



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# ANNUAL REPORT 2020

The European Medicines Agency's contribution to science, medicines and health in 2020



An agency of the European Union

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# I MISSION STATEMENT

**The mission of the European Medicines Agency is to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health.**

## Guiding principles

- We are strongly committed to public and animal health.
- We make independent recommendations based on the best scientific evidence, using state-of-the-art knowledge and expertise in our field.
- We support research and innovation to stimulate the development of better medicines.
- We value the contribution made by our partners and stakeholders to our work.
- We assure continual improvement of our processes and procedures, in accordance with recognised quality standards.
- We adhere to high standards of professional and personal integrity.
- We communicate in an open, transparent manner with all of our partners, stakeholders and colleagues.
- We promote the well-being, motivation and ongoing professional development of every member of the Agency.

## Principal activities

Working with the Member States and the European Commission (EC) as partners in a European medicines regulatory network, the European Medicines Agency (EMA):

- provides independent, science-based recommendations on the quality, safety and efficacy of medicines, and on more general issues relevant to public and animal health that involve medicines;
- applies efficient and transparent evaluation procedures to help bring new medicines to the market by means of a single, EU-wide marketing authorisation granted by the EC;
- implements measures for continuously monitoring and supervising the quality, safety and efficacy of all medicines authorised in the European Union (EU) to ensure that their benefits outweigh their risks;
- provides scientific advice and incentives to stimulate the development and improve the availability of innovative new medicines;
- recommends safe limits for residues of veterinary medicines used in food-producing animals, for the establishment of maximum residue limits by the EC;
- involves representatives of patients, healthcare professionals and other stakeholders in its work to facilitate dialogue on issues of common interest;
- publishes impartial and comprehensible information about medicines and their use;
- develops best practice for medicines evaluation and supervision in Europe, and contributes alongside the Member States and the EC to the harmonisation of regulatory standards at the international level.

### Legal role

The EMA is the EU body responsible for coordinating the existing scientific resources put at its disposal by Member States for the evaluation, supervision and pharmacovigilance of medicinal products.

The Agency provides the Member States and the EU institutions with the best-possible advice on any questions relating to the evaluation of the quality, safety and efficacy of medicinal products for human or veterinary use referred to it in accordance with the provisions of EU legislation relating to medicinal products.

# I FOREWORD

## by Christa Wirthumer-Hoche

### Chair of EMA Management Board

I am pleased to introduce EMA's annual report for 2020, a year in which the Agency was at the forefront of the largest public health emergency in modern times.

As everybody struggled with the COVID-19 pandemic around the world, the Management Board also had to get to grips with meeting in a virtual environment. We did this by adopting changes to the Board's rules of procedure so that in 2020 all our decision-making meetings with the Member States could be held virtually.

The pandemic started just as EMA was completing its relocation to the Netherlands and setting up in its new office in Amsterdam. Once again, EMA and the European medicines regulatory network worked swiftly to adapt their activities and processes to ensure a rapid response to the pandemic whilst maintaining their core activities to protect public and animal health.

The pandemic has underlined the need for rapid and close engagement of all stakeholders and partners involved in the development and supervision of medicines in the EU and globally. I am incredibly impressed by the endurance and rigour shown by all experts in the network, as well as EMA's staff and the Board, in facilitating the development and approval of COVID-19 vaccines and therapies at an unprecedented pace, without compromising on our high standards of safety, quality and efficacy.



Amid this public health crisis of unprecedented scale, there was a change at the head of EMA. Guido Rasi's mandate as EMA's Executive Director came to an end after nine years and Emer Cooke took over leadership of the Agency on 16 November 2020, following her nomination by the Board in June 2020. This change came at a time of tremendous pressure on the Agency, but thanks to their excellent cooperation, there was a seamless transition between the outgoing and the new Executive Director. The Board has full confidence that Emer will continue to lead the Agency successfully in the years to come, as we implement our network strategy to 2025, in alignment with the European Commission's pharmaceutical strategy for Europe.

On behalf of the Board, I would like to thank Guido for his remarkable leadership during an exceptionally challenging period for EMA.

We have all felt the strain of the pandemic, yet despite the immense challenges of 2020, the network and EMA have made progress in important areas. The independent audit of the future clinical trials information system began as scheduled in December 2020, with the system on track to go live, and the new EU clinical trials regulation to become applicable, in early 2022. A review of EMA's working party activities continued in 2020, with COVID-19 giving us an opportunity to reflect further on how we can serve the expertise needs of the network in an agile and sustainable way and respond to future scientific and technological challenges.

Implementation of the new veterinary regulation has progressed considerably, both in terms of new procedures and IT systems at the Agency and of delegated and implementing acts by the Commission based on the EMA's scientific opinions. We are on track to meet the legal deadline of January 2022 and, in parallel, the network has been preparing training and information materials for stakeholders to learn and adapt to the new framework.

On behalf of the Board, I wish to thank colleagues across the network, the Commission and EMA staff for all they have achieved during what was the most unusual and challenging year in EMA's history.

**March 2021**

# I INTRODUCTION

by Emer Cooke

## EMA Executive Director

2020 will be remembered as the year the COVID-19 pandemic took hold of the world, causing hardship for so many. As the scientific body in charge of the regulation of medicines, EMA had an essential part to play in ensuring treatments and vaccines would be authorised as quickly as possible to help fight this new disease, without compromising any of the EU standards for efficacy, safety and quality.

Looking back at 2020, we can be proud of how EMA and the European medicines regulatory network rose to the challenge. Just as EMA closed the chapter of its relocation and moved into its permanent headquarters in Amsterdam, the COVID-19 outbreak meant that the Agency had to shift its operations to work fully remotely and re-prioritise its plans immediately to respond to the public health need. EMA set up agile infrastructures and mobilised EU expertise to enable fast decision-making, especially through the EMA pandemic Task Force (COVID-ETF). It also launched rolling reviews as a key tool to accelerate assessments of COVID-19 vaccines and treatments.

Throughout the year, we tackled one by one the various issues presented by the pandemic. We led and coordinated EU action to prevent and mitigate shortages of medicines due to the pandemic. Our experts provided early guidance to sponsors of potential COVID-19 treatments and vaccines; they worked day and night to support fast-track approvals and prepared for effective post-marketing safety monitoring. While we did everything that was necessary to expedite our evaluation processes, we were guided by one priority: getting our recommendations right for the benefit of European citizens. With this objective in mind, we actively reached out to stakeholders and citizens to explain our work, ensured utmost transparency of our scientific assessment and conclusions, and led international collaboration efforts to streamline regulatory requirements for COVID-19 vaccines and treatments.



I took over at the helm of the Agency from my predecessor Guido Rasi on 16 November 2020, just a few weeks before EMA gave its first positive opinion for a COVID-19 vaccine. I would like to mark his tremendous contribution to shaping EMA into an organisation that was ready to support the development and approval of a vaccine against a new disease less than a year after it first emerged – a truly historic scientific achievement.

It was made possible by the extraordinary resilience of EMA staff and the tireless work behind the scenes of a high number of experts from all EU Member States. A chapter of this annual report is dedicated to EMA's response to the pandemic.

Despite the strong focus on the response to the COVID-19 pandemic, the Agency performed its core activities to the highest standards in 2020, thanks to swift and rigorous re-prioritising of activities. Altogether, EMA recommended 97 new human medicines for approval, the highest number in over 10 years. EMA continued to closely monitor the safety of medicines on the market and took action when needed to protect patients.

On the veterinary side, the Agency recommended 20 medicines for approval. The fight against antimicrobial resistance remained a priority. In addition to the annual report on the sales of veterinary antibiotics, EMA's key contribution in this area in 2020 was the publication of updated scientific advice on the categorisation of antibiotics used in people and animals. It also continued to prepare for the new EU veterinary legislation which will remain a key focus looking forward.

2020 was also the year Brexit became a reality. The meticulous preparation by EMA and the EU medicines regulatory network meant that everybody was ready to successfully transition into the new dynamic of the EU27.

In 2020, EMA celebrated its 25<sup>th</sup> anniversary. It certainly did not rest on its laurels but made sure that it was prepared for future challenges. It published its Regulatory Science Strategy to 2025, in response to the dramatic acceleration of the pace of innovation in recent years and the

need for regulators to be ready to support the development of increasingly complex human and veterinary medicines. This fed into the overarching Network Strategy to 2025, which was developed together with the Heads of Medicines Agencies (HMA), to guide the work carried out by the European medicines regulatory network in the coming years.

2020 has put EMA and the regulation of medicines in the public spotlight. While the pandemic led us on a motivating but incredibly challenging journey, it has also been an opportunity for us to demonstrate the value to public health of decision-making that is based on science – and science only. I would like to thank all those who have been part of this journey and who are at the heart of EMA's work: the members of its scientific committees, the working parties and scientific advisory groups, the Management Board and the national experts, our stakeholders and, of course, EMA's staff.

**March 2021**



# COVID-19: EUROPEAN MEDICINES REGULATORY NETWORK'S RESPONSE TO THE PANDEMIC

The COVID-19 pandemic has caused pain and hardship for hundreds of millions of people in the world. It has cost the lives of millions and has affected the health of many more.

As the SARS-CoV-2 virus ripped through societies in the EU and fundamentally reshaped how we live, work and interact with people, the scientific community rose to the challenge. Unparalleled mobilisation and sharing of information between scientists, industry, regulators, healthcare professionals, patient representatives and public health bodies around the globe resulted in the approval in the EU of a first vaccine against this new disease and another two undergoing rolling review in less than a year. Development of new treatments and vaccines is going on at an unprecedented rate, giving us confidence that pharmaceutical interventions can play an important role in getting the pandemic under control.

EMA together with its partners within the European medicines regulatory network (EMRN) played a key role in the EU's response to the pandemic from the outset. Within days of the World Health Organization declaring the novel coronavirus outbreak a public health emergency of international concern (PHEIC), WHO's highest level of alarm,

EMA initiated its public health threats plan on 4 February 2020 to be ready to support the development of new treatments and vaccines.

Lockdown measures, including factory closures, quarantine requirements and travel restrictions had a profound impact on all areas of healthcare. There were concerns that the resulting impact on global supply chains could lead to shortages, both for medicines that were critically important for use in intensive care units looking after COVID-19 victims, but also for medicines that patients across the EU were reliant upon to treat their conditions.

Limitations in hospital access for patients not suffering from COVID-19 meant that treatment protocols for certain diseases had to be changed, requiring regulatory approval. Developers of medicines required urgent guidance on how to conduct clinical trials in a situation where participants had to shield at home and could no longer attend hospital appointments.

## KEY EVENTS IN 2020



### JANUARY 20, 2020

HMA-EMA Joint Big Data task force publishes a [report](#) with recommendations to unlock the potential of big data for public health in the EU.

EMA and the network of national competent authorities (NCAs) had to adapt activities and processes to ensure a rapid response to the pandemic whilst maintaining core regulatory activities to protect public and animal health. A business continuity plan set out the principles for operating core activities; existing resources were reallocated and priorities shifted to meet these objectives.

Staff at EMA and across EMRN have demonstrated their strong commitment to the protection of the health of European citizens. Their contributions

spanned from early scientific advice during the development, the rapid evaluation and approval of treatments and vaccines to the robust safety monitoring in the post-authorisation setting. The Agency also led efforts to align regulatory requirements with international regulators, thereby further facilitating medicine development and approval. EMA and the EU network were committed from the start to maximising the transparency of their activities to build EU citizens' trust in the new medicines and vaccines and the understanding of the scientific data underpinning their recommendations.

**JANUARY 22, 2020**

EMA [welcomes two appellate judgments by the Court of Justice](#) that confirmed, in clear and unambiguous terms, the right of citizens for access to clinical study and toxicology reports submitted to EMA for the purpose of the granting of a marketing authorisation for human and veterinary medicinal products.

**JANUARY 26, 2020**

EMA celebrates [25 years of advancing public and animal health](#).

## From guided development to accelerated approval procedures

From early on in the pandemic, EMA took action promptly and adapted its procedures to achieve the authorisation of safe and effective treatments and vaccines within the shortest possible time frame.

### Rapid and agile development support

EMA activated its plan for managing emerging health threats on 4 February 2020 and, as part of this plan, encouraged developers of potential vaccines or treatments for COVID-19 to get in touch through a dedicated mailbox to discuss their strategy for evidence generation. Through these early interactions, EMA provided preliminary informal feedback on development plans and identified products that were mature enough to benefit from rapid scientific advice.

Scientific advice is one of EMA's key tools to support the sound development of medicines. During the pandemic, developers could send a request at any time for expedited advice in no more than 20 days. Developers received guidance and direction from EMA on the best methods and study designs to generate robust information for their future medicine or vaccine.

Another fast-track procedure was provided for paediatric investigation plans (PIPs). The timeline for an EMA review was reduced from 120 to 20 days. PIPs describe how a medicine will be studied in children and must be agreed with EMA ahead of any marketing authorisation application.

To further advise medicine developers, EMA also published guidance outlining the clinical evidence required for the approval of vaccines. While the exceptional context of the pandemic requires special regulatory considerations for approval, the guidance highlights that the benefits and risks of COVID-19 vaccines need to be properly assessed based on detailed information on manufacturing, non-clinical data and results of well-designed clinical trials.



#### JANUARY 28, 2020

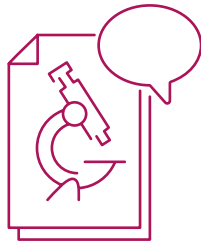
EMA publishes [updated scientific advice on the categorisation of antibiotics](#) used in animals that promotes responsible use to protect public and animal health.



#### JANUARY 29, 2020

EMA, the [Heads of Medicines Agencies \(HMA\)](#) of EU Member States and the European Commission publish [key principles outlining a harmonised approach to develop and use electronic product information \(ePI\) for human medicines across the European Union](#).

**AT THE END OF 2020**

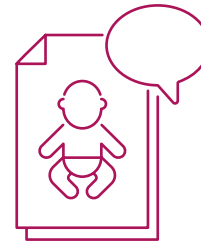


**75**

rapid scientific advice procedures had been completed;

**4**

more were in the pipeline



**5**

rapid procedures for paediatric investigation plans had been completed;

**14**

more were in the pipeline



**JANUARY 31, 2020**

The [United Kingdom formally leaves the European Union](#) and becomes a third country to the EU.



**FEBRUARY 03, 2020**

EMA's staff gather to raise the EU flags in the lobby of its new and final building in Amsterdam.

## Rolling review and fast-track approval

Once the development of a promising medicine or vaccine is nearing completion, EMA's key tool to speed up its assessment during a public health emergency is the rolling review. This tool is foreseen in EMA's public health threats plan. It was used throughout the year and allowed EU experts to scrutinise the evidence on a medicine or a vaccine as soon as it became available from ongoing studies, and before a formal marketing authorisation application was submitted. Once EMA decides that sufficient data are available, the company should then submit a formal application, which is then processed under a shortened timetable.

During the COVID-19 pandemic, EMA's conditional marketing authorisation (CMA) has been used to expedite the approval of treatments and vaccines. This is in line with EU legislation which foresees the use of this type of authorisation to fast-track the approval process during public health emergencies to save lives. It allows a marketing authorisation to be granted as soon as enough data become available to demonstrate that a medicine's benefits outweigh its risks, with robust safeguards and controls in place post-authorisation.

While a CMA is a tool to speed up the approval process, it also guarantees that the medicine assessed complies with the EU standards of safety and efficacy. It gives the EU authorities the control and safeguards needed to recommend a medicine or vaccines roll-out across the EU.

At the end of 2020, two medicines for COVID-19 were granted a CMA after having been assessed through a rolling review:

- the therapeutic Veklury
- the vaccine Comirnaty

‘The authorisation of the first COVID-19 vaccine, less than a year after the pandemic was declared, was the result of unparalleled mobilisation of scientists, industry, regulators, healthcare professionals, patient representatives and public health bodies around the globe. EMA's robust, science-based consensus opinion on the safety, efficacy and quality of the vaccine provided the EU Member States with a firm scientific foundation for the roll-out of their vaccination programmes and a continuing framework for control and supervision of the vaccine.’

**Emer Cooke**, EMA Executive Director



### FEBRUARY 04, 2020

EMA initiates public health threats plan and announces concrete actions to [accelerate the development and availability of medicinal products](#) for the treatment and prevention of the new [coronavirus disease \(COVID-19\)](#).



### FEBRUARY 06, 2020

[How does EMA support SMEs?](#) In a new video, EMA explains how it addresses the unique needs of these companies through its [SME office](#), which provides regulatory, financial and administrative assistance to small and medium-sized pharmaceutical companies.

## Safety monitoring

Once medicines for COVID-19 are authorised, EMA and the NCAs in the EU continue collecting and assessing data to ensure that they are used in the safest way, based on the most up-to-date evidence.

The safety of COVID-19 medicines is monitored according to guidance set out by EMA and NCAs in the good pharmacovigilance practices (GVP), which applies to all medicines and vaccines.

The EU has a comprehensive safety monitoring and risk management (pharmacovigilance) system, which ensures measures are in place for detecting any potential new risks, conducting rigorous scientific assessments of all safety data and introducing any necessary mitigating actions early on.

For vaccines, the [pharmacovigilance plan for COVID-19 vaccines](#) outlines how relevant new information emerging after the authorisation and uptake of COVID-19 vaccines during the pandemic will be collected and promptly reviewed. The plan comprises new obligations for companies that will have to submit monthly safety reports in addition to the regular updates foreseen by the legislation. This is particularly important for vaccines due to the exceptionally large European vaccination campaigns that involve healthy individuals.

Furthermore, EMA published guidance to support pharmaceutical companies' preparation of risk management plans (RMPs) for COVID-19 vaccines. It addresses specific aspects such as information on vaccine safety in special populations, including pregnant women, the elderly or patients with co-morbidities.

EMA also took steps to use real-world data from clinical practice to monitor the safety and effectiveness of COVID-19 treatments and vaccines and other medicines used for COVID-19. EMA contracted different consortia specialising in observational research to conduct several research projects, including on:

- early safety monitoring of COVID-19 vaccines;
- impact of COVID-19 infection and medicines in pregnancy;
- multicentre cohort studies on the use of medicines in COVID-19 patients;
- natural history of coagulopathy and use of antithrombotic agents in COVID-19 patients.

All these measures were put in place to allow regulators to collect emerging data from a wide range of sources and to take swift regulatory action to protect public health whenever needed.

Real-world monitoring complements EMA's regular safety monitoring activities. These data will provide insights into very important aspects, such as the impact of the infection and medicines in pregnancy, and will allow us to understand better the disease and adjust our recommendations as needed.

**Peter Arlett**, Head of Data Analytics and Methods Task Force at EMA



### FEBRUARY 12, 2020

For the first time, EMA makes suspected side effect reports of veterinary medicines authorised in the European Union publicly accessible through the [www.adrreports.eu](http://www.adrreports.eu) website.



### MARCH 10, 2020

The first meeting of the EU Executive Steering Group on Shortages of Medicines Caused by Major Events is held to discuss measures aimed at addressing the impact of the [outbreak of COVID-19](#) on the supply of medicines in the EU.

## Transparency

The authorisation of new medicines for COVID-19, and in particular new vaccines, will only make a difference in the fight against COVID-19 if there is a high uptake. For this reason, EMA implemented exceptional measures to maximise the transparency of its regulatory activities on medicines for COVID-19 during evaluation and after approval. This will allow healthcare professionals and citizens to take well-informed decisions about treatments and vaccines based on facts. The publication of more extensive information also allows further independent scrutiny within the scientific community.

Notably, EMA resumed its landmark policy on the publication of clinical data supporting marketing authorisations for COVID-19 medicines. This programme was suspended at the end of 2018 as a result of the Agency's move from London to Amsterdam. While it remained suspended due to business continuity linked to the COVID-19 pandemic and human resource constraints, EMA decided to exceptionally publish clinical data for COVID-19 medicines, given the unprecedented public interest in this information. By the end of 2020, EMA had published the clinical data supporting the authorisation of Veklury.



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**MARCH 18, 2020**

EMA gives advice on the use of non-steroidal anti-inflammatories for [COVID-19](#).



**MARCH 18, 2020**

EMA and the [US Food and Drug Administration \(FDA\)](#) co-chair the [first global regulatory workshop on COVID-19](#), convened under the umbrella of [International Coalition of Medicines Regulatory Authorities \(ICMRA\)](#).

## Crisis communication and stakeholder engagement

One of EMA's top priorities throughout the pandemic has been to provide the general public with factual, complete and up-to-date information about its activities to fight the pandemic in a timely manner.

EMA's approach has been to communicate proactively on complicated issues, even when uncertainties and unknowns remained. Being clear and transparent and communicating quickly and honestly to protect public health has been EMA's guiding principle.

The Agency has strengthened its engagement with the media, which serve as an important emergency information system during a crisis, through the organisation of interviews with experts and press briefings to explain complex concepts and via the dissemination of factual information on social media.

These activities have increased the Agency's visibility and public awareness of its role in fighting the pandemic, the resulting broad coverage helping to convey reliable information to the public.

More than ever, EMA has reached out to the public to respond to their questions and concerns. It has engaged with patient and healthcare professional organisations and the general public at large through information sessions, public meetings as well as consultations to increase the effectiveness of public health communications.

Two press briefings, attended by over 180 reporters, were organised in May and December 2020 to meet the huge media interest in EMA's COVID-19-related activities; 326 unique articles were published in the first 24 hours after the May press briefing.

On 11 December 2020, EMA held its first public meeting on COVID-19 to explain how the Agency assesses and monitors COVID-19 vaccines and hear directly from European citizens about their needs and concerns. The meeting was held virtually and broadcast live. It was attended by more than 3,500 people, who had the opportunity to ask questions to EMA experts live.

### Key figures on EMA communication tools:

- A special COVID-19 landing page was designed to make information related to the pandemic response more visible and easily accessible.
- 15 webpages were created reflecting the various aspects of EMA's work, from collaboration with international regulators to guidance for developers and companies. Extensive information in lay language on how vaccines for COVID-19 are developed, authorised and monitored and about data requirements for approval was also made available on the EMA website.
- 93 news announcements were published to inform the public about key milestones in medicine assessment or new initiatives about the pandemic.
- 63 media interviews and close to 1,000 direct interactions with the media and the general public.



**MARCH 19, 2020**

EMA's human medicines committee (CHMP) [urges](#) the EU research community to prioritise large randomised controlled studies.



**MARCH 20, 2020**

The European Commission, EMA and national [Heads of Medicines Agencies \(HMA\)](#) publish [recommendations for sponsors on how to manage the conduct of clinical trials in the context of the COVID-19 pandemic](#).



## Mobilising expertise from across the European network

The unprecedented mobilisation of experts through the European network proved to be one of the key success factors supporting fast-track development and marketing authorisations of safe, effective and high-quality medicines and vaccines for COVID-19.

In April 2020, as part of its health threats plan to fight COVID-19, EMA established the COVID-19 EMA pandemic Task Force (COVID-ETF). The group brought together the best expertise from the European medicines regulatory network and ensured a fast and coordinated response to the pandemic.

It was instrumental in:

- conducting exploratory reviews of investigational products;
- identifying the most appropriate regulatory pathway for ensuring that potential treatments and vaccines are approved and available as swiftly as possible;
- providing rapid scientific advice on questions from medicine developers on their development plans, endorsed by EMA's Committee for Medicinal Products for Human Use (CHMP);
- interacting with academia or sponsors/ investigators of clinical trials not funded by industry;
- advising on start of rolling reviews and timing of CMA applications.

‘Thanks to its agile structure and strong human commitment, COVID-ETF has been instrumental in bringing together all the best expertise from across the European medicines regulatory network and facilitating fast decision-making by EMA scientific committees.’

**Marco Cavaleri**, Head of Biological Health Threats and Vaccines Strategy at EMA



### MARCH 25, 2020

EMA publishes a [report looking at the main achievements over the last ten years](#) of the [MUMS/limited market policy](#) for the classification of veterinary medicines, which was established by the Agency in 2009.



### MARCH 31, 2020

EMA publishes its newly adopted [Regulatory Science Strategy to 2025](#). It provides a plan for advancing regulatory science over the next five years, covering both human and veterinary medicines.

## Coordinating the network's response to shortages

Ensuring the continued availability of medicines for European patients during the COVID-19 pandemic has been high on the agenda of EMA and the European medicines regulatory network.

