific advice is also one of the **main sources for updating EMA scientific guidelines** on medicine development, including, in particular, disease-specific guidelines.

More information

- How to submit a scientific advice or protocol assistance request
- Qualification of novel methodologies for medicine development
- Parallel joint scientific consultation with regulators and health technology assessment bodies
- Scientific advice and protocol assistance: Regulatory and procedural guidance

Publications

- The Added Value of Patient Engagement in Early Dialogue at EMA: Scientific Advice as a Case Study

Related documents

European Medicines Agency guidance for applicants seeking scientific advice and protocol assistance (PDF/512.19 KB)

First published: 22/01/2009
Last updated: 04/04/2022
EMA/4260/2001 Rev. 13

CHMP protocol assistance scientific advice briefing document template (DOC/92.5 KB)

First published: 18/06/2010
Last updated: 12/02/2016
Rev. 1

Dates of 2023 Scientific Advice Working Party (SAWP) meetings and submission deadlines scientific advice, protocol assistance, qualification of biomarkers and EMA/EUnetHTA parallel consultation requests (PDF/145.8 KB)

First published: 14/06/2022
EMA/569289/2019

Dates of 2022 Scientific Advice Working Party (SAWP) meetings and submission deadlines scientific advice, protocol assistance, qualification of biomarkers and EMA/EUnetHTA parallel consultation requests (PDF/191.58 KB)

First published: 01/09/2021

Last updated: 15/11/2021
EMA/569288/2019 Rev. 2

From lab to patient: journey of a medicine

Follow the journey of a medicine for human use assessed by EMA in this interactive timeline. It explains all stages from initial research to patient access, including how EMA supports medicine development, assesses the benefits and risks and monitors the safety of medicines.

The full text is available as a booklet .

Contact point

For early support, including applying scientific advice and marketing authorisation:

- 2019-ncov@ema.europa.eu or pheerlyinteractions@ema.europa.eu

For support with clinical trials:

- phesupportct@ema.europa.eu

Topics

- Scientific advice

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