The EU network is continuously monitoring the supply chains of human and veterinary medicines in the EU and the impact of the increased use of these medicines during the pandemic.

Although most medicine shortages are normally dealt with at national level, during the COVID-19 pandemic, EMA acted as a central coordinator, supporting Member States' activities in preventing and mitigating supply disruptions.

In March 2020, the EU Executive Steering Group on Shortages of Medicines Caused by Major Events was established to provide strategic leadership for urgent and coordinated action.

“The European medicines regulatory network established key pillars in 2020 to help prevent and mitigate medicine shortages. Moving forward, this system will be further developed and contribute to strengthening the network's overall response to supply issues, in particular during public health emergencies.”

**Noël Wathion**, EMA Deputy Executive Director

In April, it launched an enhanced fast-track monitoring system with an initial focus on medicines used in COVID-19 patients in intensive care units (ICUs) that were in high demand early in the pandemic, such as anaesthetics, antibiotics, resuscitation medicines and muscle relaxants.

The monitoring system allows regulators to:

- detect and monitor common issues across Member States;
- spot patterns in medicines supply;
- anticipate future supply disruptions early;
- identify EU/EEA-wide measures to address disruption issues.

Each pharmaceutical company had to appoint an industry single point of contact (i-SPOC) responsible for reporting on ongoing or anticipated shortages of medicines used to treat COVID-19 patients. EMA compiles the information it receives from the i-SPOCs and shares it with the steering group for decision-making.

Although the supply situation of some medicines improved in the course of 2020, global supply challenges remain.



**APRIL 09, 2020**

EMA establishes the [COVID-19 EMA pandemic Task Force \(COVID-ETF\)](#) to take quick and coordinated regulatory action related to COVID-19 medicines.



**APRIL 10, 2020**

EMA publishes [guidance](#) on adaptations to the regulatory framework to address challenges arising from the COVID-19 pandemic, with a particular focus on crucial medicines for use in COVID-19 patients.

## International collaboration

As Chair of the International Coalition of Medicines Regulatory Authorities (ICMRA), EMA led the global efforts to streamline and align regulatory requirements to facilitate medicine development and approval. Throughout 2020, EMA chaired or co-chaired a series of workshops and strategic meetings to exchange information and provide joint directions and recommendations on key aspects of medicine development and benefit-risk evaluation during the pandemic.

One of the key recommendations of the coalition was to stress the need for large, well-designed, controlled clinical trials to generate sound evidence on the effects of therapeutics or vaccines against COVID-19. This type of conclusive evidence is necessary to enable rapid development and approval of treatments and vaccines against COVID-19.

The group also outlined principles for trial design, specified concrete actions that COVID-19 clinical trial investigators should take when collecting, analysing and reporting data, and issued a pledge towards medicine developers to continue running clinical trials for as long as feasible, as this will allow the collection of critical data in support of further regulatory actions and vaccine deployment.

EMA shared the study protocols and code books with other regulators in ICMRA to facilitate joint utilisation and safety evaluation, as well as building more sustainable infrastructure for benefit-risk evaluation in pregnancy after the pandemic.



### APRIL 20, 2020

The European Commission, EMA and the national competent authorities agree a series of [measures](#) to mitigate the impact of disruptions caused by COVID-19 on the conduct of inspections of manufacturing facilities or other sites relevant for medicinal products in the European Union.



### APRIL 21, 2020

EMA, together with the pharmaceutical industry and the EU Member States, launches its enhanced fast-track monitoring system to help prevent and mitigate supply issues with crucial medicines used for treating patients with [COVID-19](#).

## Early lessons from the COVID-19 response

Building on the experience from the 2009 H1N1 pandemic, EMA expanded the rolling review as a systematic tool to fast-track the assessment of data and prepare for speedier approvals. By allowing EU experts to scrutinise emerging evidence and question applicants early on, it proved to be a key enabler of fast-track assessment. Combined with the CMA, this approach allowed experts to reach a robust, science-based consensus opinion within the shortest time frame while ensuring that the medicine or vaccine meets the rigorous EU standards for safety, efficacy and quality and that comprehensive data will still be generated post-approval.

Early dialogue with medicine developers and academia helped EMA and experts of the EU network to keep abreast of emerging new technologies and prepare for them. The COVID-ETF supported this scientific work throughout the process, from the provision of advice to developers early in the development to steering scientific discussions at key milestones. The group played a major role in bringing together the best and most relevant expertise from across the EU network in an agile and proactive manner, and allowed quick and coordinated regulatory actions, based on sound scientific assessment. The critical role of the COVID-ETF in supporting the EU Member States and the European Commission with the rapid authorisation of medicines and vaccines was fully acknowledged. As a result, the EC announced in October 2020 that EMA will be tasked with formally establishing such a task force to lead the scientific response to any future public health emergency as part of the Agency's extended mandate.

International cooperation that took place under the umbrella of ICMRA allowed steering research efforts and emphasised the need for the sound development and generation of robust data. Reaching agreements amongst regulators from all corners of the world on key aspects of medicine development and vaccine safety monitoring was a significant achievement and paved the way for even further cooperation and regulatory alignment.

Also, the public meeting organised by the Agency to explain how EMA assesses and monitors COVID-19 vaccines was acknowledged as an important tool for explaining complex concepts to the public, addressing some misunderstandings and responding to the public's questions and concerns. Following the positive feedback received after the meeting, it was agreed that similar meetings would be held throughout the pandemic.



### APRIL 28, 2020

EMA endorses the [joint COVID-19 statement](#), published by the [International Coalition of Medicines Regulatory Authorities \(ICMRA\)](#), committing to a strengthening of global collaboration in the fight against [coronavirus disease](#).



### APRIL 30, 2020

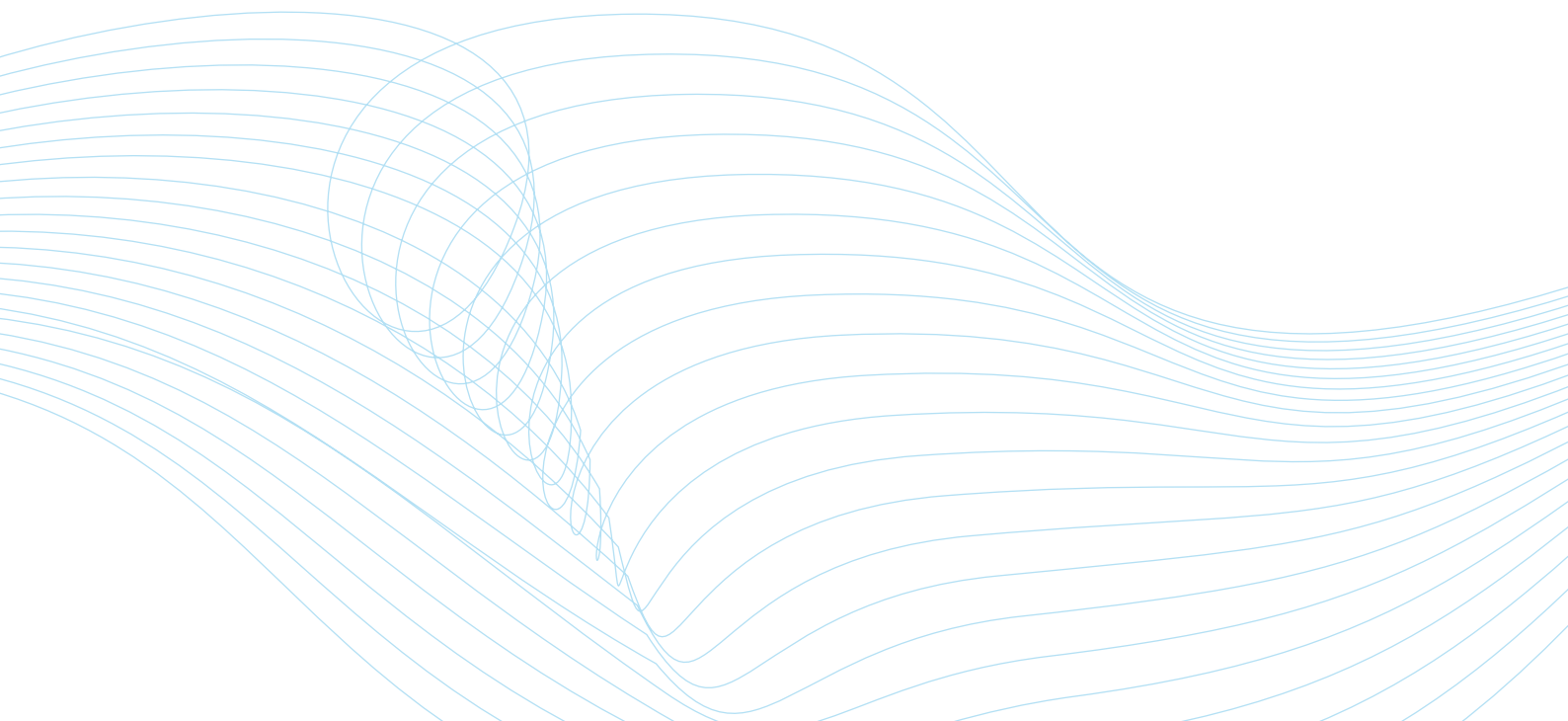
EMA's human medicines committee (CHMP) recommends the suspension of all [ranitidine medicines](#) in the EU due to the presence of low levels of an impurity called N-nitrosodimethylamine (NDMA).

# CHAPTER 1

## KEY ACHIEVEMENTS IN 2020



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# EVALUATION AND MONITORING OF MEDICINES: HIGHLIGHTS

## Human medicines

### Medicines recommended for approval

Authorisation of new medicines is essential to advancing public health as they bring new opportunities to treat certain diseases. In 2020, EMA recommended 97 medicines for marketing authorisation. Below is a selection of medicines approved in 2020 that represent significant progress in their therapeutic areas:



**Zolgensma**, to treat babies and young children with spinal muscular atrophy, a rare and often fatal genetic disease that causes muscle weakness and progressive loss of movement.



**Zabdeno** and **Mvabea**, the two components of a new vaccine that provides active immunisation to prevent Ebola virus disease in individuals aged one year and older.



**Givlaari**, the first treatment for acute hepatic porphyria in adults and adolescents aged 12 years and older.



**Idefix**, the first treatment for adult patients waiting for a kidney transplant, who are highly sensitised against tissue from the donor and who have a positive crossmatch test against an available kidney from a deceased donor.



**Rybelsus**, for the treatment of adults with insufficiently controlled type 2 diabetes to improve glycaemic control as an adjunct to diet and exercise. It is the first glucagon-like peptide (GLP-1) receptor agonist treatment – a class of non-insulin medicines for people with type 2 diabetes – developed for oral use, providing patients with another option to treat the disease without injections.



**Kaftrio**, the first triple combination therapy for the treatment of cystic fibrosis in patients aged 12 years and older who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or heterozygous for F508del in the CFTR gene with a minimal function (MF) mutation.



**Enerzair Breezhaler**, the first asthma triple combination therapy that includes an optional electronic sensor to collect data on the use of the inhaler by the patient.

#### APRIL 30, 2020

EMA starts the [first rolling review](#) of a COVID-19 medicine – the antiviral medicine remdesivir.

#### MAY 04, 2020

The European Commission, EMA and the [Coordination Group for Mutual Recognition and Decentralised Procedure – Veterinary \(CMDv\)](#) issue guidance on adaptations to the regulatory framework for companies that develop, manufacture and distribute veterinary medicines in order to address some of the constraints posed by the COVID-19 pandemic.



**Blenrep**, to treat adult patients with relapsed and refractory multiple myeloma (a cancer of the bone marrow) who no longer respond to treatment with an immunomodulatory agent, a proteasome inhibitor and a CD-38 monoclonal antibody.



**Tecartus**, for the treatment of adult patients with a rare cancer of white blood cells called mantle cell lymphoma (MCL) when the symptoms or the disease come back (relapse) or when they are not responding (refractory) after two or more lines of systemic therapy.



**Oxlumo**, for the treatment of the rare inherited disorder primary hyperoxaluria type 1.



**Libmeldy**, to treat metachromatic leukodystrophy (MLD), a rare inherited metabolic disease that affects the nervous system.



**Rekambys** and **Vocabria**, to be used together for the treatment of patients with human immunodeficiency virus type 1 (HIV-1) infection. They are the first antiretroviral (ARV) medicines that come in a long-acting injectable formulation.



**Rozlytrek**, for the treatment of patients whose solid tumours have a neurotrophic tyrosine receptor kinase gene fusion, or patients with ROS1-positive advanced non-small cell lung cancer.

## 11<sup>th</sup> medicine recommended for use outside the EU

In July 2020, the CHMP adopted a positive opinion for Dapivirine Vaginal Ring (dapivirine) used to reduce the risk of infection with HIV-1, in combination with safer sex practices when oral pre-exposure prophylaxis (PrEP) is not used, cannot be used or is not available. Placed in the vagina, the ring slowly releases the antiretroviral medicine dapivirine over a period of 28 days.

This is the 11<sup>th</sup> medicine recommended by EMA under [EU Medicines for all \(EU-M4All\)](#), a mechanism that allows the CHMP to assess and give opinions on medicines that are intended for use in countries outside the EU under Article 58 of Regulation (EC) No 726/2004.



### MAY 04, 2020

EMA publishes an [overview](#) of initiatives for the acceleration of development support and evaluation procedures for COVID-19 treatments and vaccines.



### MAY 15, 2020

EU regulators [call](#) for a comprehensive international coordination mechanism to allow the conduct of adequately powered, randomised controlled trials, which can generate sound evidence on the effects of therapeutics or vaccines against COVID-19.



## Spotlight on COVID-19

EMA is contributing to tackling the COVID-19 pandemic by expediting the development and approval of safe and effective treatments and vaccines.

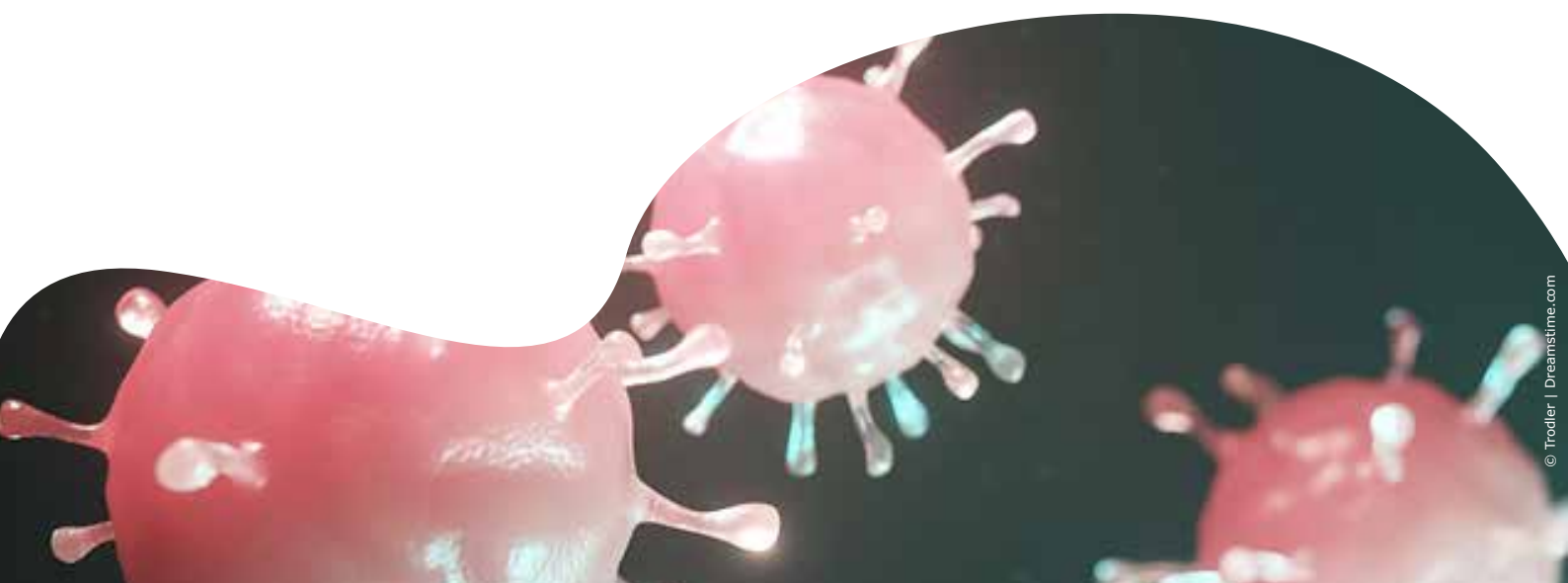
In December 2020, the CHMP recommended granting a CMA for the vaccine Comirnaty, developed by BioNTech and Pfizer, to prevent COVID-19 in people from 16 years of age.

By the end of the year, the Committee was already reviewing the formal marketing authorisation application for another vaccine (Moderna's mRNA-1273 COVID-19 vaccine) and rolling reviews of two additional vaccines were also ongoing – one for the vaccine being developed by AstraZeneca with the University of Oxford and one for the vaccine from Janssen-Cilag.

In June 2020, the CHMP recommended granting a CMA for Veklury (remdesivir) for the treatment of COVID-19 in adults and adolescents from 12 years of age with pneumonia who require supplemental oxygen. In December, the Committee recommended to use Veklury only in COVID-19 patients who require supplementary oxygen but do not need mechanical ventilation.

In September 2020, the Committee completed its review of results from the RECOVERY study arm that involved the use of the corticosteroid medicine dexamethasone in the treatment of patients with COVID-19 admitted to hospital and concluded that dexamethasone can be considered a treatment option for patients who require oxygen therapy (from supplemental oxygen to mechanical ventilation).

Earlier in the year, EMA warned healthcare professionals to closely monitor patients with COVID-19 who received chloroquine or hydroxychloroquine, given the serious side effects that can result from treatment with these medicines. Both chloroquine and hydroxychloroquine, which are authorised for malaria and certain autoimmune diseases, were used early in the pandemic to treat patients with COVID-19 but their beneficial effects in these patients have not been established.



### MAY 26, 2020

For [observational studies of real-world data in COVID-19](#), EMA calls for transparency for protocols and results, and collaboration between researchers, to ensure high-quality, powerful studies.



### MAY 28, 2020

EMA, together with EU Member States and the European Commission publishes a [plan outlining principles](#) for how the network will ensure that core public and animal health regulatory activities, such as the authorisation, maintenance and supervision of human and veterinary medicines, will continue to be carried out during the ongoing [COVID-19 pandemic](#).

## EARLY ACCESS TO MEDICINES THAT ADDRESS PUBLIC HEALTH NEEDS

In 2020, **six medicines** received a recommendation for marketing authorisation following an **accelerated assessment**: **Blenrep, Enhertu, Givlaari, Mvabea, Oxlumo** and **Zabdeno**. This mechanism is reserved for medicines that are able to address unmet medical needs. It allows for faster assessment of eligible medicines by EMA's scientific committees (within a maximum of 150 days rather than 210 days).

**Thirteen medicines** received a recommendation for a **CMA**, one of the possibilities in the EU to give patients early access to new medicines: **Adakveo, Aynakyt, Blenrep, Comirnaty, Enhertu, Hepcludex, Idefirix, Dovprela, Retsevmo, Rozlytrek, Tecartus, Veklury** and **Zolgensma**

The conditional authorisation allows for early approval on the basis of less complete clinical data than normally required, because the benefits of earlier patient access outweigh the potential risks of limited data. This is particularly important in the response to a public health emergency such as COVID-19. These authorisations are subject to specific post-authorisation obligations to generate complete data on the medicines.

**Five medicines (Elzonris, Lumoxiti, Mvabea, Obiltoxaximab SFL and Zabdeno)** were authorised under exceptional circumstances, a route that allows patients' access to medicines that cannot be approved under a standard authorisation as comprehensive data cannot be obtained. This can be the case if there are only very few patients with the disease, if the collection of complete information on the efficacy and safety of the medicine would be unethical, or if there are gaps in the scientific knowledge. These medicines are subject to specific post-authorisation obligations and monitoring.

The enhanced development support provided by EMA's PRIME scheme aims at helping patients to benefit as early as possible from promising medicines that target an unmet medical need by optimising the generation of robust data and enabling accelerated assessment. This year, **eight PRIME-designated medicines** were recommended for approval (**Blenrep, Givlaari, Hepcludex, Idefirix, Oxlumo, Rozlytrek, Tecartus** and **Zolgensma**).

20 medicines under development were included in the scheme in 2020: oncology (5), haematology-haemostaseology (3), endocrinology-gynaecology-fertility-metabolism (2), vaccines (2), cardiovascular diseases (2), and one each for ophthalmology, infectious diseases, neurology, pneumology-allergology, gastroenterology-hepatology, immunology-rheumatology-transplantation.



### JUNE 04, 2020

EMA updates patients' and healthcare professionals' organisations about its COVID-19 activities. At a [virtual meeting with the Patients' and Consumers' Working Party and the Healthcare Professionals' Working Party](#) on Tuesday 2 June 2020, the Agency presented an overview of its contribution to the pandemic response and provided updates on [COVID-19 treatments and vaccines](#) under development.



### JUNE 08, 2020

EMA receives an application for [conditional marketing authorisation](#) (CMA) of remdesivir, the first antiviral medicine for the treatment of COVID-19, and formally starts evaluation.

## MEDICINES FOR RARE DISEASES

The EU framework for orphan medicines aims to encourage the development and marketing of medicines for patients with rare diseases by providing incentives for developers.

Orphan designations are reviewed by EMA's Committee for Orphan Medicinal Products (COMP) at the time of approval to determine whether the information available to date allows maintaining the medicine's orphan status and granting the medicine ten years of market exclusivity. Among the 97 medicines recommended for marketing authorisation in 2020, **22 had their orphan designation confirmed** by the end of the year.

In 2020, the following applications lost their orphan status before receiving marketing authorisation, which means they were still authorised as medicinal products but not as orphan medicinal products: Calquence and Sarclisa. More information can be found in the [COMP monthly reports](#).

## NEW USES FOR EXISTING MEDICINES

**83** extensions of indication were recommended in 2020. The extension of the use of a medicine that is already authorised for marketing in the EU can offer new treatment opportunities for patients. Important extensions of indication included:



**Orfadin**, to include the treatment of alkaptonuria in adult patients.



**Velphoro**, to include control of serum phosphorus levels in children aged 2 years or older with chronic kidney disease (CKD) stages 4-5 or with CKD on dialysis.



**Olumiant** (baricitinib), to include the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy.

## NEGATIVE OPINIONS

The CHMP adopted a **negative opinion for two<sup>1</sup> medicines** in 2020: **Gamifant** and **Turalio**.

When the Committee cannot reach an agreement on a positive benefit-risk balance, it issues a negative opinion on the marketing authorisation application and elaborates on the grounds for this opinion. Applicants have the right to request a re-examination of the negative opinion within 15 days of receipt of the notification.

**93% of all opinions** (positive and negative) **were reached by consensus** among the 27 CHMP members, which means that, following in-depth discussions, the experts agreed on all aspects of the marketing authorisations and there were no divergent opinions.

<sup>1</sup> This figure does not include the initial negative opinion adopted by the CHMP on Elzonris (tagraxofusp) in July 2020. The applicant for this medicine requested re-examination of the Committee's negative opinion and, after considering the grounds for this request, the CHMP recommended granting a marketing authorisation for Elzonris in November 2020.



### JUNE 18, 2020

EMA endorses two statements about the importance, safety and effectiveness of vaccines published by the [International Coalition of Medicines Regulatory Authorities \(ICMRA\)](#).



### JUNE 22, 2020

The European Commission, EMA and FDA agree new priorities to strengthen their [collaboration](#) on medicines during their 2020 bilateral regulatory dialogue meeting.

Around **70% of applicants who were granted a positive opinion for their medicine had received scientific advice** from EMA during their product's development phase. This early engagement with developers allows EMA to clarify what kind of evidence is required to later evaluate a medicine for authorisation. This encourages generation of more robust data for regulatory assessment, and thus protects patients from taking part in unnecessary or poorly designed clinical trials.

## Keeping patients safe

### MONITORING MEDICINES AFTER THEIR AUTHORISATION – OPTIMISING SAFE AND EFFECTIVE USE

Once a medicine has been authorised, EMA and the EU Member States continuously monitor the quality, safety and the benefit-risk balance of the medicine used in real life on the market. This is to optimise how the medicine is used by patients to achieve its full benefit and to protect patients from avoidable side effects. Regulatory measures range from a change to the product information to the suspension or withdrawal of a medicine or recall of a limited number of batches.

Important new safety advice issued in 2020 included:

- Restrictions in the use of **cyproterone acetate** due to risk of meningioma (brain tumour). The risk of meningioma increases with increasing cumulative doses. The use of cyproterone acetate is contraindicated in patients with a meningioma or a history of meningioma.
- Recommendation to update the safety information for **hormone replacement therapy** (HRT) used to treat symptoms of the menopause. As already indicated in the product information of HRT medicines, women should only take hormone replacement therapy for the treatment of symptoms of menopause at the lowest dose and for the shortest possible time that works for them. The updates are based on evidence from a large study published in *The Lancet* in August 2019, which confirmed the known higher risk of breast cancer in women using HRT. The results showed that the risk may continue to be increased for ten years or more after stopping HRT, if it has been used for more than five years.
- The product information for **fluoroquinolone antibiotics** was updated to reflect that systemic and inhaled fluoroquinolones may increase the risk of heart valve regurgitation/incompetence.
- Recommendation to restrict the use of medicines containing **ulipristal acetate 5 mg** (Esmya and generic medicines) as a result of cases of serious liver injury. The medicines can now only be used to treat uterine fibroids in premenopausal women for whom surgical procedures are not appropriate or have not worked. The medicines must not be used for controlling symptoms of uterine fibroids while awaiting surgical treatment.



**JUNE 23, 2020**

EMA [announces](#) it will provide free scientific advice for academia developing medicines for rare diseases.



**JUNE 23, 2020**

The [European medicines regulatory network](#) issues recommendations on impurities in medicines following the conclusion of an exercise to draw on lessons learnt from the presence of nitrosamines in a class of blood pressure medicines known as sartans.

- Recommendation to use **fosfomycin** medicines given by infusion (drip) into a vein only to treat serious infections when other antibiotic treatments are not suitable. Fosfomycin medicines given by mouth can continue to be used to treat uncomplicated bladder infections in women and adolescent girls. They can also be used to prevent infection in men undergoing a procedure whereby a tissue sample is taken from their prostate (biopsy). Fosfomycin medicines given by mouth to children (under 12 years of age) and intramuscular formulations (fosfomycin medicines for injection into a muscle) should no longer be used as there are insufficient data available to confirm their benefits to patients.
- Recommendation to test patients for the lack of the enzyme dihydropyrimidine dehydrogenase (DPD) before starting cancer treatment with **fluorouracil** given by injection or infusion (drip) and related medicines containing capecitabine and tegafur. Patients who completely lack DPD must not be given these fluorouracil medicines because of high fluorouracil toxicity which can have a fatal outcome.
- Recommendation to limit the use of high-strength **creams containing 100 micrograms/gram (0.01%) of estradiol** to a single treatment period of up to 4 weeks. Data on these creams showed that in postmenopausal women who use them, the levels of estradiol in the blood were higher than normal postmenopausal levels. The absorption of estradiol into the bloodstream is of concern and could result in side effects such as venous thromboembolism (formation of blood clots in the veins), stroke, endometrial cancer (cancer of the lining of the womb) and breast cancer.
- Updated recommendations for **dimethyl fumarate** to help minimise the risk of progressive multifocal leukoencephalopathy (a rare brain infection) in patients treated with this medicine. Dimethyl fumarate is authorised in the EU for the treatment of adults with relapsing-remitting multiple sclerosis.
- Recommendation on measures to avoid handling errors in preparation and administration of **leuprorelin** depot medicines, which are used to treat prostate cancer, breast cancer, certain conditions that affect the female reproductive system and early puberty. Handling errors resulted in some patients receiving insufficient amounts of their medicine.
- The data from the *Tsepamo* study confirmed that there is no indication of an overall increased risk of major birth defects in children exposed to **dolutegravir** (anti-HIV treatment) during pregnancy. Furthermore, the signal for a potentially increased risk of neural tube defects has weakened when the number of exposed patients has increased. The product information was updated accordingly.



#### JUNE 25, 2020

The EMA Management Board nominates Emer Cooke as the [new Executive Director of the Agency](#). At an extraordinary virtual session on 25 June, the Board selected Emer Cooke from a shortlist of candidates created by the European Commission.



#### JUNE 25, 2020

EMA's human medicines committee ([CHMP](#)) recommends granting a [conditional marketing authorisation](#) to Veklury (remdesivir), the first medicine for the treatment of COVID-19 in adults and adolescents from 12 years of age with pneumonia who require supplemental oxygen.

- Update of product information, introduction of a patient card and prescriber checklist to minimise the risk of fatal outcomes as a result of interaction between **brivudine** and **fluoropyrimidines** (e.g. fluorouracil, capecitabine, tegafur, flucytosine). At least 4 weeks must be awaited after the end of brivudine treatment before starting treatment with a fluoropyrimidine.
- Recommendation to perform a liver function test before starting a treatment with **pirfenidone**, and subsequently every month for the first 6 months and then every 3 months for the duration of the treatment, to prevent drug-induced liver injury. Pirfenidone is an anti-fibrotic and anti-inflammatory medicine indicated for the treatment of idiopathic pulmonary fibrosis.
- Recommendation to suspend all **ranitidine** medicines in the EU due to the presence of low levels of an impurity called *N*-nitrosodimethylamine (NDMA). Ranitidine medicines are used for reducing levels of stomach acid mainly in patients with conditions such as heartburn and stomach ulcers. NDMA is classified as a probable human carcinogen (a substance that could cause cancer), based on animal studies. More information is available in the next section.

## ENSURING INTEGRITY OF CLINICAL TRIAL CONDUCT AND THE MANUFACTURE AND SUPPLY OF MEDICINES

Medicine development and manufacturing is global. It is important for regulators to ensure that EU standards are adhered to no matter where clinical trials or manufacturing takes place.

In 2020, EMA undertook several reviews to provide recommendations to marketing authorisation holders (MAHs) to avoid/mitigate the risk of presence of **nitrosamine impurities** in medicines.

In April 2020, EMA recommended to suspend all ranitidine medicines in the EU due to the presence of low levels of an impurity called *N*-nitrosodimethylamine (NDMA). The available safety data did not show that ranitidine increased the risk of cancer, and any possible risk was likely to be very low. However, NDMA had been found in several ranitidine medicines above levels considered acceptable, and there were unresolved questions about the source of this impurity and potential increase of NDMA over the shelf life. Companies were asked to provide reassuring data on degradation of ranitidine and endogenous formation of NDMA to support a positive benefit-risk balance and lift the suspended marketing authorisations.

The product information for 490 centrally authorised medicines was updated on the basis of new safety data in 2020. Every year, the recommendations of EMA's safety committee (PRAC) on safety warnings are also included in the product information of many thousands of nationally authorised products (NAPs). The revised information is expected to help patients and healthcare professionals to make informed decisions when using or prescribing a specific medicine.

### JUNE 30, 2020

EMA and the [Ministry of Food and Drug Safety of the Republic of Korea \(MFDS\)](#) sign an agreement that allows them to share confidential information on medicines intended for the treatment, diagnosis, or prevention of COVID-19. COVID-19 is a global public health emergency.

### JULY 01, 2020

EMA endorses a joint [statement on prioritisation of COVID-19 clinical trials](#) published by the [International Coalition of Medicines Regulatory Authorities \(ICMRA\)](#).



In June 2020, EMA finalised its review of nitrosamine impurities in human medicines and recommended companies to review their manufacturing processes and, where necessary, take measures to limit the presence of nitrosamines in human medicines. These measures are meant to ensure that nitrosamines are either not present or are present below levels identified to protect public health.

In November 2020, the Agency adopted an opinion on the impact of the above review on the outcome of the review for sartans with a tetrazole ring that was finalised in January 2019. This led to an amendment of the previous conclusions, now requiring companies to carry out risk assessments, establish control strategies and carry out testing for nitrosamines at the level of the finished product.

In 2020, EMA recommended to suspend the marketing authorisations for generic medicines tested by **Panexcell Clinical Laboratories Priv. Ltd** at its site in Mumbai, India. This was due to irregularities found by inspectors in how the company carried out bioequivalence studies, which are used to show that a generic medicine delivers the same amount of active substance in the body as the reference medicine.

Applications for three centralised marketing authorisations and one type II-variation were withdrawn due to non-compliance with **good clinical practice (GCP)**. The CHMP adopted one negative opinion (refusing the granting of the marketing authorisation) for a medicine for which there were GCP-related non-compliance issues in the clinical study submitted by the applicant.



#### JULY 06, 2020

EMA and the [Heads of Medicines Agencies \(HMA\)](#) launch a public consultation on their [joint strategy](#) for the next five years that details how the European medicines agencies' network can continue to enable the supply of safe and effective medicines that meet patients' needs in the face of challenges posed by ever-accelerating developments in science, medicine, digital technologies, globalisation as well as emerging health threats, such as the COVID-19 pandemic.

## Veterinary medicines

### New medicines to benefit animal health in Europe

In 2020, EMA recommended 20 veterinary medicines for marketing authorisation; 13 of these contain a new active substance (i.e. one that had not previously been authorised in the EU). Among the 20 medicines recommended for marketing authorisation, ten were vaccines – more than double the number of vaccines authorised in 2019. Of these, eight were biotechnological vaccines.

The Agency's Committee for Medicinal Products for Veterinary Use (CVMP) also recommended the granting of a marketing authorisation for two immunological products that were developed through biotechnological processes. **Solensia** is the first monoclonal antibody to manage osteoarthritis in cats. **Librela** is a new canine monoclonal antibody for alleviation of pain associated with osteoarthritis in dogs.

**NexGard Combo** was recommended for marketing authorisation under EMA's minor use minor species (MUMS)/limited market programme. This scheme aims to stimulate development of new veterinary medicines for minor species and for rare diseases in major species that would otherwise not be developed under current market conditions.

**NexGard Combo** is an antiparasitic veterinary medicine for the treatment of cats with, or at risk from mixed infections by cestodes, nematodes and ectoparasites



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#### JULY 09, 2020

EMA's human medicines committee ([CHMP](#)) issues an opinion requiring companies to take measures to limit the [presence of nitrosamines](#) in human medicines as far as possible and to ensure levels of these impurities do not exceed set limits.



## Optimising the safe and effective use of veterinary medicines

Once a veterinary medicine has been put on the market, EMA and EU Member States continuously monitor the quality and benefit-risk balance of the medicine. The aim is to optimise the safe and effective use of the veterinary medicine, to achieve its full benefit and to protect animals and users from avoidable adverse effects. If the benefit-risk balance of a veterinary medicine changes, EMA can take regulatory measures that range from an amendment to the product information to the suspension or withdrawal of a medicine. The Agency can also recommend recalling batches of the medicine concerned.

### Important new safety advice issued in 2020

The product information for 12 medicines was updated on the basis of new safety data. The revised information is expected to help animal owners and healthcare professionals to make informed decisions when using or prescribing a medicine.

- Addition of further information in the package leaflet for special precautions for use of **Activyl Tick Plus** in animals.
- Amendment to the product information in relation to the use during pregnancy and lactation and other special precautions for use of **Advocate** in animals.
- Addition of further information in the package leaflet on potential side effects following administration of **Cardalis** in dogs, such as gastrointestinal signs and pruritus.
- Addition of further information in the package leaflet on potential side effects following administration of **Convenia** in dogs, such as haematological reactions, gastrointestinal signs, neurological signs and hypersensitivity reactions.



### JULY 21, 2020

EMA sets up an [infrastructure](#) to support the monitoring of the [efficacy](#) and safety of [COVID-19](#) treatments and vaccines when used in day-to-day clinical practice. This is underpinned by three contracts for observational research that EMA has signed with academic and private partners over recent months, to be ready to effectively monitor vaccines in the real world as soon as they are authorised and support the safe and effective use of COVID-19 vaccines and medicines.

- Addition of further information in the package leaflet on potential side effects following administration of **Credelio** in dogs and cats, such as neurological and gastrointestinal signs.
- Clarification of the information in the package leaflet on potential side effects following administration of **Galliprant** in dogs, in relation to gastrointestinal signs.
- Addition of special precautions to the product information for **Metacam/Novem** to ensure the safety of the person handling and administering the treatment to cattle, pigs, horses, dogs, cats and guinea pigs.
- Amendment to the product information on potential side effects following administration of **Neptra** in dogs to include eye disorders.
- Amendment to the product information on potential side effects following administration of **Onsior** in cats and dogs to include renal disorders.
- Amendment to the product information on potential side effects following administration of **Purevax FeLV** in cats to include gastrointestinal signs and anaphylaxis. Update of the frequency of the adverse reactions.
- Modification of special precautions for **Vectra Felis** to include transient adverse reactions after accidental ingestion by cats.
- Amendment to the product information for **Vectra 3D** in dogs to clarify the potential follow-up of rare application site reactions.

The CVMP adopted two positive opinions for extensions of existing authorisations, broadening the use of the medicines concerned:

- **Aivlosin**, to be also used for the treatment and metaphylaxis of swine respiratory disease associated with *Mycoplasma hyopneumoniae* and *Pasteurella multocida* in pigs.
- **Cytopoint**, to be also used for the treatment of pruritus associated with allergic dermatitis in dogs.

## PROTECTING CONSUMERS

If a medicine is intended to be used in a food-producing animal, it needs to be safe for people to eat the food that comes from this animal. The maximum residue limits (MRLs) recommended by EMA reflect the level of residues of the veterinary medicine in food derived from a treated animal that can be considered safe for consumption. The MRL is established before the medicine for food-producing animals is authorised in the EU.

In 2020, positive opinions were adopted recommending the establishment of MRLs for the following active substances:

- Bupivacaine and Lidocaine in medicines for pigs and cattle.
- Imidacloprid in medicines for finfish.

More information and figures on veterinary medicines are available in chapter 2.



### SEPTEMBER 14, 2020

The HMA-EMA Joint Big Data Steering Group publishes its first [workplan](#), which sets actions to be delivered in 2020-21. With the [European medicines regulatory network](#) focused on the response to the COVID-19 pandemic, the workplan aims to progress evolution to data-driven regulation through smart working, leveraging collaboration with stakeholders and the use of remote expert workshops.

# I ANTIMICROBIAL RESISTANCE

Antimicrobial resistance (AMR) is a serious global public health threat. It occurs when bacteria and other microorganisms change over time and develop resistance to antibiotics and other antimicrobial medicines, making them less effective. This constitutes a threat to the effective treatment of infections caused by bacteria and other microorganisms.

AMR affects both human and veterinary medicines and EMA and the European medicine regulatory network have a pivotal role in bringing those two aspects together. The global challenge posed by AMR can only be tackled by increasing coordination in the EU and worldwide to develop new treatments and tests while using the existing therapies wisely and responsibly, both in the treatment of humans and animals.

This is why AMR is one of the six strategic areas included in the '[European medicines agencies network strategy to 2025](#)', which details the strategic objectives and work plans of EMA and the NCAs of the EU Member States.

In 2020, EMA contributed to the global fight against AMR by:

- supporting the development of new antimicrobial agents;
- collecting data on the consumption of veterinary antimicrobials;
- encouraging and advising on responsible use of antimicrobials.

## DEVELOPMENT OF NEW ANTIMICROBIAL AGENTS

In 2020, four new antibacterial agents received a positive opinion from the CHMP: Fetcroja (cefiderocol) is an antibiotic used in adults to treat infections caused by certain bacteria (aerobic Gram-negative bacteria). This medicine is for use when other antibiotic treatments might not work and there are limited treatment options for patients. Xenleta (lefamulin) is an antibiotic used in adults to treat a lung infection caught outside hospital when other antibiotic medicines are not suitable or do not work. Devprela (pretomanid) is a medicine for treating adults with tuberculosis that is resistant to antibiotics. Tigecycline Accord (tigecycline) is a medicine used to treat adults and children older than eight years with complicated infections of the tissue below the skin when other antibiotics are not suitable.



### SEPTEMBER 22, 2020

EMA hosts a [virtual workshop](#) with its Patient and Consumers' [Working Party](#) (PCWP) and Healthcare Professionals' [Working Party](#) (HCPWP) to gather views from stakeholders on their experiences, concerns and expectations regarding the safe use of medicines by women who are pregnant or breastfeeding.



### SEPTEMBER 23, 2020

EMA publishes a [10-year analysis of the European Union Incident Management Plan \(EU-IMP\)](#) on how incidents with medicines are managed in the EU.

## DATA ON VETERINARY ANTIBIOTIC CONSUMPTION

The 10<sup>th</sup> annual report on the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC), published by EMA in October 2020 and presenting data from 30 countries from the European Economic Area and Switzerland, shows that European countries continue to reduce the use of antibiotics in animals. The overall sales of veterinary antibiotics in European countries dropped by more than 34% between 2011 and 2018.

Also, total sales of certain veterinary antimicrobial agents belonging to antibiotic classes that are considered critically important in human medicine noticeably decreased between 2011 and 2018.

The ESVAC project was conceived and developed to support and harmonise the collection of sales data of veterinary antibiotics. The report is used by scientists, veterinarians and other health professionals, risk assessors and risk managers in Member States as a reference for antimicrobial policies and for guidance on the responsible use of antimicrobials.

## RESPONSIBLE USE OF ANTIMICROBIALS

### Updated categorisation of antibiotics in animals

In January 2020, EMA published its updated scientific advice on the categorisation of antibiotics. The scientific advice ranks antibiotics by considering both the risk that their use in animals causes to public health through the possible development of AMR and the need to use them in veterinary medicine. The classification comprises four categories, from A to D: Avoid (A), Restrict (B), Caution (C) and Prudence (D).

Veterinarians are encouraged to consult the infographic when deciding which antibiotic to prescribe to animals. It can also be used as a tool to draft treatment guidelines.



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### OCTOBER 06, 2020

EMA's human medicines committee (CHMP) starts a 'rolling review' of data on a [vaccine for COVID-19](#) known as BNT162b2, which is being developed by BioNTech in collaboration with Pfizer.

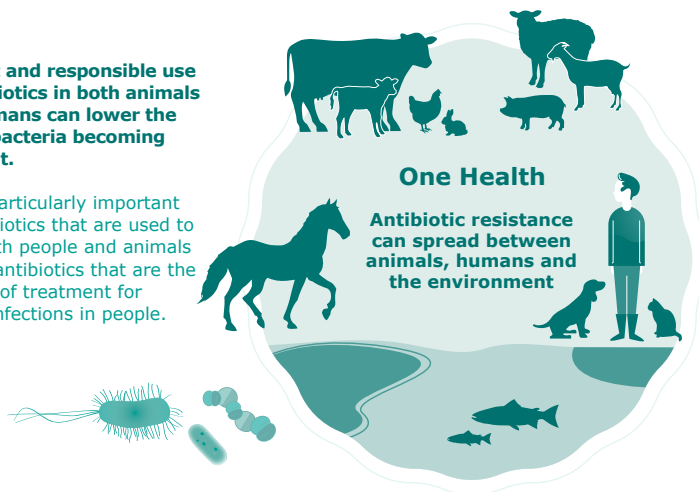
### OCTOBER 19, 2020

EMA launches a new online platform for scientific advice. As from 19 October 2020, developers of [human](#) or [veterinary](#) medicines should use EMA's [IRIS Regulatory & Scientific Information Management Platform](#) to request [scientific advice](#).

**CATEGORISATION OF ANTIBIOTIC CLASSES FOR VETERINARY USE**  
(WITH EXAMPLES OF SUBSTANCES AUTHORISED FOR HUMAN OR VETERINARY USE IN THE EU)

**Prudent and responsible use of antibiotics in both animals and humans can lower the risk of bacteria becoming resistant.**

This is particularly important for antibiotics that are used to treat both people and animals and for antibiotics that are the last line of treatment for critical infections in people.



**The Antimicrobial Advice Ad Hoc Expert Group (AMEG) has categorised antibiotics based on the potential consequences to public health of increased antimicrobial resistance when used in animals and the need for their use in veterinary medicine.**

The categorisation is intended as a tool to support decision-making by veterinarians on which antibiotic to use.

**Veterinarians are encouraged to check the AMEG categorisation before prescribing any antibiotic for animals in their care.** The AMEG categorisation does not replace treatment guidelines, which also need to take account of other factors such as supporting information in the Summary of Product Characteristics for available medicines, constraints around use in food-producing species, regional variations in diseases and antibiotic resistance, and national prescribing policies.

**Category A**  
**Avoid**

- antibiotics in this category are not authorised as veterinary medicines in the EU
- should not be used in food-producing animals
- may be given to companion animals under exceptional circumstances

**Category B**  
**Restrict**

- antibiotics in this category are critically important in human medicine and use in animals should be restricted to mitigate the risk to public health
- should be considered only when there are no antibiotics in Categories C or D that could be clinically effective
- use should be based on antimicrobial susceptibility testing, wherever possible

**Category C**  
**Caution**

- for antibiotics in this category there are alternatives in human medicine
- for some veterinary indications, there are no alternatives belonging to Category D
- should be considered only when there are no antibiotics in Category D that could be clinically effective

**Category D**  
**Prudence**

- should be used as first line treatments, whenever possible
- as always, should be used prudently, only when medically needed

**For antibiotics in all categories**

- unnecessary use, overly long treatment periods, and under-dosing should be avoided
- group treatment should be restricted to situations where individual treatment is not feasible
- check out the European Commission’s guideline on prudent use of antibiotics in animals: <https://bit.ly/2s7LUF2>

AMEG is the acronym for EMA's Antimicrobial Advice Ad Hoc Expert Group. It brings together experts from both human and veterinary medicine. They work together to provide guidance on the impact on public health of the use of antibiotics in animals.




**OCTOBER 21, 2020**

EMA publishes the 10<sup>th</sup> [annual report](#) on the [European Surveillance of Veterinary Antimicrobial Consumption \(ESVAC\)](#). It shows that European countries continue to reduce the use of antibiotics in animals.


<b>A</b>	<b>Aminopenicillins</b> mecillinam pivmecillinam	<b>Carbapenems</b> meropenem doripenem	<b>Drugs used solely to treat tuberculosis or other mycobacterial diseases</b> isoniazid ethambutol pyrazinamide ethionamide	<b>Glycopeptides</b> vancomycin	<b>AVOID</b>
	<b>Ketolides</b> telithromycin	<b>Lipopeptides</b> daptomycin		<b>Glycylcyclines</b> tigecycline	
	<b>Monobactams</b> aztreonam	<b>Oxazolidinones</b> linezolid		<b>Phosphonic acid derivates</b> fosfomicin	
	<b>Rifamycins (except rifaximin)</b> rifampicin	<b>Riminoferazines</b> clofazimine	<b>Other cephalosporins and penems (ATC code J01DI), including combinations of 3rd-generation cephalosporins with beta lactamase inhibitors</b> ceftobiprole ceftaroline ceftolozane-tazobactam faropenem	<b>Pseudomonic acids</b> mupirocin	
	<b>Carboxypenicillin and ureidopenicillin, including combinations with beta lactamase inhibitors</b> piperacillin-tazobactam	<b>Sulfones</b> dapsona		<b>Substances newly authorised in human medicine following publication of the AMEG categorisation</b> to be determined	
<b>B</b>	<b>Cephalosporins, 3rd- and 4th-generation, with the exception of combinations with β-lactamase inhibitors</b> cefoperazone cefovecin cefquinome ceftiofur	<b>Polymyxins</b> colistin polymyxin B	<b>Quinolones: fluoroquinolones and other quinolones</b> cinoxacin danofloxacin difloxacin enrofloxacin flumequine ibafloxacin		<b>RESTRICT</b>
<b>C</b>	<b>Aminoglycosides (except spectinomycin)</b> amikacin apramycin dihydrostreptomycin framycetin gentamicin kanamycin neomycin paromomycin streptomycin tobramycin	<b>Aminopenicillins, in combination with beta lactamase inhibitors</b> amoxicillin + clavulanic acid ampicillin + sulbactam	<b>Amphenicols</b> chloramphenicol florfenicol thiamphenicol	<b>Macrolides</b> erythromycin gamithromycin oleandomycin spiramycin tildipirosin tilmicosin tulathromycin tylosin tylvalosin	<b>CAUTION</b>
		<b>Cephalosporins, 1st- and 2nd-generation, and cephamycins</b> cefacetrile cefadroxil cefalexin cefalonium cefalotin cefapirin cefazolin	<b>Lincosamides</b> clindamycin lincomycin pirlimycin		
			<b>Pleuromutilins</b> tiamulin valnemulin	<b>Rifamycins: rifaximin only</b> rifaximin	
<b>D</b>	<b>Aminopenicillins, without beta-lactamase inhibitors</b> amoxicillin ampicillin metampicillin	<b>Aminoglycosides: spectinomycin only</b> spectinomycin	<b>Sulfonamides, dihydrofolate reductase inhibitors and combinations</b> formosulfathiazole phthalylsulfathiazole sulfacetamide sulfachlorpyridazine sulfaclozine sulfadiazine sulfadimethoxine sulfadimidine sulfadoxine sulfafurazole sulfaguandine	<b>Nitroimidazoles</b> metronidazole	<b>PRUDENCE</b>
	<b>Tetracyclines</b> chlortetracycline doxycycline oxytetracycline tetracycline	<b>Anti-staphylococcal penicillins (beta-lactamase-resistant penicillins)</b> cloxacillin dicloxacillin nafcillin oxacillin	<b>Cyclic polypeptides</b> bacitracin	<b>Nitroimidazoles</b> metronidazole	
	<b>Natural, narrow-spectrum penicillins (beta lactamase-sensitive penicillins)</b> benzathine benzylpenicillin benzathine phenoxymethylpenicillin benzylpenicillin penethamate hydriodide	<b>Anti-staphylococcal penicillins (beta-lactamase-resistant penicillins)</b> pheneticillin phenoxymethylpenicillin procaine benzylpenicillin	<b>Steroid antibacterials</b> fusidic acid	<b>Nitroimidazoles</b> metronidazole	

**Other factors to consider**

The **route of administration** should be taken into account alongside the categorisation when prescribing antibiotics. The list below suggests routes of administration and types of formulation ranked from the lowest to the highest estimated impact on antibiotic resistance.



- Local individual treatment (e.g. udder injector, eye or ear drops)
- Parenteral individual treatment (intravenously, intramuscularly, subcutaneously)
- Oral individual treatment (i.e. tablets, oral bolus)
- Injectable group medication (metaphylaxis), only if appropriately justified
- Oral group medication via drinking water/milk replacer (metaphylaxis), only if appropriately justified
- Oral group medication via feed or premixes (metaphylaxis), only if appropriately justified





**OCTOBER 22, 2020**

EMA [marks 25 years](#) of work to protect public and animal health with a virtual conference. Since its establishment in 1995, the Agency has harmonised and improved the evaluation of medicines, stimulated innovation, improved safety monitoring and risk management, fostered transparency and dialogue, built relationships with international partners and helped to make medicines accessible to those who need them.

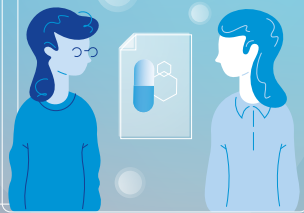
## Responsible use of antibiotics – What's your role? – European Antibiotic Awareness Day 2020

On the occasion of European Antibiotic Awareness Day in 2020, EMA highlighted the importance of using antibiotics responsibly in a social media campaign. The Agency also developed a set of info-cards that focuses on what patients, healthcare professionals, veterinarians, health leaders, journalists and the pharmaceutical industry in their respective roles can do to make sure that these important medicines are used wisely.

### Responsible use of antibiotics: what's your role?

As a **healthcare professional** you can explain to your patients that taking antibiotics and antimicrobial resistance are related.

Keep track of the most up-to-date clinical guidelines and antibiotics product information.



EUROPEAN MEDICINES AGENCY  
EMA

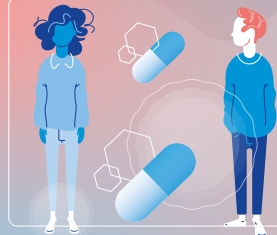
#EAAD #AMR #AntimicrobialResistance

### Responsible use of antibiotics: what's your role?

As a **patient** you should use antibiotics only when and as prescribed by your doctor.

Talk to your doctor or pharmacist for more information.

Never share antibiotics that were prescribed to you!



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#EAAD #AMR #AntimicrobialResistance

### Responsible use of antibiotics: what's your role?

As a **patient**, by using antibiotics responsibly you can protect people who are especially vulnerable to infections.

- ▶ Pregnant women and newborns
- ▶ Older people
- ▶ Cancer patients
- ▶ Patients who have undergone a transplant
- ▶ People living with immunodeficiency



EUROPEAN MEDICINES AGENCY  
EMA

#EAAD #AMR #AntimicrobialResistance

### Responsible use of antibiotics: what's your role?

Antibiotics don't work against viral infections. Don't use them to treat a cold or flu.

Always complete the prescribed course of antibiotics and never share them!



EUROPEAN MEDICINES AGENCY  
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#EAAD #AMR #AntimicrobialResistance

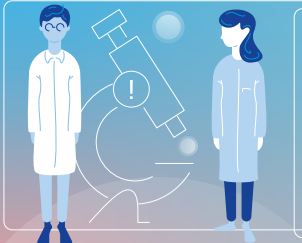
#### SEPTEMBER 23, 2020

EMA holds a [workshop](#) with the Patients' and Consumers' Working Party (PCWP) and Healthcare Professionals' Working Party (HCPWP) on the application of the General Data Protection Regulation (GDPR) in the area of health and secondary use of data for medicines and public health purposes.

#### SEPTEMBER 24, 2020

EMA publishes its draft [Guideline on registry-based studies](#) for a three-month public consultation.

**Responsible use of antibiotics: we all have a role**



The world needs new antibiotics and new tools to monitor antimicrobial resistance.

**Pharmaceutical companies** need to boost their research and development efforts.



#EAAD #AMR #AntimicrobialResistance

**Responsible use of antibiotics: what's your role?**

As a **veterinarian** you can promote the responsible use of antibiotics with animal owners.

Keep track of the most up-to-date clinical guidelines and report lack of or reduced effectiveness.



#EAAD #AMR #AntimicrobialResistance

**Responsible use of antibiotics: what's your role?**



**Global health leaders** and decision-makers can increase incentives for new antibiotics and reward companies that develop them.

Join the global coalition combating antimicrobial resistance through a 'One Health' approach.



#EAAD #AMR #OneHealth #ICMRA

**Responsible use of antibiotics: what's your role?**

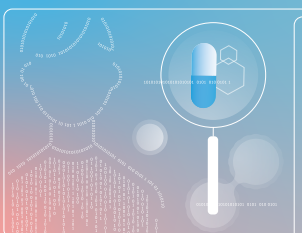
**Global medicines regulators** have a role in combating antimicrobial resistance.

Join our efforts to work towards safe, effective, and innovative solutions to antimicrobial resistance.



#AMR #AntimicrobialResistance #ICMRA

**Responsible use of antibiotics: what's your role?**



Continued **research** in all aspects of antimicrobial resistance is crucial for fighting superbugs.

Continuous monitoring of the effectiveness of existing antimicrobial agents and active surveillance of emerging antimicrobial resistance is a key task in this fight.



#AMR #AntimicrobialResistance #ICMRA

**Responsible use of antibiotics: what's your role?**

People need to be aware of the risks of antimicrobial resistance.

As a **journalist**, you can join the fight by keeping antimicrobial resistance at the forefront of the news cycle to increase public attention to this global health threat.



#AMR #AntimicrobialResistance #ICMRA



**SEPTEMBER 29, 2020**

EMA hosts a [workshop](#) on the General Data Protection Regulation (GDPR) and secondary use of data for medicines and public health purposes.



**OCTOBER 01, 2020**

EMA's human medicines committee ([CHMP](#)) starts the first 'rolling review' of a [COVID-19 vaccine](#), which is being developed by the company AstraZeneca in collaboration with the University of Oxford.



# I BREXIT AND RELOCATION

## Move to Amsterdam

In January 2020, EMA relocated to its new permanent headquarters in the Zuidas business district of Amsterdam. This marked the end of the Agency's physical relocation from London to Amsterdam, which had started in March 2019 in a temporary building in Amsterdam Sloterdijk made available by the Dutch government.

EMA's permanent premises, a tailor-made building with approximately 33,000 square metres and 1,300 working spaces, was commissioned by the Dutch government and built by the Central Government Real Estate Agency (CGREA) with a consortium of construction companies. The building was completed in record time: it took a little over two years between the decision in November 2017 of the EU Member States to

relocate EMA to Amsterdam, following the United Kingdom's decision to leave the EU, and the move-in of EMA staff at the beginning of January 2020.

At the beginning of February 2020, EMA staff gathered in the lobby to raise again the EU flags, thus closing the chapter of its relocation to the Netherlands.



### OCTOBER 29, 2020

EMA hosts a [symposium](#) to discuss new approaches to facilitating and using input from cancer patients to inform medicine development and regulatory decision-making.



### OCTOBER 30, 2020

EMA implements two [extra transparency](#) measures for [COVID-19](#) medicines, by publishing both the clinical data in support of the authorisation of [Veklury](#) (remdesivir) and information on the [COVID-19 treatments](#) and vaccines that have received [scientific advice](#) or informal guidance from [EMA's pandemic Task Force \(COVID-ETF\)](#).

## Preparing for Brexit

The UK formally left the EU on 31 January 2020 and became a third country (a country outside the European Union and European Economic Area). The EU-UK Withdrawal Agreement provided for a transition period ending on 31 December 2020, during which EU pharmaceutical law continued to apply to the UK. Throughout 2020, the UK therefore continued to receive all documentation from EMA procedures, and the procedures carried out at EU-level applied to the UK. The UK also kept access to all EMA systems and databases.

The most immediate change of the UK's departure was that as of 1 February 2020, delegates representing, appointed by or nominated by the UK could no longer participate in any EMA scientific committee or working party meetings, or in the Agency's Management Board.

As part of Brexit preparedness planning, EMA and the EU27 Member States had anticipated the loss of UK experts in their day-to-day operations. Since July 2019, the portfolio of medicines previously managed by the UK was already fully under the responsibility of new rapporteurs and co-rapporteurs from other EU Member States, Iceland and Norway.

From May 2017, EMA, the European Commission and national competent authorities in Member States worked closely together to minimise the impact of Brexit on the supply of medicines. This work continued throughout 2020 as the end of the transition period drew to a close. Companies were advised on how to apply for and implement the necessary regulatory changes so that their medicines could remain on the EU market after Brexit and were encouraged to plan and take action early.

By November 2020, as was required to ensure a smooth transition, all MAHs for centrally authorised medicines previously based in the UK had moved to an EU Member State. Most MAHs had made the necessary changes, notably as regards the relocation of qualified persons for pharmacovigilance (QPPVs) and pharmacovigilance master files (PMFs), by the end of 2020. Thanks to early planning and good anticipation of the changes needed, no medicine shortage occurred.



### NOVEMBER 06, 2020

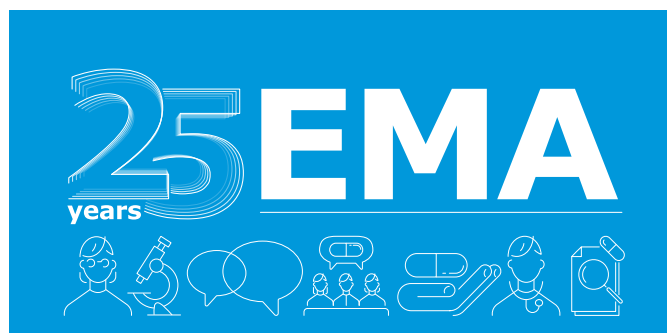
EMA endorses a statement jointly developed by the [International Coalition of Medicines Regulatory Authorities \(ICMRA\)](#) and the [World Health Organization \(WHO\)](#) that have [committed to working together](#) to ensure that patients have access to safe and effective medicines against COVID-19 as early as possible, while the existing rigorous scientific standards for the evaluation and safety monitoring of treatments and vaccines are maintained at all times.

# I EMA'S 25<sup>TH</sup> ANNIVERSARY

In 2020 EMA celebrated its 25<sup>th</sup> anniversary. Since the Agency's creation on 26 January 1995, the environment in which EMA operates has undergone fundamental scientific, technological, legislative and social changes. But its mission has remained: bringing the best experts from around the EU together to create an efficient and robust system for the evaluation and supervision of human and veterinary medicines that serves citizens throughout the EU. This has allowed EMA to remain agile and adapt to continuous extensions of its legal mandate and to [deliver for public and animal health](#) in Europe.

## 25 years of advancing public and animal health

To mark its 25th anniversary, EMA organised a series of events in 2020 together with its stakeholders. Due to the pandemic restrictions, not all planned events could take place. The meetings and conferences that could not be cancelled were held virtually, underlining EMA's successful transition into an online-based meeting environment.



### Programme of events to celebrate EMA's 25<sup>th</sup> anniversary

- **2-3 April 2020** - [International awareness session on science and regulation for animal health and welfare, public health and the environment](#);
- **22 September 2020** - [Workshop on benefit-risk of medicines used during pregnancy and breastfeeding](#);
- **22 October 2020** - [25 Years of EMA: building, learning and adapting to new challenges](#);
- **29 October 2020** - [EMA 25th anniversary symposium: New approaches in patient-focused cancer drug development](#);
- **30 November 2020** - [Workshop on regulatory support for development of orphan medicines](#).



#### NOVEMBER 13, 2020

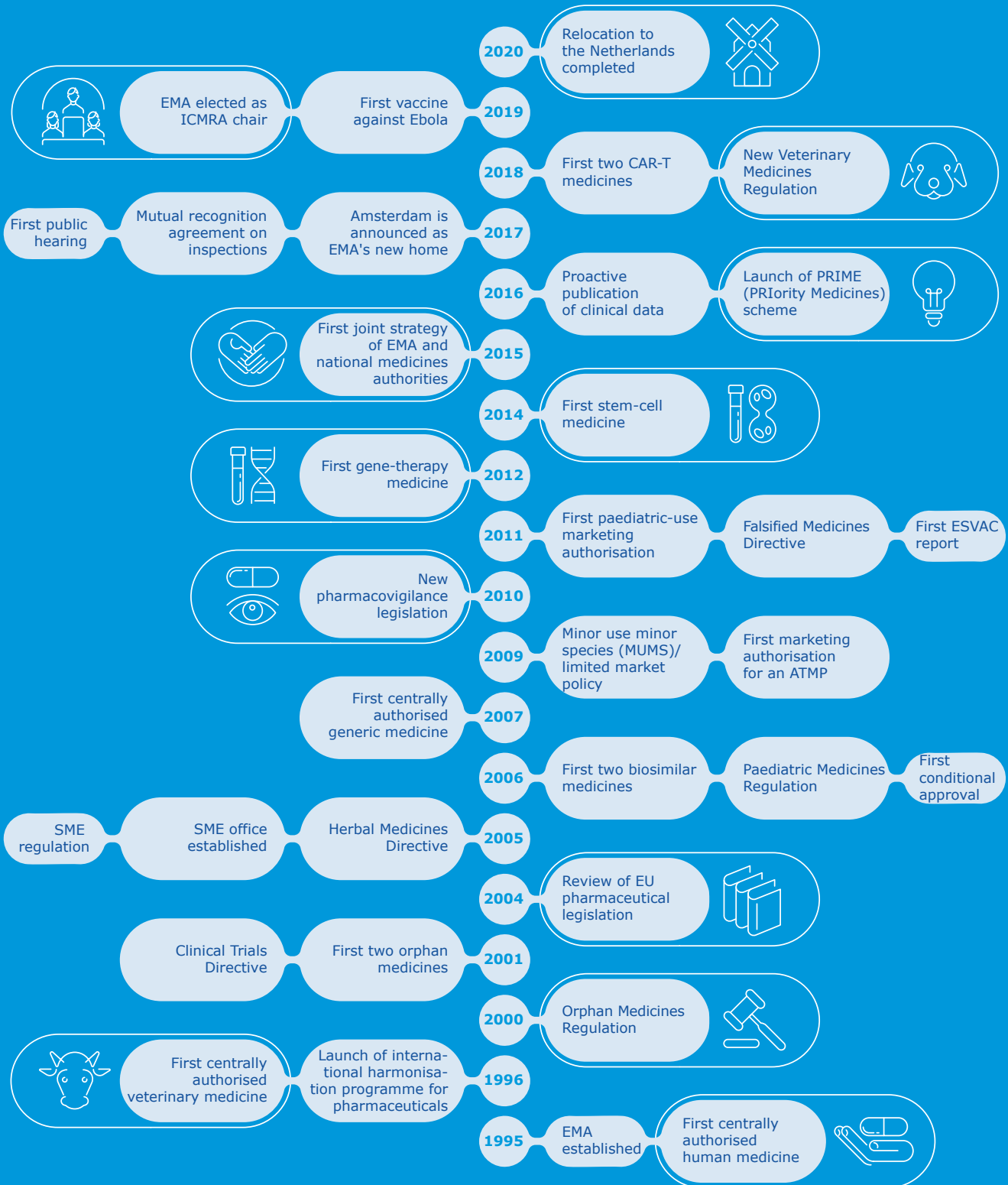
EMA's human medicines committee (CHMP) aligns recommendations for limiting [nitrosamine impurities](#) in sartan medicines with recent [recommendations](#) it issued for other classes of medicines.



#### NOVEMBER 13, 2020

EMA publishes a message from EMA's outgoing [Executive Director](#), Guido Rasi, on his last day as Executive Director of EMA. He emphasised that his mandate comes to an end in the middle of the biggest [public health emergency](#) in a century.

## 25 YEARS OF ADVANCING PUBLIC AND ANIMAL HEALTH - TIMELINE



**NOVEMBER 13, 2020**

EMA publishes a [safety monitoring plan and guidance on risk management planning for COVID-19 vaccines](#) prepared with the [national competent authorities](#) (NCAs) in EU Member States.



**NOVEMBER 16, 2020**

Emer Cooke begins her mandate as [Executive Director](#) of EMA.

The main anniversary event in 2020 was a virtual conference titled '[25 Years of EMA: building, learning and adapting to new challenges](#)', organised on 22 October 2020. The aim of the meeting was to highlight key achievements and learnings from recent years as well as to elaborate further on

key strategic areas looking forward, given the challenges and continually evolving landscape.

EMA's 25<sup>th</sup> anniversary coincided with anniversaries in a number of policy areas of EMA.

## 20 years of orphan medicines regulation

December 2020 marked the 20<sup>th</sup> anniversary of the [Orphan Regulation](#). The EU's orphan designation programme offers incentives to encourage the development of medicines that otherwise would not be developed to help diagnose and treat patients with rare diseases. These are often debilitating and life-threatening diseases that place a huge burden on the patients, their families and carers, and represent an enormous challenge for countries' public health systems.

Since the EU orphan regulation entered into force in 2000, EMA has given orphan status to over 2,300 medicines. By the end of 2020, 192 medicines with orphan status received a marketing authorisation. The European Commission completed an evaluation of the Regulation in August 2020. It has been an EU success story and it is delivering in public health terms. It has helped many, but many disease areas have still not attracted sufficient attention and more dedicated research is needed to help patients to access new or better treatments. The findings

from this evaluation are being considered as part of the recently launched Pharmaceutical Strategy for Europe.

On 30 November 2020, EMA held a workshop with academia, companies, patients and healthcare professionals. The aim was to review and raise awareness of the range of currently available development support tools and encourage early and efficient interactions with the regulators. A [meeting report](#) outlines the key findings.

With the establishment of the [Committee for Orphan Medicinal Products](#) (COMP) in 2000, EMA opened its doors to patients and healthcare professionals and their contributions. Today, representatives of patients, healthcare professionals and civil society take part in most of EMA's scientific committees as full members, adding their unique perspective and experiences to the debate. They play an increasingly important role in the assessment of the risks and benefits of medicines.



### NOVEMBER 16, 2020

EMA's human medicines committee (CHMP) starts a '[rolling review](#)' of data on a [vaccine for COVID-19](#) known as mRNA-1273, which is being developed by Moderna Biotech Spain, S.L. (a subsidiary of Moderna, Inc.).



### NOVEMBER 18, 2020

EMA marks [European Antibiotic Awareness Day](#), the annual European Union initiative to raise awareness of [antimicrobial resistance](#) as an increasing global public health threat and to promote the prudent use of antibiotics.

## 15 years of SME regulation

The 15<sup>th</sup> anniversary of the implementation of the [SME regulation](#) was another policy milestone in 2020. EMA held a virtual round-table meeting with stakeholders on 27 November 2020 to mark the introduction of this successful initiative.

The objectives of the meeting were to:

- provide an update on EU support for small and medium-sized enterprises (SMEs);
- highlight the achievements of [EMA's SME initiative](#);
- present the [results of an SME survey](#) launched by the Agency in 2020;

- exchange views on achievements, challenges and future opportunities to support SMEs and innovation in the pharmaceutical sector.

Representatives of the European Commission, the European Investment Bank (EIB), the EU Agencies Network, industry organisations representing SMEs and service providers in the human, veterinary and med-tech sectors participated in the round-table meeting. The outcomes of the discussion are summarised in a [meeting report](#).

## 10 years of minor use minor species (MUMS)/limited market policy

In March 2020, EMA published a [report](#) looking at the main achievements of the [policy for classification and incentives for veterinary medicinal products indicated for MUMS/limited market](#) over the last ten years.

The MUMS/limited market policy is a joint activity between EMA and the European medicines regulatory network. It was established to stimulate the development of new veterinary medicines for minor species and for rare diseases in major species that would otherwise not be researched under current market conditions. The incentives provided by the policy include reduced data requirements as well as fee exemptions or reductions.

The experience over the last 10 years has shown that the MUMS/limited market scheme is successful in incentivising the development of new medicines or addition of new indications for existing medicines intended for MUMS/limited market. These medicines are starting to fill some gaps in animal health, meeting the objective of increasing availability of veterinary medicines.

The new [Veterinary Medicines Regulation \(EU\) 2019/6](#), which entered into force in January 2019 and will become applicable in January 2022, will introduce specific provisions in the EU legislation to further boost the development of new medicines for limited markets, building on the success of EMA's experience applying the MUMS/limited market policy over the last ten years.



### NOVEMBER 20, 2020

EMA and the [Heads of Medicines Agencies \(HMA\)](#) encourage [marketing authorisation holders](#) to submit their applications through the [centralised procedure](#) in order to ensure that those vaccines reach all Member States at the same time, with no unfair access in the Union.



### NOVEMBER 27, 2020

EMA holds a multi-stakeholder [webinar](#) to support the implementation of Article 117 of the Medical Devices Regulation (MDR) 2017/745 on drug-device combinations

# I PREPARING FOR THE FUTURE

In 2020, EMA made preparations to ensure that it was fit to tackle future scientific and technological challenges and able to deal with new responsibilities.

## Regulatory Science Strategy to 2025

EMA published its [Regulatory Science Strategy to 2025](#) in March 2020, following its adoption by the Management Board. Developed over two years in consultation with a wide range of stakeholders, including healthcare professionals, patients, the pharmaceutical industry, academia and regulatory bodies, the strategy aims at advancing regulatory science over the next five years, covering both human and veterinary medicines. It is the Agency's response to the dramatic acceleration of the pace of innovation in recent years and the need for regulators to be ready to support the development of increasingly complex human and veterinary medicines that combine different technologies.

The COVID-19 pandemic underlines the need for rapid and close engagement of all stakeholders and partners involved in the development and supervision of medicines in the EU and globally, which is one of the fundamental principles of this strategy. The learnings from this public health crisis and how the European medicines regulatory network dealt with it will be incorporated so that processes can be adapted in real time, where needed.

The strategy sets out key areas where new or enhanced engagement of the [EU network](#) is essential and where advances in regulatory science are necessary. It identifies strategic goals for such engagement for human and veterinary medicines and includes core recommendations and underlying actions to support these.

The five key goals of the strategy include:

- catalysing the integration of science and technology in medicine development;
- driving collaborative evidence generation – improving the scientific quality of evaluations;
- advancing patient-centred access to medicines in partnership with healthcare systems;
- addressing emerging health threats and availability/therapeutic challenges;
- enabling and leveraging research and innovation in regulatory science.

The goals, and the recommendations and actions stemming from them, aim to ensure that regulators can advance public health and that medicine regulation in the coming years is designed in a way that delivers optimal outcome for the European citizens.

Deliverables of the Regulatory Science Strategy continue to be embedded in EMA's multiannual work programmes and implementation plans of EMA's scientific committees, working parties and other groups involved in medicine evaluation.



### NOVEMBER 27, 2020

EMA [endorses a statement](#) by the [International Coalition of Medicines Regulatory Authorities \(ICMRA\)](#) that urges all stakeholders, including vaccines researchers and investigators, academia, regulators and the pharmaceutical industry, to continue [COVID-19](#) vaccine trials beyond the time when the pre-defined cases of COVID-19 disease for final analysis in a trial have been reached.



## Future-proofing EMA – organisational changes that came into effect in 2020

One of the first concrete outcomes of the Regulatory Science Strategy was the implementation of a new, more agile organisational structure to ensure that the Agency operates as efficiently as possible to deliver high-quality outputs for public and animal health. The changes were implemented in March 2020 and took into account the rapidly evolving landscape for pharmaceutical research and development that requires regulators to keep up with advances in science and technology and prepare for future challenges at an ever-accelerating pace. They were also driven by the need to recalibrate to a reduced workforce following the [relocation of the Agency to Amsterdam](#) in 2019, while also dealing with an increased workload due to the pandemic and the implementation of various new pieces of legislation extending the scope of EMA's activities.

The main, high-level changes were as follows:

Operations in the area of human medicines have been integrated into one [Human Medicines Division](#), which is now led by [Alexis Nolte](#). The structure of the [Veterinary Medicines Division](#), under the leadership of [Ivo Claassen](#), remains unchanged.

In addition, four mission-critical task forces were established to support the human and veterinary medicines divisions, bringing together expertise to drive transformational change in the following high-priority areas:

- The [Digital Business Transformation](#) task force is responsible for driving complex, digital change initiatives that have a profound impact on the strategy of EMA, its structure and operations in relation to the network, its partners and stakeholders. It includes adapting EMA operations to fundamental changes brought by legislative initiatives, digital technologies and global trends to meet stakeholders' needs and expectations throughout the phases of digital business transformation. [Zaide Frias](#) leads this taskforce.
- The [Data Analytics and Methods](#) task force is responsible for building up capability and capacity within EMA and across the network to deliver robust evidence for benefit-risk decision-making. This will be achieved through a series of projects and initiatives in line with the Big Data Steering Group workplan. These will strengthen [scientific advice](#) on products under development, underpin support to

### NOVEMBER 30, 2020

EMA holds a [workshop](#) to discuss the benefits and impact of early regulatory interactions and [incentives for the development of medicines for rare diseases](#).



### DECEMBER 01, 2020

EMA receives an application for [conditional marketing authorisation \(CMA\)](#) of Moderna COVID-19 vaccine.



[marketing authorisation](#) assessments and deliver expert methods advice and data analysis for medicines on the market. All this will be pursued in close cooperation with legal and data protection internal experts to guarantee compliance with data protection 'by design' and 'by default' principles. [Peter Arlett](#) heads this task force.

- The [Regulatory Science and Innovation](#) task force enables the continuous 'future-proofing' of the Agency and the network by addressing key scientific and technological trends and their translation through the development of EMA's [regulatory science strategy](#) (see above), planning and governance. It also seeks to offer an enhanced first point of contact service to developers, in particular [SMEs](#) and [academia](#). This task force is led by [Anthony Humphreys](#).

- The [Clinical Studies and Manufacturing](#) task force is responsible for developing and guiding Agency strategy at EU and global level to support the facilitation of clinical studies and manufacturing. [Fergus Sweeney](#) leads this task force.

Further reviews and operational changes were introduced in the course of 2020, with the aim of continually improving the quality of EMA's regulatory and scientific output and level of service for its stakeholders. This included the new structure of the Information Management Division, which came into effect on 1 July and aims to evolve the delivery and maintenance of information systems to be more customer-focused, agile, integrated and innovative and to provide stakeholders with the right information management tools, technologies and services to deliver quality medicines to EU citizens. The division is led by [Hilmar Hamann](#).

## Future-proofing: Legal aspects

Regular contacts with the European Data Protection Supervisor (EDPS), DG JUST and DG SANTE's Data Protection Coordinator were intensified in the second half of the year in respect of topics such as secondary uses of health data, use of real-world data in regulatory activities and use of cloud-based platforms and software.



### DECEMBER 08, 2020

EMA and the [Heads of Medicines Agencies](#) (HMA) publish their [joint strategy](#) for the next five years. It details how the European medicines regulatory network can continue to enable the supply of safe and effective medicines that meet patients' needs in the face of challenges posed by ever-accelerating developments in science, medicine, digital technologies, globalisation as well as emerging health threats, such as the COVID-19 pandemic.

## European medicines agencies network strategy to 2025

The Regulatory Science Strategy also fed into the overarching '[European medicines agencies network strategy to 2025](#)', which was developed together with the [Heads of Medicines Agencies](#) (HMA), and in consultation with the European Commission and stakeholders to guide the work carried out by the [European medicines regulatory network](#) in the coming years.

The strategy was published in December 2020, following its adoption by the EMA Management Board and HMA. The strategy details how the network can continue to enable the supply of safe and effective medicines that meet patients' needs in the face of challenges posed by ever-accelerating developments in science, medicine, digital technologies, globalisation as well as emerging health threats, such as the COVID-19 pandemic.

‘The COVID-19 pandemic has highlighted the pivotal role of medicine regulation for the protection of public health. Lack of availability of medicines, either because they are not marketed or due to supply disruptions, has shown to pose serious threats to patient and animal health, animal disease control programmes and sustainable livestock production. This strategy ensures that we join forces across the EU to effect tangible improvements for citizens’

**Emer Cooke**, EMA Executive Director



### DECEMBER 11, 2020

EMA holds the first in a series of [public meetings](#) to inform European citizens about the [EU regulatory processes for the approval of COVID-19 vaccines](#) and the Agency's role in their development, evaluation, approval and safety monitoring.

The 'European medicines agencies network strategy to 2025' outlines six priority areas for the network:

- the availability and accessibility of medicines;
- data analytics, digital tools and digital transformation;
- innovation;
- antimicrobial resistance and other emerging health threats;
- supply chain challenges;
- the sustainability of the network and operational excellence.

It identifies strategic goals for each of these areas, which will be translated into concrete actions in the detailed work plans of EMA and the [national competent authorities](#) in EU Member States in the coming five years. Lessons from some recent developments related to the COVID-19 pandemic have been incorporated and further learnings will continue to be taken into account in subsequent work plans on an ongoing basis.

The strategy was open for public consultation from July to September. The extensive and helpful feedback from the consultation, which captured input from a broad range of stakeholder groups, was carefully analysed and reviewed in order to refine and finalise the strategy. Details on the comments received and the network's analysis of these comments were also [published](#).

The strategy was developed in close collaboration with the European Commission and its key themes are aligned with those covered in the Commission's [Pharmaceutical Strategy](#) (see below), which will provide direction for future pharmaceutical policy for human medicines in the EU.

The network will review the strategy in 2022 to assess whether the goals and objectives remain appropriate, and to adjust them if necessary in the light of the changing environment and ongoing engagement with stakeholders.



#### DECEMBER 15, 2020

EMA held the first [EU Big Data Stakeholder Forum](#) to inform stakeholders and citizens about the work of the HMA-EMA Big Data Task Force and opportunities for stakeholder collaboration in this area.

## Building a European Health Union: EMA's new role in crisis preparedness and management

In 2020, EMA welcomed the European Health Union package proposed by the European Commission to strengthen the EU's preparedness for crisis situations and response. The proposals included a possible extension of EMA's mandate.

The Commission's proposal for an extended EMA mandate reflects and strengthens several of the structures and processes that the Agency had voluntarily and proactively established to respond to the COVID-19 crisis, for example the coordination of the monitoring of shortages of critical medicines and the creation of a scientific Emergency Task Force that can swiftly advise clinical trial sponsors and medicine developers during public health emergencies. The proposal acknowledged that the work done so far by the Agency together with the national medicines authorities has been effective.

The Commission also proposed a new role for EMA in the medical devices area, including two very specific tasks building on EMA's experience in setting up systems for the monitoring of medicines and working with scientific experts in

various clinical areas, as well as EMA's important role within the network in the implementation of the medical device legislation. These new tasks include monitoring and management of shortages of critical medical devices and the management of expert panels responsible for conducting the clinical evaluation of and providing advice with respect to high-risk medical devices and in vitro diagnostics.

Finally, the Commission proposed to strengthen the mandate of EMA by providing an explicit legal basis to access and analyse real-world healthcare data and by establishing, jointly with the European Centre for Disease Prevention and Control (ECDC), a vaccine safety and effectiveness monitoring platform.

An Extended Mandate Task Force (EMTF) was set up by the Agency's Executive Board in December 2020 to define the scope of the changes that EMA will have to introduce to implement the new legal mandate foreseen, to analyse the consequences of these changes and to draft a high-level roadmap for its implementation.



### DECEMBER 21, 2020

EMA recommends granting a [conditional marketing authorisation](#) for the first COVID-19 vaccine [Comirnaty](#), developed by BioNTech and Pfizer, to prevent COVID-19 in people from 16 years of age.

# CHAPTER 2

## KEY FIGURES IN 2020



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# I HUMAN MEDICINES

## Supporting research and development

EMA provides guidance and support to medicine developers. This includes scientific and regulatory information on how to design and run clinical trials, compliance standards, and obligations and incentives for developers of specialised medicines.

### Scientific advice

During a medicine's development, a developer can request 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. This is known as scientific advice.

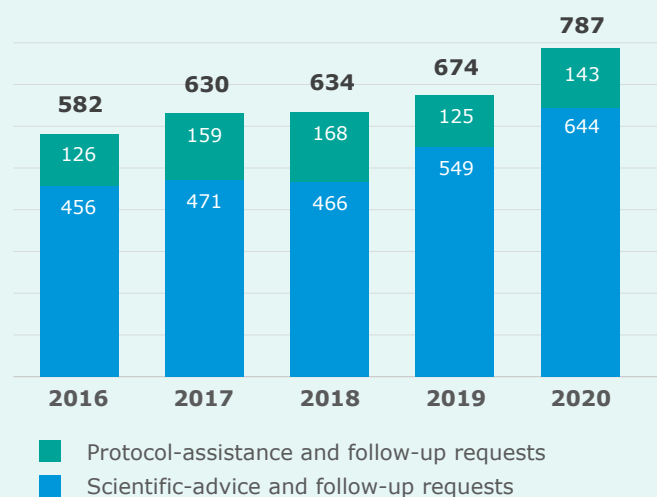
Scientific advice is one of the Agency's key instruments for supporting the development of high-quality, effective and safe medicines, for the benefit of patients. Early dialogue and scientific advice lead to better development plans, promote the collection of high-quality data, and most importantly, help to ensure that patients only take part in those clinical trials that are likely to be robust enough to generate data that are relevant to support the evaluation of a marketing authorisation application or extension of indication.

In 2020, EMA received a total of 565 requests for scientific advice, which represents an increase of 3% compared to 2019. In addition, 79 requests for scientific advice on COVID-19 development programmes were received.

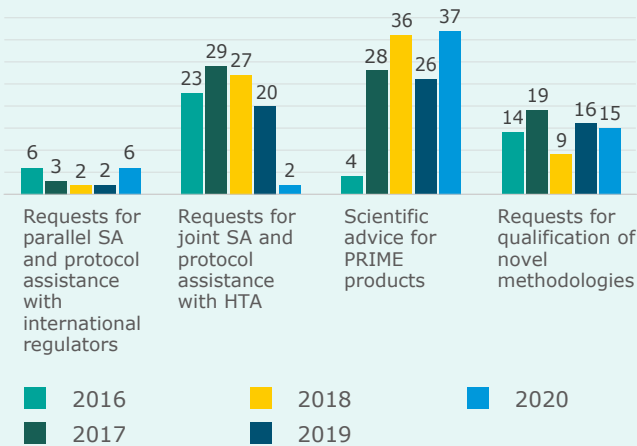
Protocol assistance is the special form of scientific advice for developers of designated orphan medicines for rare diseases. The requests for protocol assistance increased by 14%, from 125 requests in 2019 to 143 in 2020.

A total of 97 patients participated as experts in several scientific-advice procedures.

Scientific advice and protocol-assistance requests received - total



### Scientific advice and protocol-assistance requests received - special programmes

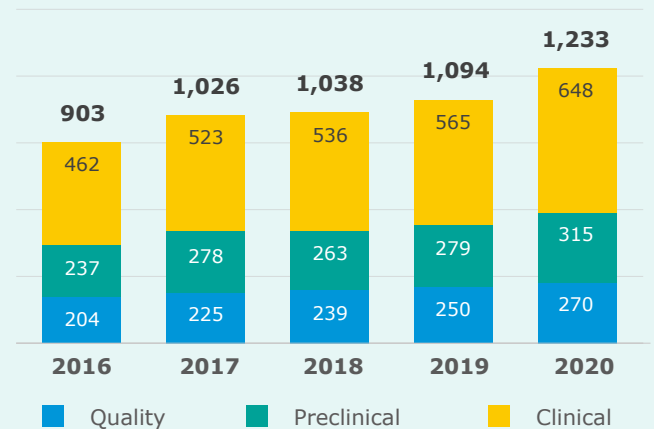


The qualification of novel methodologies leads to publicly available opinions on innovative methods validated for use in a specific pharmaceutical development context. EMA can also provide letters of support for methodologies that have not yet qualified but shown promise towards a potential future qualification. In 2020, there were 15 requests for such qualifications. Among the notable published opinions in 2020 was a Clinical Outcome Assessment (COA) instrument that served as an efficacy endpoint in clinical trials for multiple sclerosis drug development, and on recurrent event endpoints for clinical trials, which is relevant in several developments such as for chronic heart failure treatment.

Scientific advice is the core of many of EMA’s special programmes to encourage development and availability of new and innovative medicines. The Agency received 37 requests for scientific advice for PRIME products in 2020, the highest number since the scheme was launched in 2016. PRIME is EMA’s support scheme for early and enhanced dialogue with developers of promising new medicines that address an unmet medical need.

The requests for joint scientific advice and protocol assistance with HTA bodies dropped significantly due to reprioritisation of this activity by the European Network for Health Technology Assessment (EUnetHTA), in view of the COVID-19 pandemic. The two requests in 2020 were for orphan medicines, one in the blood and blood-forming organs and the other for nervous system therapeutic areas. One of them was also an advanced therapy medicinal product (ATMP).

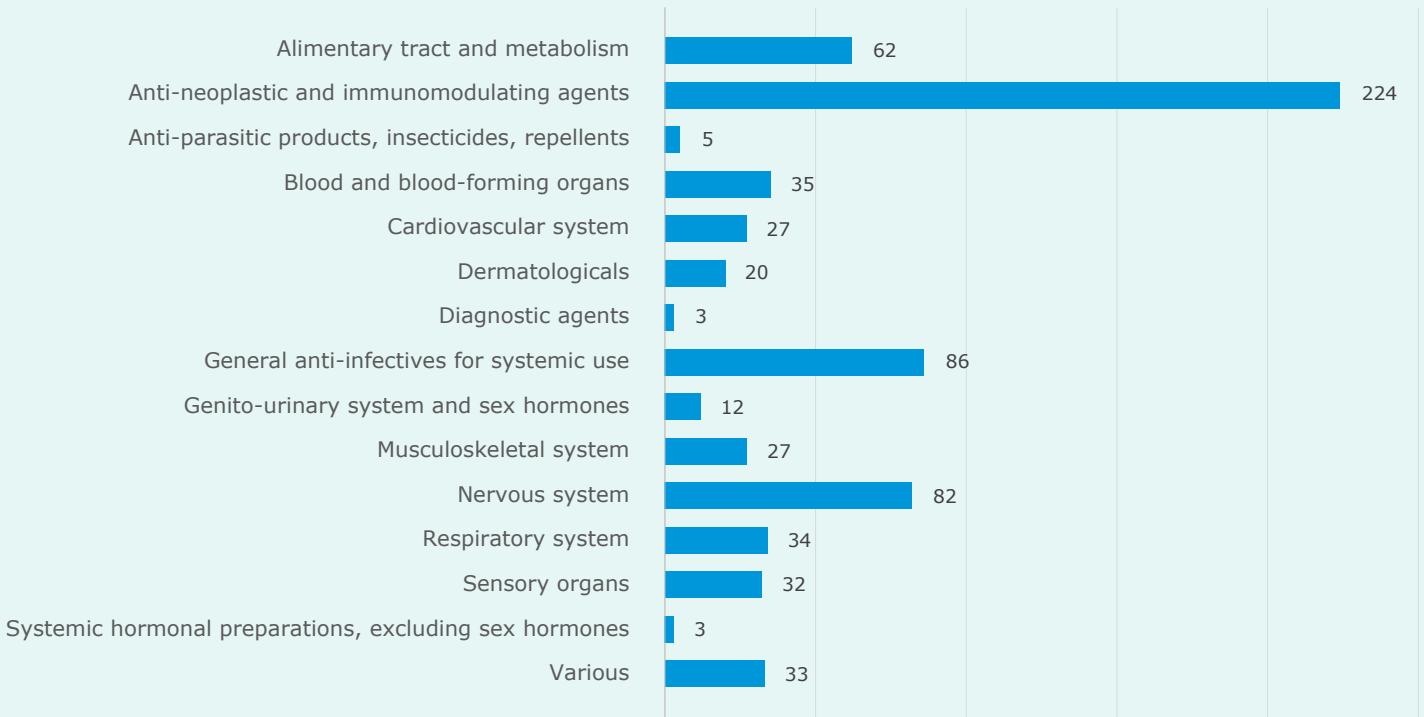
### Scientific advice requests by topic



As in previous years, more than half of the requests for scientific advice related to clinical issues, 26% to preclinical issues and 22% to quality issues. In terms of development stage, 60% of requests related to medicines in phase III, 27% to medicines in phase II, 11% to medicines in phase I and 2% to medicines in phase IV of their clinical development.



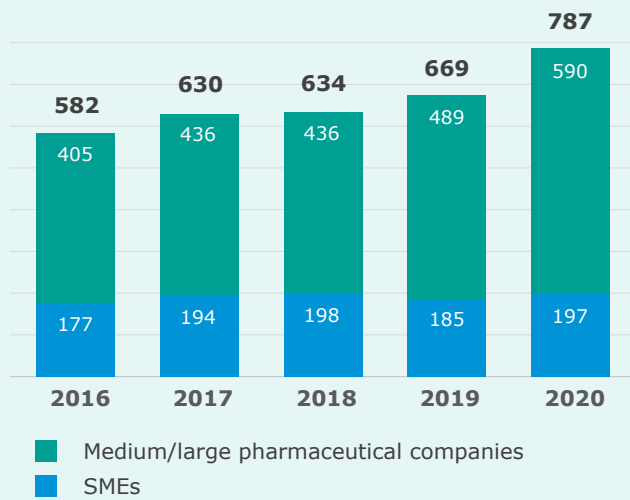
Scientific advice requests by therapeutic area\* (2020)



\* Excludes biomarker qualification as well as unclassified cases.

25% of the total number of requests came from SMEs.

Scientific advice requests by affiliation of requester



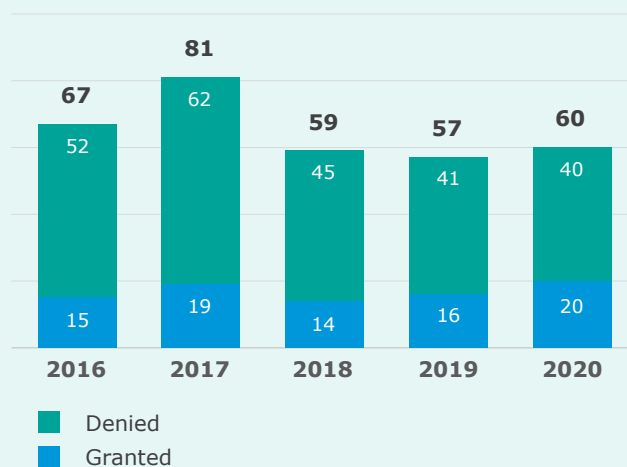
## PRIME

Launched in March 2016, PRIME aims to support and optimise medicine development so that patients who have no or only unsatisfactory treatments for their disease have access to new medicines that enable them to live healthier lives. In 2020, EMA received 69 PRIME eligibility requests and adopted 60 recommendations. Twenty medicines under development were included in the scheme in 2020.

PRIME eligibility requests increased by 15% in 2020 (69 requests received in 2020 compared to 60 in 2019).

PRIME is reserved for the most promising medicines and EMA focuses its attention on medicines that have the potential to bring a major therapeutic advantage. That is why only a limited number of applications (20 out of 60 in 2020) are accepted into the scheme. However, the rate of products granted access to the scheme has been increasing over recent years: from 23% in 2018 to 33% in 2020. 8 PRIME-designated medicines were recommended for approval (Blenrep, Rozlytrek, Tecartus, Givlaari, Hepcludex, Zolgensma, Idefirix and Oxlumo) in 2020.

**PRIME - eligibility recommendations**



## Support for SMEs

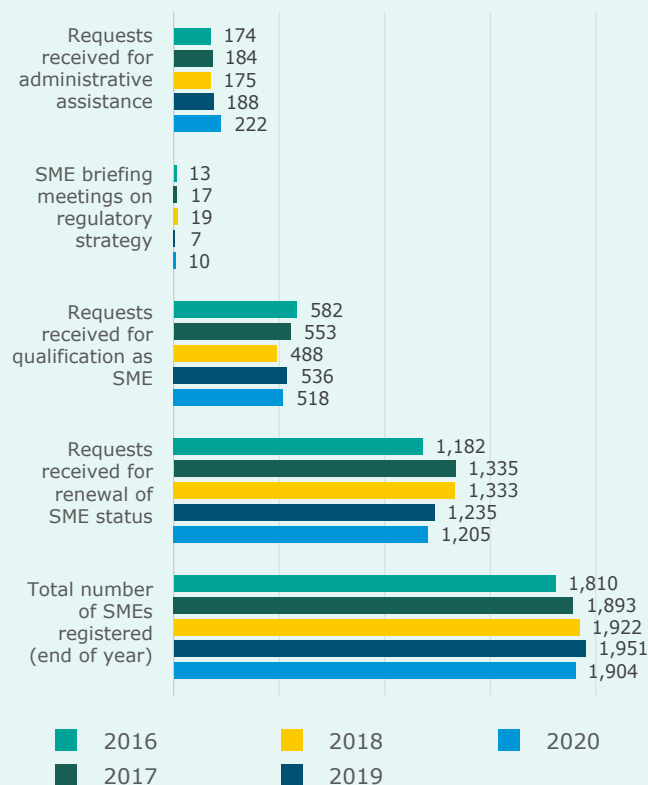
SMEs are recognised as a driver of innovation in the EU. The Agency promotes innovation and the development of medicines by SMEs through regulatory and administrative support to these companies. EMA put the SME initiative in place in 2005 to promote innovation and development of medicines by SMEs. The Agency's SME office provides advice and guidance, organises topical workshops and produces a dedicated newsletter for SMEs registered with EMA. These companies also have access to various fee incentives to support their medicine development programmes.

In 2020, the SME office received 222 requests for direct assistance on administrative or regulatory aspects and organised 10 briefing meetings to assist SMEs that were unfamiliar with the EU regulatory system. A total of 1,904 SMEs were registered at the Agency by the end of 2020.

In 2020, SMEs submitted 23 marketing authorisation applications, which is 19% of all applications received in 2020. Out of the 23 applications, 13 were for orphan-designated medicines.

The CHMP gave a positive opinion for 16 medicines developed by SMEs. This is the highest number in the past five years and represents 18% of all positive opinions in 2020. Half of the medicines developed by SMEs (8) contained a new active substance.

### SME-related activities - requests received (human and veterinary medicines)



### Initial evaluation applications and SMEs (human medicines)

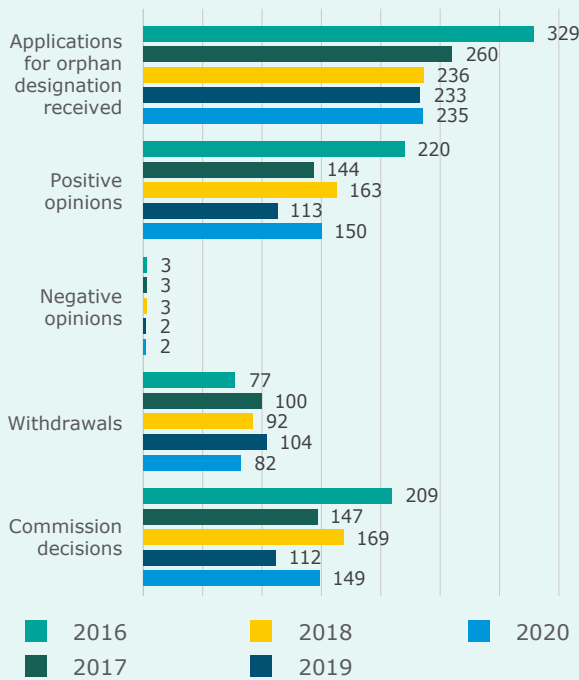
	2016	2017	2018	2019	2020
Initial marketing authorisation applications submitted by SMEs	27	20	15	24	23
Positive opinions	4	12	13	8	16
Negative opinions	1	2	5	1	1
Withdrawals	5	7	5	3	1

## Orphan medicine designation

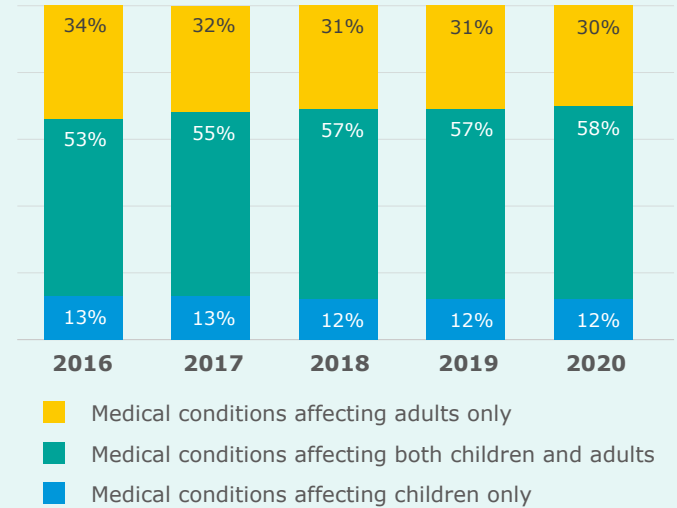
The EU framework for orphan medicines aims to encourage the development and marketing of medicines for patients with rare diseases by providing incentives for developers.

Medicines with an EU orphan designation benefit from ten years of market exclusivity if they are granted a marketing authorisation. During the development of an orphan medicine, other incentives such as a fee reduction for scientific advice (protocol assistance) are also available for medicine developers. EMA’s COMP is responsible for assessing orphan designation applications.

### Orphan medicine designation procedures



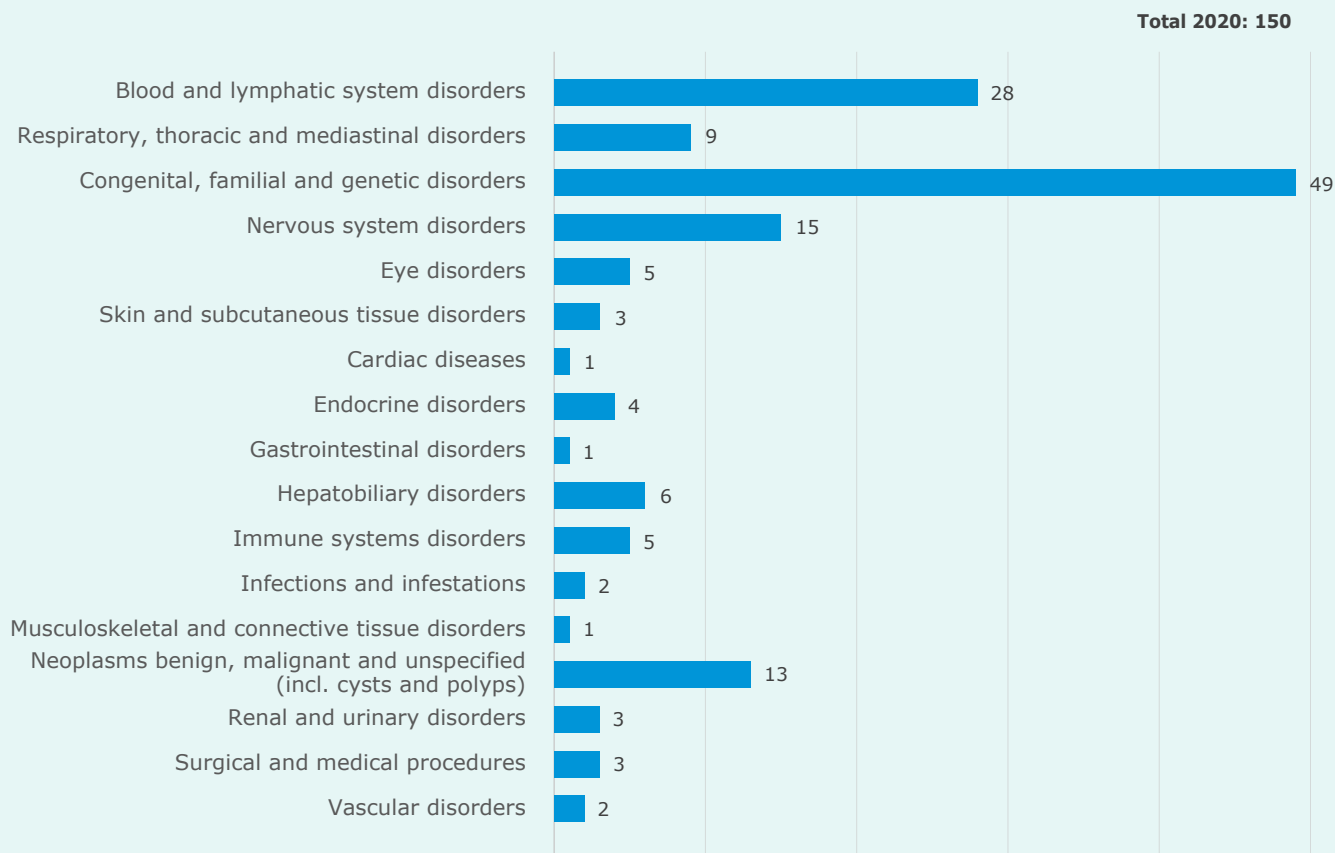
### Designated orphan medicines for the treatment of children and adults



The number of applications for orphan designation was 235 in 2020. Of these applications, 150 were granted a designation, allowing them to benefit from the incentives under the EU Orphan Framework. 82 applications were withdrawn and 2 received a negative opinion from the COMP.

The EC supported the development of medicines for rare diseases financially, with more than €11 million in 2020. More than 54% of the Commission’s special contribution was used to provide protocol assistance to medicine developers and more than 36% for the assessment of applications for marketing authorisation.

### Opinions on orphan designation by therapeutic area (2020)



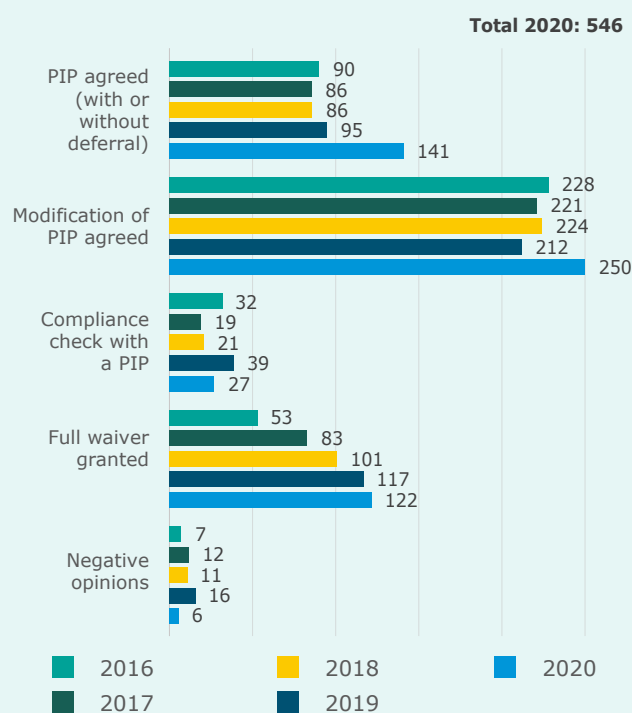
### Medicines for children

The Agency also promotes the development of medicines for children. EMA’s Paediatric Committee (PDCO) assesses and agrees PIPs as well as PIP waivers for medicines that are unlikely to benefit children. The committee also checks compliance with a PIP at the time of the submission of a marketing authorisation. To support research and development of medicines in children, EMA provides the secretariat for the European Network of Paediatric Research at EMA (Enpr-EMA).

A PIP is a development plan aimed at ensuring that the necessary data are obtained through studies in children to support the authorisation of a medicine for children. Where studies in children are inappropriate or unnecessary, a waiver may be granted. In 2020, the PDCO agreed 141 initial PIPs, the highest number in the past five years.

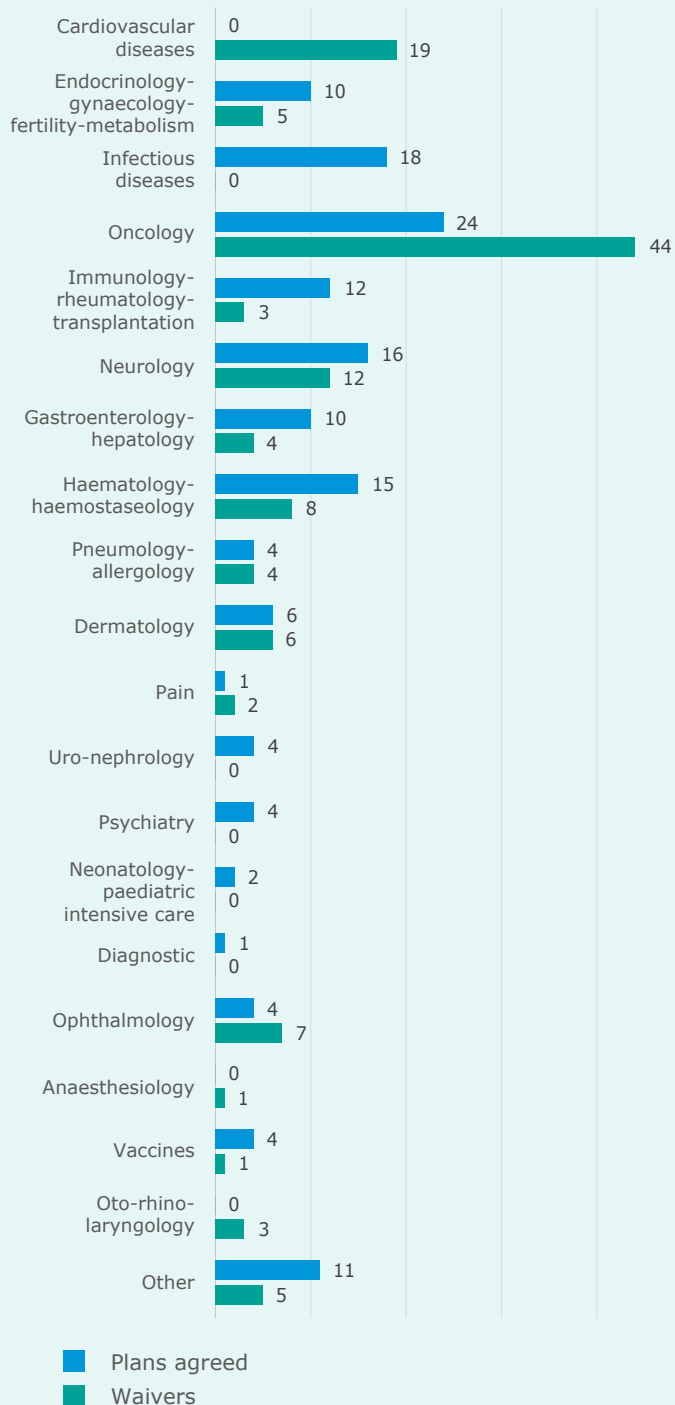
Requests for scientific advice on paediatric issues decreased by 9%, from 161 requests in 2019 to 147 in 2020.

### Opinions on PIPs and waivers



Article 46 of the Paediatric Regulation requires MAHs to submit studies on the use of medicines already authorised in children to regulatory authorities. This ensures that all paediatric studies are assessed by the relevant competent authorities. In 2020, EMA assessed 129 paediatric studies in the context of Article 46. These studies are available to the public through the EU Clinical Trials Register.

### Paediatric investigation plans agreed and waivers granted (2020)

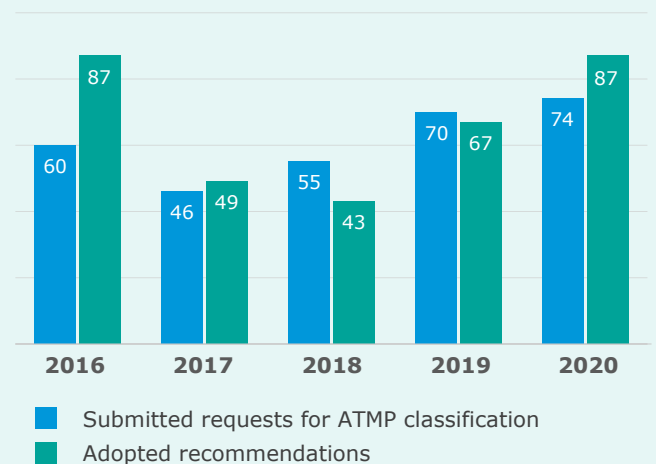


### Advanced-therapy medicinal products

ATMPs are medicines based on genes or cells that have the potential for groundbreaking new treatments. They are particularly important for severe, untreatable or chronic diseases for which conventional approaches have proven to be inadequate.

The Committee for Advanced Therapies (CAT) is responsible for assessing the quality, safety and efficacy of ATMPs. It prepares a draft opinion on each ATMP application before the CHMP adopts a final opinion for the medicine concerned. The CAT also reviews requests for the certification of quality and non-clinical data for SMEs developing ATMPs and provides scientific recommendations on the classification of a medicine as an ATMP.

### Scientific recommendations on advanced therapy classifications



In 2020, the CAT received 74 requests for ATMP classification (6% more than in 2019) and adopted 87 recommendations, an increase of 30% compared to 2020. These figures confirm an upwards trend since 2017 and indicate a strong pipeline for the development of ATMP medicines in the future.

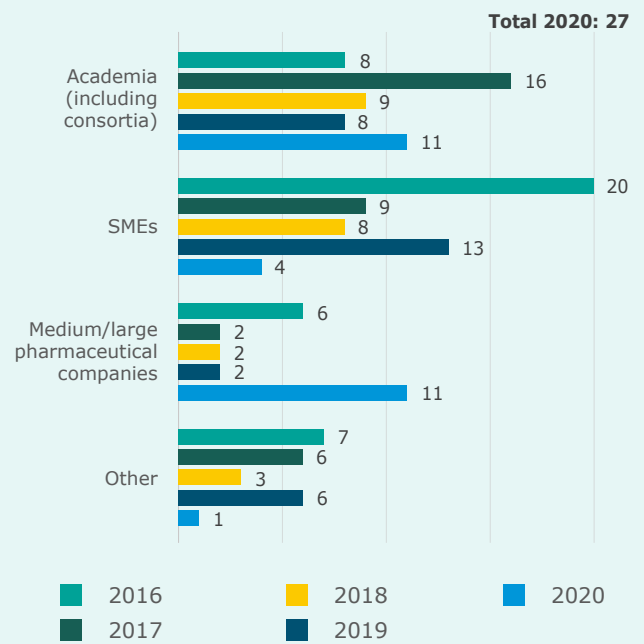
Three ATMPs were recommended for marketing authorisation by the CHMP in 2020: **Libmeldy**, for the treatment of metachromatic leukodystrophy; **Tecartus**, for the treatment of relapsed or refractory mantle cell lymphoma, and **Zolgensma**, for the treatment of spinal muscular atrophy.

## Innovation Task Force

The Innovation Task Force (ITF) is a multidisciplinary group that includes scientific, regulatory and legal competences. It provides a forum for early dialogue with applicants, in particular SMEs and academic sponsors, to proactively identify scientific, legal and regulatory issues linked to innovative therapies and technologies.

The Agency received 73 requests for briefing meetings in 2020 (compared to 35 in 2019) and held 27 meetings in 2020 (compared to 29 in 2020). 41% of these 27 meetings were attended by developers from academia and another 41% by medium or large pharmaceutical companies. 30% of the meetings concerned innovative methods to support the development of medicines, and 22% manufacturing technologies.

ITF briefing meetings by affiliation



## Key scientific guidelines

The Agency develops scientific guidelines to provide advice to applicants or MAHs, competent authorities and other interested parties on the most appropriate way to test and monitor the safety, efficacy and quality of medicines. The Agency's work on guideline development and revision continued to be suspended or scaled back due to focus on COVID-19.

Guidelines are drafted by EMA working parties comprised of experts from across Europe. The objective is to reflect the latest scientific developments and experience gained through scientific advice and the evaluation and monitoring of medicines.

A selection of reflection papers and guidance issued or revised in 2020 is listed below.

Topic	Content
<b>Guidance on the management of clinical trials during the COVID-19 pandemic</b>	The guidance provides concrete information on changes and protocol deviations which may be needed in the conduct of clinical trials to deal with extraordinary situations. It includes a harmonised set of recommendations, to ensure the utmost safety of trial participants across the EU while preserving the quality of the data generated by the trials.
<b>Questions and answers on regulatory expectations for medicinal products for human use during the COVID-19 pandemic</b>	The Q&A document outlines areas where regulatory flexibility is possible to address some of the constraints marketing authorisation holders may be faced with in the context of COVID-19. The measures introduced cover different areas of the regulation of medicines such as marketing authorisations and regulatory procedures, manufacturing and importation of active pharmaceutical ingredients and finished products, quality variations, and labelling and packaging requirements with flexibility to facilitate the movement of medicinal products within the EU.
<b>Consideration on core requirements for risk management plans (RMPs) for COVID-19 vaccines</b>	The RMP guidance for COVID-19 vaccines complements the <a href="#">existing guidelines on the RMP format in the EU</a> and guidance on <a href="#">good pharmacovigilance practices</a> , which apply to all medicines. Additional specific considerations in this guidance address, for example: <ul style="list-style-type: none"> <li>• further information on vaccine safety that might be generated after the marketing authorisation in special populations;</li> <li>• core requirements for lists of adverse events of special interest (AESI), methods used for signal detection, and follow-up of any safety signals identified in clinical trials;</li> <li>• submission of monthly summary safety reports.</li> </ul>



# Recommendations for marketing authorisation

## Applications for initial evaluation

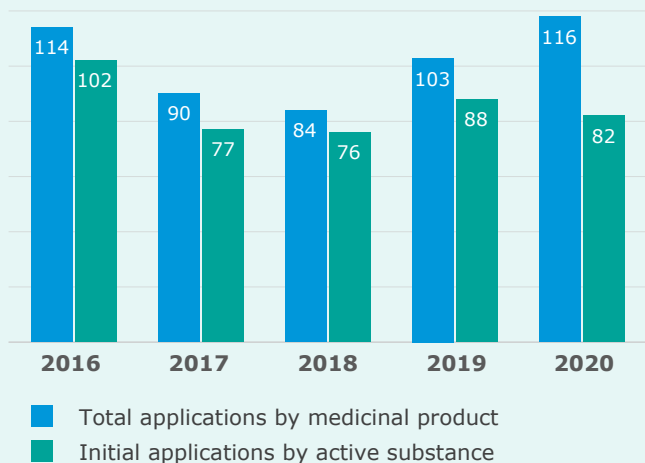
EMA’s scientific committees carry out robust scientific evaluations of medicines and issue recommendations for the EC, which ultimately decides whether or not to authorise a medicine for marketing throughout the EU.

The initial evaluation covers all activities relating to the processing of marketing authorisation applications for new medicines which have never been assessed before, from the pre-submission discussion with future applicants, through to the evaluation by the CHMP and the granting of the marketing authorisation by the EC.

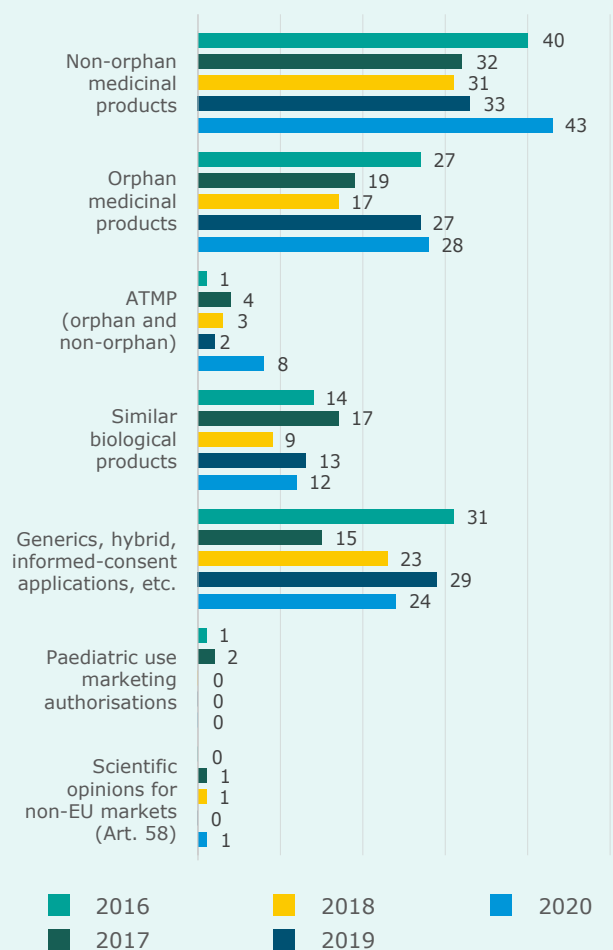
A total of 116 applications were received in 2020.

The number of applications for ATMPs increased significantly, from 2 in 2019 to 8 in 2020. This is the highest number in the past five years.

**Initial-evaluation applications**



**Initial-evaluation applications by type of application**



Note: Number of applications for initial evaluation corrected from the 2019 Annual Report, which counted 117 applications.

# Outcome of initial evaluation

## Medicines recommended for approval

### Cancer



- Aybintio ●
- Ayvakyt** ●●
- Bienrep** ●●●●
- Cabazitaxel Accord
- Daurismo** ●
- Enhertu** ●●
- Equidacent ●
- Lenalidomide Mylan
- Nubeqa**
- Nyvepria ●
- Onbevi
- Phelinun
- Phesgo**
- Piqray
- Retsevmo** ●
- Rozlytrek** ●●
- Sarclisa** ●
- Sunitinib Accord
- Tecartus** ●●●●
- Tukysa**
- Zercepac ●

### Haematology/ Haemostaseology



- Adakveo** ●●
- Arsenic trioxide medac
- Arsenic trioxide Mylan
- Azacitidine betapharm
- Azacitidine Mylan
- Calquence**
- Elzonris** ●●
- Inrebic** ●●
- Lenalidomide Krka
- Lenalidomide Krka d.d.
- Lenalidomide Krka d.d. Novo mesto
- Lumoxiti** ●●
- Reblozyl ●
- Ruxience ●

### Pneumology/ Allergology



- Arikayce liposomal ●
- Ateectura Breezhaler
- Bemrist Breezhaler
- Budesonide/Formoterol Teva Pharma B.V.
- Enerzair breezhaler
- Gencebok
- Kafrio** ●
- Palforzia
- Trepulmix ●
- Triexo Aerosphere
- Zimbus Breezhaler

### Endocrinology



- Cinacalcet Accordpharma
- Givlaari** ●●●●
- Insulin aspart Sanofi ●
- Kixelle ●
- Lyumjev
- Ogluo
- Rybelsus

### Immunology/ Rheumatology/ Transplantation



- Idefixir** ●●●●
- Jyseleca**
- Livogiva ●
- Nepexto ●
- Qutavina ●
- Yuflyma ●

### Infections



- Fetcroja
- Hepcludex** ●●●●
- Hepelisav B
- Obiltoxaximab SFL** ●●
- Dovprela** ●●
- (previously Pretomanid FGK)
- Rekamby
- Rukobia**
- Tigecycline Accord
- Vocabria**
- Xenleta**
- Xofluza**

### Neurology



- Fampridine Accord
- Fingolimod Accord
- Fintepla ●
- Libmeldy** ●●
- Zeposia
- Zolgensma** ●●●●

### Vaccines



- Fluad Tetra
- MenQuadfi
- Mvabea** ●●
- Supemtek**
- Vaxchora**
- Zabdeno** ●●

### Cardiovascular



- Apixaban Accord
- Leqvio
- Rivaroxaban Accord

### COVID-19



- Comirnaty** ●
- Veklury** ●

### Metabolism



- Nilemdo**
- Nustendi**

### Pain



- Zynrelef
- Exparel

### Uro-nephrology



- Oxlumo** ●●●●
- Sibnaya ●

### Diagnostic agents



- Methylthioninium chloride Cosmo

### Dermatology



- Staquis**

### Ophthalmology



- Roclanda

### Psychiatry

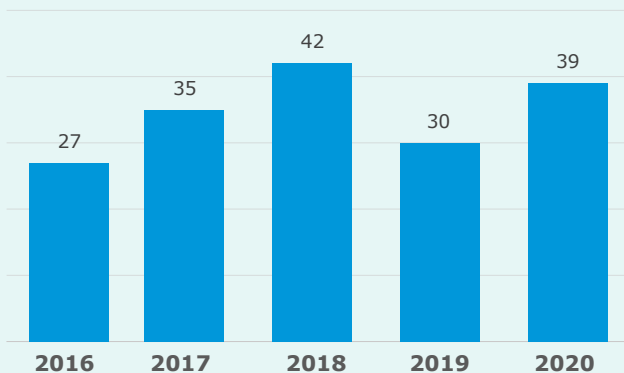


- Paliperidone Janssen-Cilag International

● PRIME ● ATMP ● Orphan medicine ● Accelerated assessment ● Conditional marketing authorisation  
 ● Approval under exceptional circumstances ● Biosimilar

Medicines that contain a new active substance are highlighted in bold

### Positive opinions - new active substances



In 2020, EMA recommended 97 medicines for marketing authorisation. Of these, 39 had a new active substance which had never previously been authorised in the EU.

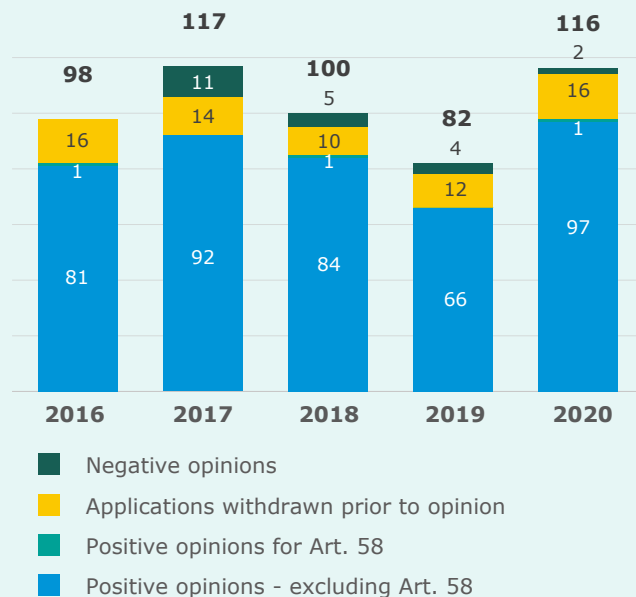
The CHMP adopted a negative opinion for two medicines in 2020: Gamifant and Turalio. This figure does not include the initial negative opinion adopted by the CHMP on Elzonris in July 2020. The applicant for this medicine requested re-examination of the Committee’s negative opinion and, after considering the grounds for this request, the CHMP recommended granting a marketing authorisation for Elzonris in November 2020.

The applications for 16 medicines were withdrawn by the applicants prior to the CHMP adopting an opinion, in most cases because the data included in the application were insufficient to support a marketing authorisation.

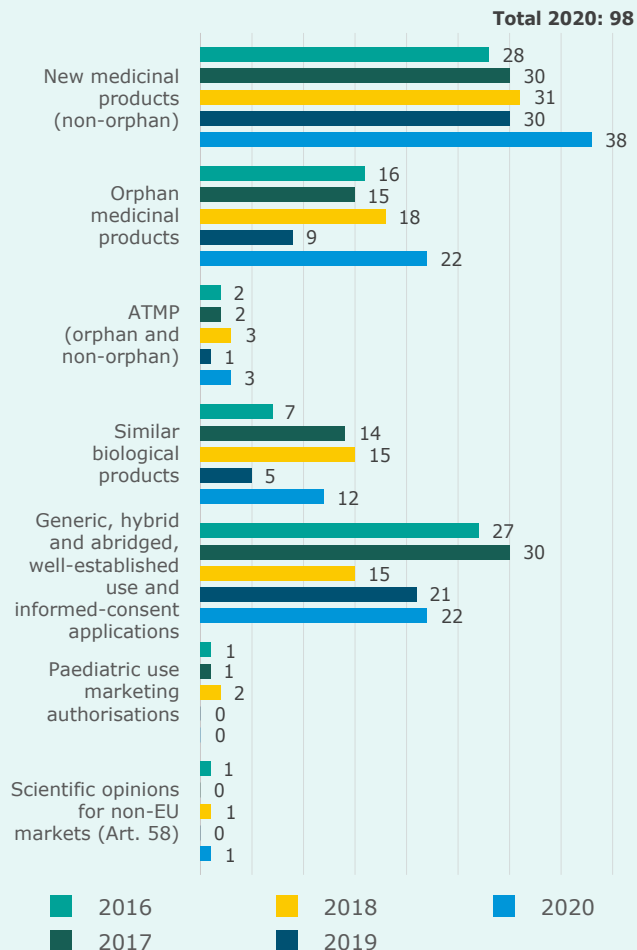
In July 2020, the CHMP adopted a positive opinion for Dapivirine Vaginal Ring, used to reduce the risk of infection with HIV-1. This is the 11<sup>th</sup> medicine recommended by EMA under EU Medicines for all (EU-M4All), a mechanism that allows the CHMP to assess and give opinions on medicines that are intended for use in countries outside the EU under Article 58 of Regulation (EC) No 726/2004.

Applicants for 70% of the medicines granted a positive opinion by the CHMP in 2020 had received scientific advice during the development phase of their medicine.

### Outcome of initial-evaluation applications



### Positive opinions by type of procedure



## Conditional marketing authorisations

In 2020, 13 medicines received a recommendation for a CMA, one of the possibilities in the EU to give patients early access to new medicines: Adakveo, Ayvakyt, Blenrep, Comirnaty, Enhertu, Hepcludex, Idefirix, Dovprela, Retsevmo, Rozlytrek, Tecartus, Veklury and Zolgensma.

As these medicines address unmet medical needs, the conditional authorisation allows for early approval on the basis of less complete clinical data than normally required (products for use in emergency situations may have less complete pharmaceutical or non-clinical data). These authorisations are subject to specific post-authorisation obligations to generate complete data on the medicines.

In 2020, two medicines (Bavencio and Ervebo) that had previously received a CMA were granted a recommendation for a full marketing authorisation by the CHMP after fulfilling its post-authorisation obligations.

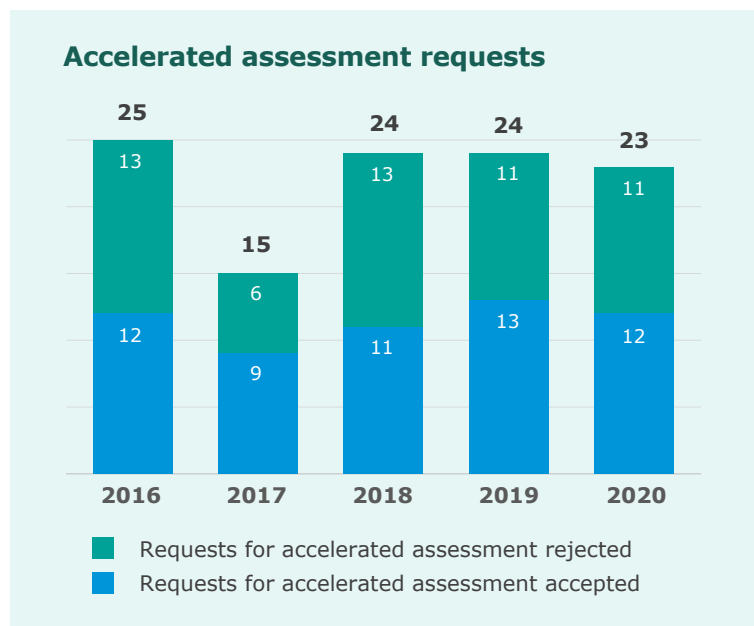
Since the introduction of CMAs in 2006, 23 medicines out of 59 have been granted a full marketing authorisation following a CMA. On average, it took around 3.5 years for companies to fulfil their post-authorisation obligations and get their products fully authorised.

CMA and switch to standard marketing authorisation (excluding withdrawals)					
	2016	2017	2018	2019	2020
Positive opinions for CMAs	8	3	1	8	13
Opinions recommending switch of CMA to standard marketing authorisation	2	5	2	1	2

## Accelerated assessment

Six medicines (Blenrep, Enhertu, Givlaari, Mvabea, Oxlumo and Zabdeno) received a recommendation for marketing authorisation following an accelerated assessment in 2020. This mechanism is reserved for medicines that can address unmet medical needs. It allows for faster assessment of eligible medicines by EMA’s scientific committees.

In 2020, 12 requests from applicants for accelerated assessment of their medicine were accepted and 11 were rejected. The main reasons for rejection were either that the unmet medical need the medicine was expected to address was not adequately justified or that the data provided did not justify the applicants’ claims that their products were of major public health interest.



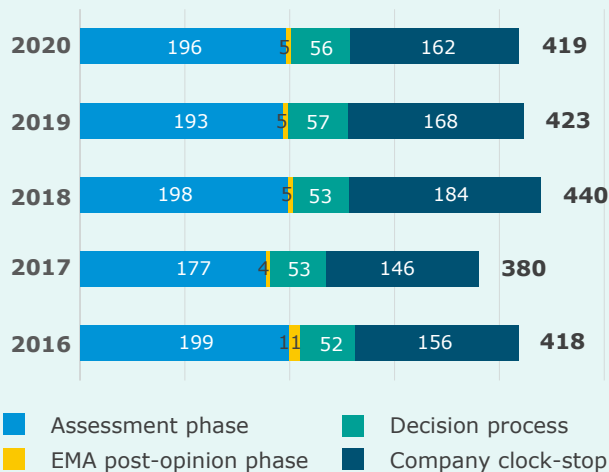
## Average assessment time

EMA has a maximum of 210 active days to carry out its assessment. Within this time frame, the CHMP must issue a scientific opinion on whether the medicine under evaluation should be authorised. During the assessment, concerns with the application may be identified requiring further information or clarification from the company. In this case, the clock is stopped to give the company time to reply to the Agency. Once the reply has been received, the timetable and counting of active days of assessment continues.

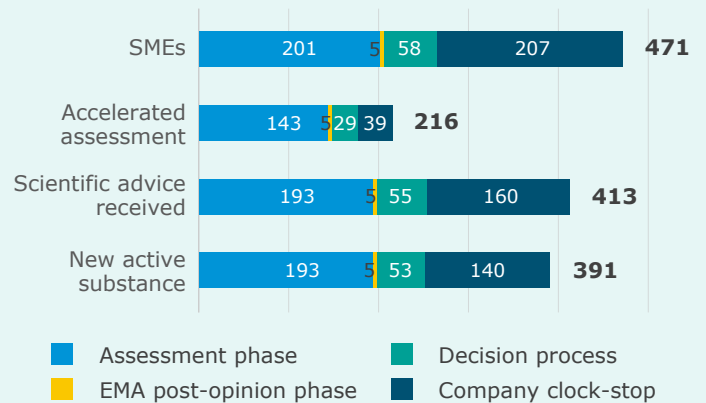
Once issued, the CHMP opinion is transmitted to the EC, which has the ultimate authority to grant a marketing authorisation and will take a decision within 67 days of receipt of the CHMP opinion.

The overall total time required for the centralised procedure, from the start of the evaluation process to the adoption of a decision by the European Commission, was an average of 419 days in 2020, 4 days less than in 2019.

### Average number of days for centralised procedures - positive opinions



### Average number of days for centralised procedures - subset (2020)



Note: The average time for the decision process includes, in the case of orphan medicinal products, the time for the finalisation of the review of orphan designations carried out by EMA's COMP.

For medicines evaluated under the accelerated procedure, the total time from the start of the assessment until the granting of authorisation was reduced by around 6.8 months (from 419 to 216 days), potentially facilitating the subsequent decision-making steps at a national level and ultimately speeding up patient access to medicines that fulfil unmet medical needs.

## Post-authorisation activities

In 2020, the CHMP gave 83 positive recommendations for extension of the therapeutic indication of already authorised medicines. Almost one-third of these extensions of indication related to cancer medicines.

Important extensions of indication included:

- Orfadin, to include the treatment of alkaptonuria in adult patients.
- Velphoro, to include control of serum phosphorus levels in children aged 2 years or older with chronic kidney disease (CKD) stages 4-5 or with CKD on dialysis.

- Olumiant (baricitinib), to include the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy.

In line with previous years, in 2020 EMA received applications for:

- 3,989 type-IA variations
- 2,675 type-IB variations
- 1,274 type-II variations
- 35 extensions of marketing authorisations

The product information for 490 authorised medicines was updated as new safety data were made available and assessed by EMA.

# Safety monitoring of medicines

EMA and EU Member States are responsible for coordinating the EU’s safety monitoring of medicines, also known as ‘pharmacovigilance’. The regulatory authorities constantly monitor the safety of medicines and can take action on an indication that a medicine’s safety profile or benefit-risk balance has changed since its authorisation. EMA’s safety committee, the PRAC, plays a key role in overseeing the safety of medicines in the EU as it covers all aspects of safety monitoring and risk management.

The Agency’s main responsibilities in relation to the safety monitoring of medicines include coordination of the European pharmacovigilance system, setting standards and guidelines for pharmacovigilance, provision of information on the safe and effective use of medicines, detecting new safety issues for centrally authorised products, managing assessment procedures, e.g. for periodic safety update reports (PSURs), and the operation and maintenance of the EudraVigilance system.

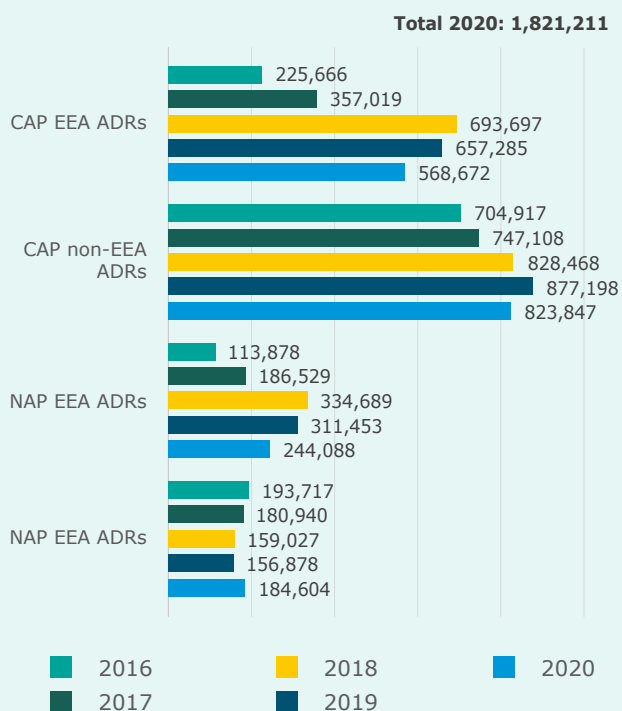
## EudraVigilance – collecting suspected adverse drug reaction reports

Both EMA and the NCAs are legally required to continuously monitor the adverse drug reaction (ADR) data reported to EudraVigilance to determine whether new or changed risks have been identified and whether these risks have an impact on a medicine’s overall benefit-risk balance.

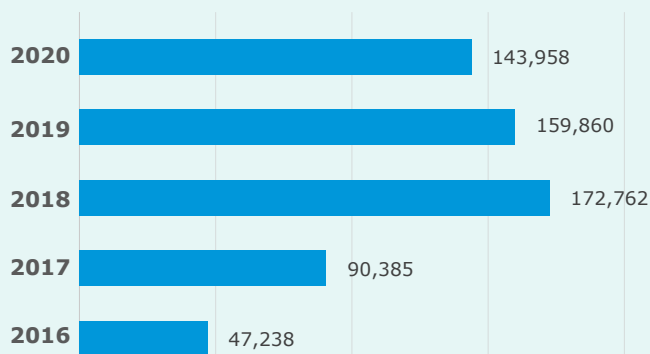
The number of reports submitted by European patients and consumers remained high, with 143,958 reports submitted in 2020. This shows patients’ commitment to reporting side effects as a result of EU and national information campaigns and, since November 2017, the inclusion of non-serious EEA reports in EudraVigilance.

Over 1.8 million ADR reports were submitted to EudraVigilance in 2020, representing a slight decrease (9%) compared with 2019. Over 60% of all reports in EudraVigilance originated in the EEA.

EEA and non-EEA ADR reports received



Number of reports from patients



Note: Following the launch of the new EudraVigilance system in November 2017, figures include reports of non-serious suspected adverse drug reactions since 2017.

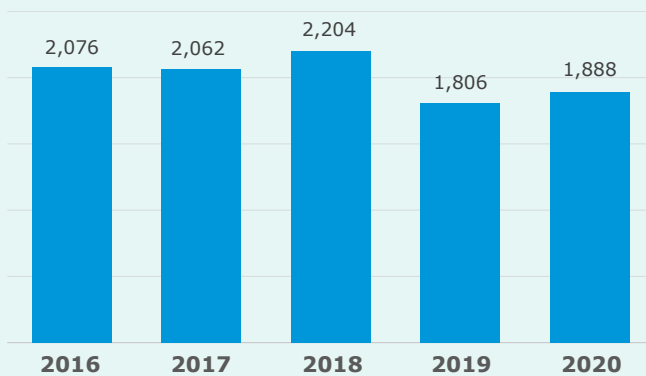
## Signal detection

A safety signal is information on a new or known adverse event that is potentially caused by a medicine and warrants further investigation. Signals are generated from several sources, such as spontaneous reports of suspected adverse reactions, clinical studies and the scientific literature. The evaluation of a safety signal is a routine pharmacovigilance activity to establish whether there is a causal relationship between a reported adverse event and the use of a medicine.

In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary. This mainly comprises changes in the information on medicines available for patients (in the package leaflet) and prescribers (in the summary of product characteristics).

In 2020, 1,888 potential signals were reviewed by EMA, about as many as in 2019. Approximately 81% of these signals originated from monitoring the EudraVigilance database, highlighting its central role in safety monitoring. There was a decrease in the number of signals validated by EMA and assessed by the PRAC (39 in 2020 vs 50 in 2019) due to normal fluctuations from year to year, while the number of signals validated by Member States and assessed by the PRAC remained relatively stable (42 vs 46). In addition to signal detection activities and assessments at PRAC level, experts from the NCAs, in collaboration with EMA, provided a major contribution to the development of signal detection methods and continuous process improvement.

Signals reviewed by EMA



## OUTCOME OF SIGNAL ASSESSMENT

1,888 potential signals reviewed by EMA



81 confirmed signals were prioritised and assessed by the PRAC

Of these, 39 signals were detected and validated by EMA

42 signals were detected and validated by EU Member States



Out of 81 confirmed signals



37 signals led to a product information update; 2 of these also included a Direct Healthcare Professional Communication (DHPC) to highlight important new safety information to prescribers



16 signals led to a recommendation for routine pharmacovigilance

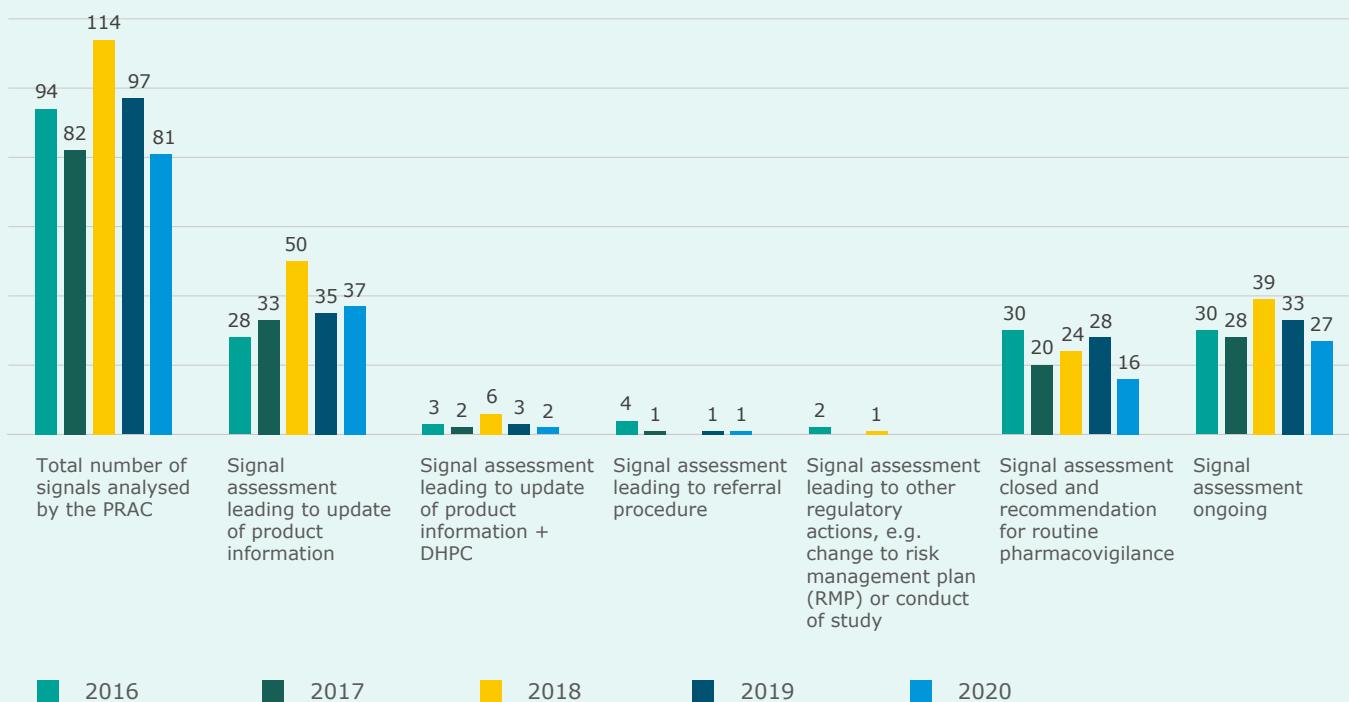


27 signals were still under review by the PRAC at the end of 2020 as further data were required



1 signal led to a referral procedure to further investigate the issue

### Signal assessment



### Periodic safety update reports (PSURs)

MAHs are required to submit a report on the evaluation of a medicine’s benefit-risk balance to the regulatory authorities at regular, predefined intervals following the authorisation of a medicine. These reports summarise data on the benefits and risks of a medicine and take into consideration all related studies carried out, both in authorised and unauthorised indications.

The Agency is responsible for procedures supporting the analysis of these reports for both centrally authorised products (CAPs) and nationally authorised products (NAPs) that are authorised in more than one Member State. These reports are called PSURs. When the assessment procedure involves more than one medicinal product with the same active substance, the procedure is referred to as periodic safety update single assessment or PSUSA.

In 2020, the PRAC started the assessment of 829 PSURs and PSUSAs, of which 30% represent single assessments of active substances only contained in NAPs. 774 recommendations were issued by the PRAC based on the assessment of PSURs and PSUSAs, of which around a quarter consisted of single assessments of active substances only contained in NAPs.

Close to one in five assessments led to changes in the product information to optimise the safe and effective use of medicines by patients and healthcare professionals.





PSURs and PSUSAs finalised	2016	2017	2018	2019	2020
PSURs stand-alone (CAPs only) finalised	511	540	537	558	516
PSURs single assessment finalised	280	302	364	270	258
PSURs single assessment (CAPs with NAPs) finalised	16	39	43	48	49
PSURs single assessment (NAPs only) finalised	264	263	321	222	209
<b>Total outcomes</b>	<b>791</b>	<b>842</b>	<b>901</b>	<b>828</b>	<b>774</b>

PRAC outcomes of PSURs and PSUSAs	2016	2017	2018	2019	2020
<b>Maintenance</b>	<b>637</b>	<b>680</b>	<b>735</b>	<b>655</b>	<b>630</b>
NAPs only		207	245	166	161
CAPs/NAPs and CAPs only		473	490	489	469
<b>CHMP Variation</b>	<b>154</b>	<b>162</b>	<b>166</b>	<b>173</b>	<b>144</b>
NAPs only		56	76	56	48
CAPs/NAPs and CAPs only		106	90	117	96
<b>Total outcomes</b>	<b>791</b>	<b>842</b>	<b>901</b>	<b>828</b>	<b>774</b>

## Post-authorisation safety studies and post-authorisation efficacy studies

A post-authorisation safety study (PASS) can be carried out after a medicine has been authorised to obtain further information on its safety, or to determine the effectiveness of risk-management measures. A PASS can be imposed on MAHs as part of their post-authorisation obligations.

The PRAC is responsible for assessing the protocols of imposed PASS and their results. The PRAC also reviews protocols of large numbers of voluntarily submitted PASS in the context of risk management plan assessments.

In 2020, the PRAC assessed 13 imposed PASS protocols that were requested to obtain further information on a medicine's safety, a similar number compared with 2019. The Committee assessed 167 non-imposed PASS protocols.

In addition, the PRAC started to assess the results of four imposed PASS.

Post-authorisation safety studies					
	2016	2017	2018	2019	2020
Imposed PASS protocol procedures started	12	6	17	12	17
Imposed PASS protocol procedures finalised	10	5	9	13	13
Non-imposed PASS protocol procedures started		333	195	144	158
Non-imposed PASS protocol procedures finalised		265	196	180	167
PASS amendment	12 (started), 7 (finalised)	11 (started), 10 (finalised)	11 (started), 11 (finalised)	11 (started), 9 (finalised)	19 (started), 14 (finalised) + 9 follow up amendments (started) and 7 (finalised)
Imposed PASS result procedures started	3	6	8	3	4
Imposed PASS result procedures finalised	3	3	8	3	2
PASS scientific advice through SAWP	3	0	3	3	1

Post-authorisation efficacy studies (PAES) are also conducted after a medicine has been granted a marketing authorisation, to collect data on aspects

of the benefits in its approved indication that can only be explored once the medicine is marketed.

## Notification of withdrawals

Companies are required to report the cessation of the marketing of a medicine in any Member State for reasons affecting patient safety so that regulatory authorities can ensure that the same action is taken across all Member States. For centrally authorised medicines, companies also need to notify EMA of withdrawals for commercial reasons. The Agency is responsible

for coordinating these actions across the EU. These notifications are forwarded to all NCAs in the EEA. The list of withdrawn products is published on the EMA website.

The number of notifications of withdrawn products rose by 10% between 2019 and 2020.

## Other pharmacovigilance activities

**Additional monitoring** aims primarily to enhance ADR reporting for certain types of medicines. The list of medicines under additional monitoring is reviewed every month by the PRAC and is available on EMA's website and also published by the NCAs. In 2020, 343 medicines were subject to additional monitoring, in line with 2019. These medicines are identified by an inverted black triangle on their packaging.

The EU **incident management plan** is coordinated by EMA and aims to ensure that concerned bodies in the EU take appropriate action whenever new events or information (known in this context as incidents) arise concerning human medicines. It covers medicines authorised centrally, nationally and through the decentralised and mutual recognition procedures. The plan's operation involves representatives from EMA, the EC and regulatory authorities in the Member States. In 2020, six incidents triggered the plan. Overall, a declining trend in the numbers of Incident Review Network meetings related to safety issues has been observed in recent years. This is probably associated with the robust tools and processes introduced with the revised pharmacovigilance legislation, which enabled most incidents to be managed by using routine, established pathways.

The **European pharmacovigilance issues tracking tool (EPITT)** is a database developed by EMA to promote the discussion of pharmacovigilance and risk management issues between the Agency and Member States. It provides access to documents related to the safety of medicinal products/substances authorised in the EEA. EPITT helps medicines regulatory authorities in the EEA and EMA to track signals at EU level. In 2020, 15 non-urgent information or rapid alert notifications were submitted via EPITT.

**Scientific and medical literature** is an important source of information for identifying suspected adverse reactions with medicines authorised in the EU. EMA is responsible for monitoring a number of substances and selected medical literature to identify suspected adverse reactions with such medicines, and for entering the relevant information into the EudraVigilance database. In 2020, 9,550 Individual Case Safety Reports (ICSRs) were triggered by EMA's medical literature monitoring (MLM) service, in line with 2019.

Other pharmacovigilance activities	2016	2017	2018	2019	2020
Cumulative number of products on the list of products to be subject to additional monitoring	301	336	351	342	343
Number of incident management plans triggered	7	4	11	3	6
Number of non-urgent information or rapid alert notifications submitted through EPITT	49	61	44	43	15
Number of external requests for EV analyses	34	32	17	13	15
Number of MLM ICSRs created	8,495	14,193	13,275	9,676	9,550

## Referral procedures

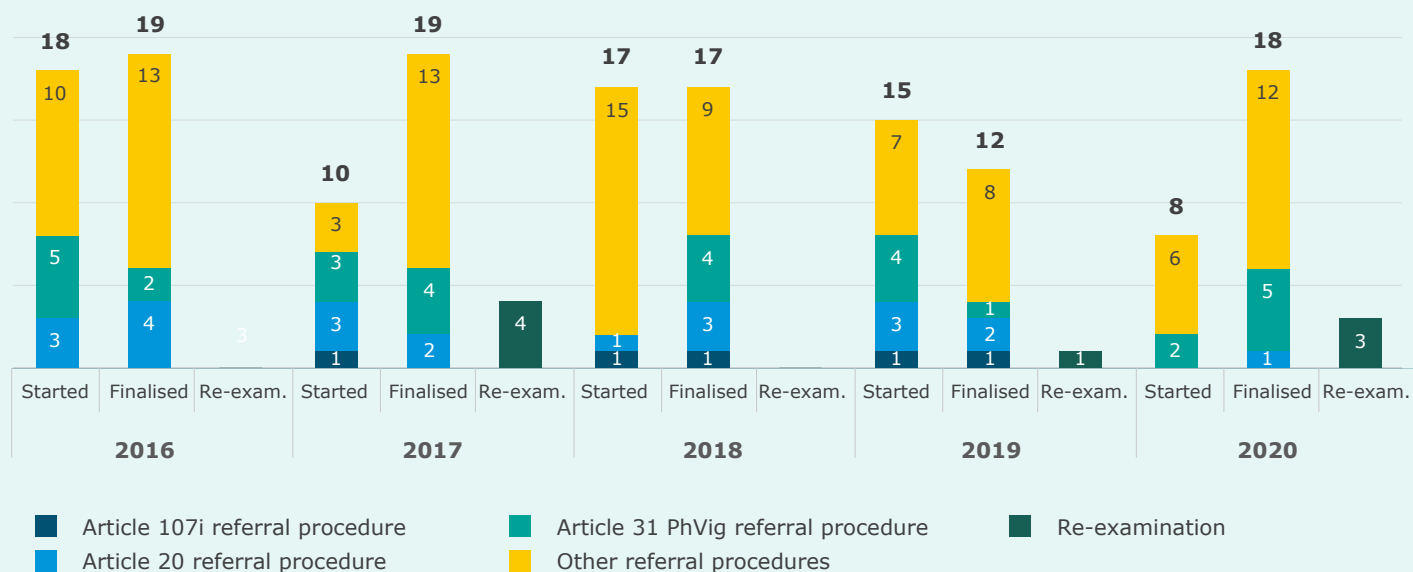
Referral procedures are initiated to address concerns over the safety or benefit-risk balance of a medicine, as well as to deal with disagreement among Member States on the use of a medicine. In a referral, EMA is requested, on behalf of the EU, to conduct a scientific assessment of a particular medicine or class of medicines and issue a recommendation. Following this recommendation, the EC will issue a legally binding decision for the EU. Less often, in cases where only nationally authorised products are concerned, the decision is taken by the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh). In cases where the CMDh position is agreed by a majority (not by consensus), the EC will issue a final decision applicable throughout the EU.

In 2020, 18 referral procedures were finalised, of which six were related to the safety of medicines, initiated under Articles 31, 20 or 107i of the pharmacovigilance legislation. Five procedures led to changes in the product information, and one resulted in the suspension of the marketing authorisation.

The remaining 12 referral procedures aimed to address either:

- efficacy or quality concerns with certain medicines;
- a need for EU-wide harmonisation of the product information;
- differences between the Member States in the mutual recognition and decentralised procedures.

Referrals for human medicines finalised or re-examinations



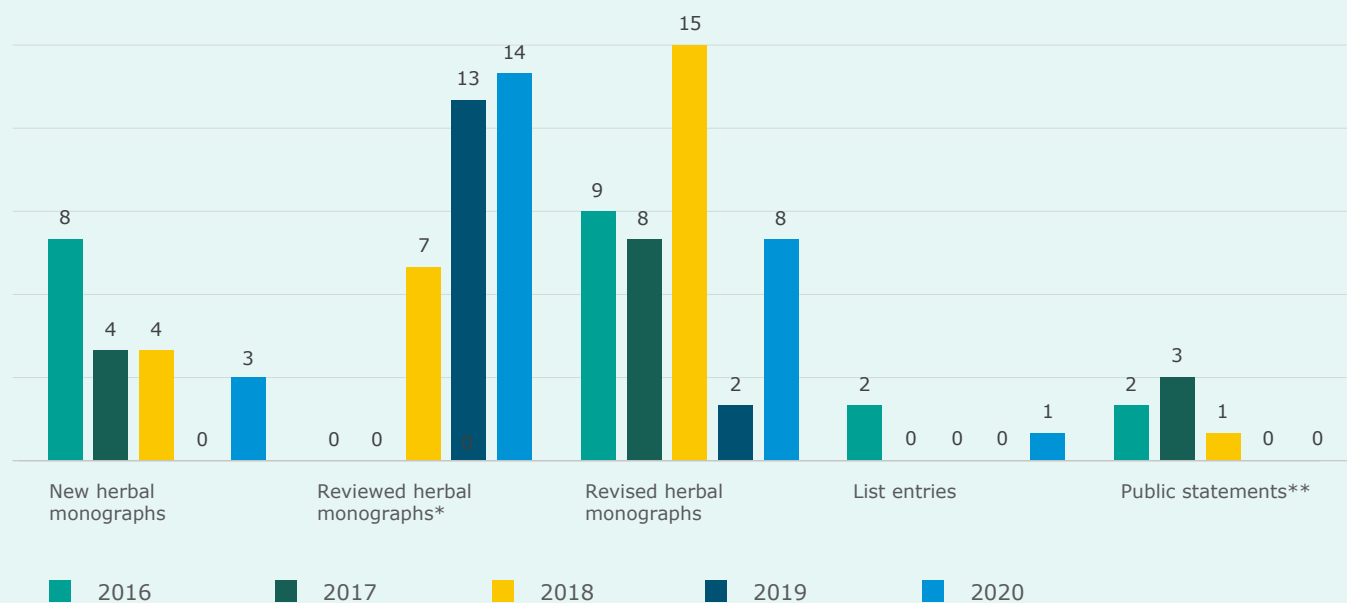
# Herbal medicines

The Agency’s Committee on Herbal Medicinal Products (HMPC) is responsible for preparing opinions on herbal medicines with the aim of promoting an increasingly harmonised process for licensing and information on herbal substances across the EU. The HMPC establishes EU monographs for traditional and well-established herbal medicines, as well as

draft entries to the EC’s list of herbal substances, preparations and combinations thereof for use in traditional medicines.

In 2020, 14 monographs were updated following a systematic review of newly available data.

## Herbal monographs and list of herbal substances, preparations and combinations thereof



\* When, after the review of new data, no change is required in the monograph, an addendum to the previous assessment report is prepared (otherwise start of revision procedure leading to a revised monograph).

\*\* When the assessment does not lead to a monograph, a public statement is prepared.

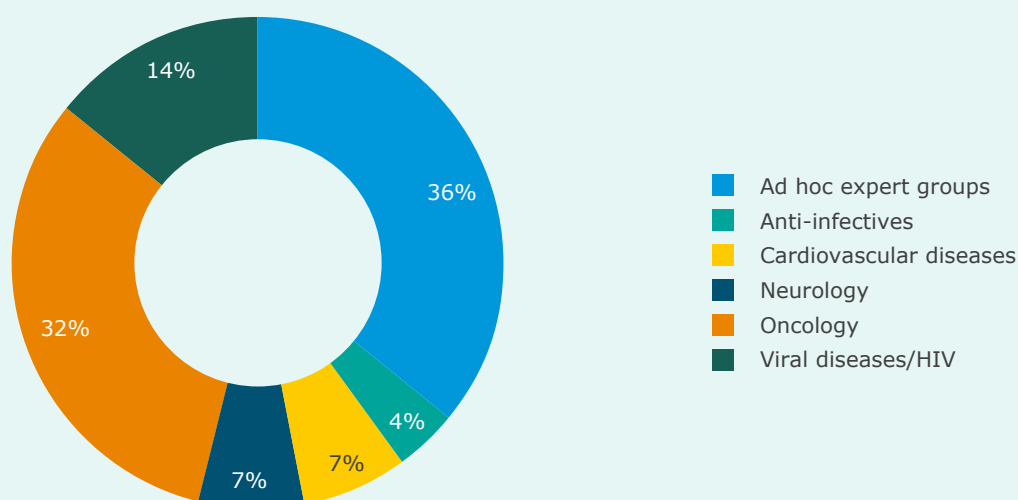
Note: A complete list of recommendations on herbal medicines can be found in the annexes.

## Contribution of experts, patients and healthcare professionals to scientific assessments

EMA's scientific committees can consult additional experts, patients and healthcare professionals to enrich their scientific assessment of medicines. These external parties may be involved in scientific advisory groups (SAGs) or ad hoc expert groups.

A total of 28 consultations took place in 2020 in the form of SAG meetings, similar to 2019.

Areas of discussions - SAGs and ad hoc expert group meetings (2020)



Procedures with SAG or ad hoc expert group involvement (number of consultations)	2016	2017	2018	2019	2020
Marketing authorisation (new MAA, new MAA re-examination, Art. 58)	8	14	19	15	18
Extension of indication (including line extensions)	6	3	10	3	7
Referral (including re-examination)	5	11	3	6	0
Guideline	0	1	0	1	0
Other topics (renewal, PSUR, signal, class review)	0	1	0	2	3
<b>Total</b>	<b>19</b>	<b>30</b>	<b>32</b>	<b>27</b>	<b>28</b>

## Involvement of patients and healthcare professionals

Patients and healthcare professionals are involved in a wide range of EMA activities. They bring a valuable real-life perspective to scientific discussions on medicines, which is expected to lead to better outcomes of the regulatory process. Patients and healthcare professionals participate by:

- contributing as members of scientific committees and the Management Board;
- being consulted on disease-specific requests by the scientific committees and working parties;
- taking part in discussions on the development and authorisation of medicines;
- reviewing written information on medicines prepared by the Agency;
- being involved in the preparation of guidelines;
- taking part in the Agency's conferences and workshops.

Patient involvement in EMA activities (interactions)	2016	2017	2018	2019	2020
Scientific advice/protocol assistance	82	158	107	143	97
SAGs/ad hoc expert meetings	28	46	37	46	42
Scientific committee/working party consultations	50	104	112	355	227
Patient membership in MB, committees, working parties	58	59	59	57	57
EMA Management Board	2	2	2	2	2
Scientific committees	15	15	15	11	14
Patients' and Consumers' Working Party	41	42	42	44	41
Document reviews conducted by patients and consumers	120	176	178	169	203
EPAR summaries	36	39	43	40	50
Package leaflets	58	79	75	101	123
Safety communications	26	24	35	11	16
Herbal summaries		34	25	17	14
<b>Total cases of patient/stakeholder engagement in EMA activities</b>	<b>769</b>	<b>950</b>	<b>493</b>	<b>770</b>	<b>594</b>

HCP involvement in EMA activities (interactions)	2016	2017	2018	2019	2020
Scientific advice/protocol assistance	1	1	0	2	1
SAGs/ad hoc expert meetings	26	40	31	36	39
Scientific committee/working party consultations	31	74	47	68	28
HCP membership in MB, committees, working parties	51	54	54	58	62
EMA Management Board	2	2	2	2	2
Scientific committees	12	12	12	12	12
Healthcare Professionals' Working Party	37	40	40	44	48
Document reviews conducted by healthcare professionals	55	33	80	48	46
Safety communications	48	20	40	35	42
DHPCs	7	13	40	13	4
<b>Total cases of HCP engagement in EMA activities</b>	<b>399</b>	<b>450</b>	<b>212</b>	<b>212</b>	<b>176</b>





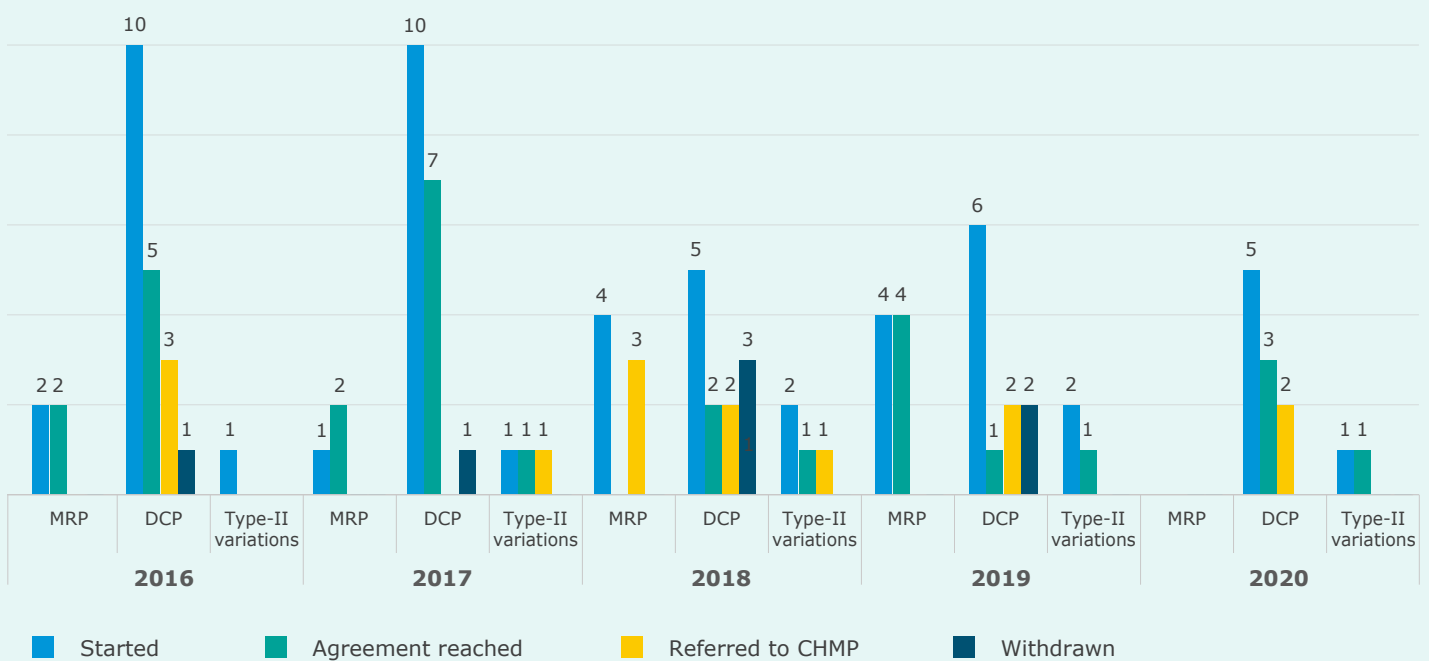
# Mutual-recognition and decentralised procedures

90% of the medicines entering the EU market are nationally authorised. These are mainly generics which reach the market through the mutual recognition procedure (MRP) and the decentralised procedure (DCP), the primary authorisation routes for generic applications within the EU. The CMDh, a separate body from EMA which represents the EU Member States plus Iceland, Liechtenstein and Norway, plays a key role, together with its working

parties, in the authorisation and maintenance of these medicines. EMA provides secretarial support to the CMDh in accordance with the approved rules of procedure.

Detailed information about the work of the CMDh in 2020 in relation to pharmacovigilance and referrals can be found on the [HMA website](#).

Applications referred to the CMDh



# I VETERINARY MEDICINES

## Activities supporting research and development

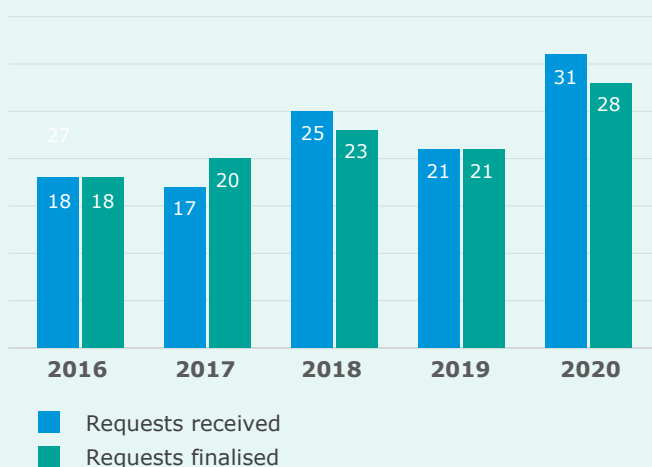
The Agency provides pre-authorisation support to medicine developers to boost innovation and research and enhance the availability of safe and effective veterinary medicines. This is achieved through activities and incentives offered to companies prior to submitting an application for marketing authorisation. These tools facilitate interaction and dialogue with the Agency from the very early stages of medicine development.

### Scientific advice

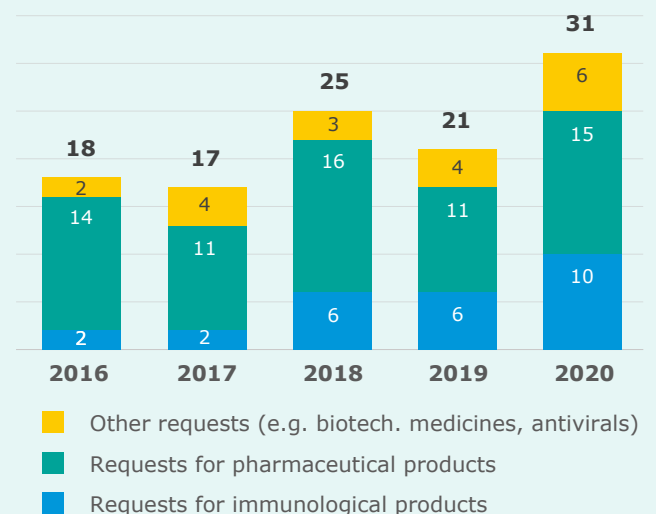
Scientific advice is provided on any aspect of research and development relating to the quality, safety or efficacy of medicines for veterinary use, and to the establishment of maximum residue limits. Scientific advice is a means of facilitating and improving the availability of new veterinary medicines. EMA received 31 requests for scientific advice in 2020 and finalised 28, including some pending from 2019. The number of requests has grown after a decline in 2019, indicating an

increased interest from medicine developers in engaging early with the Agency. Almost a third of all scientific advice requests received were for immunologicals, including vaccines. These types of medicine play a major role in protecting animal health by preventing and controlling serious epizootic diseases. They also have an impact on human health by ensuring safe food supplies and preventing animal-to-human transmission of infectious diseases.

**Scientific-advice requests received and finalised**



**Scientific-advice requests received and finalised**



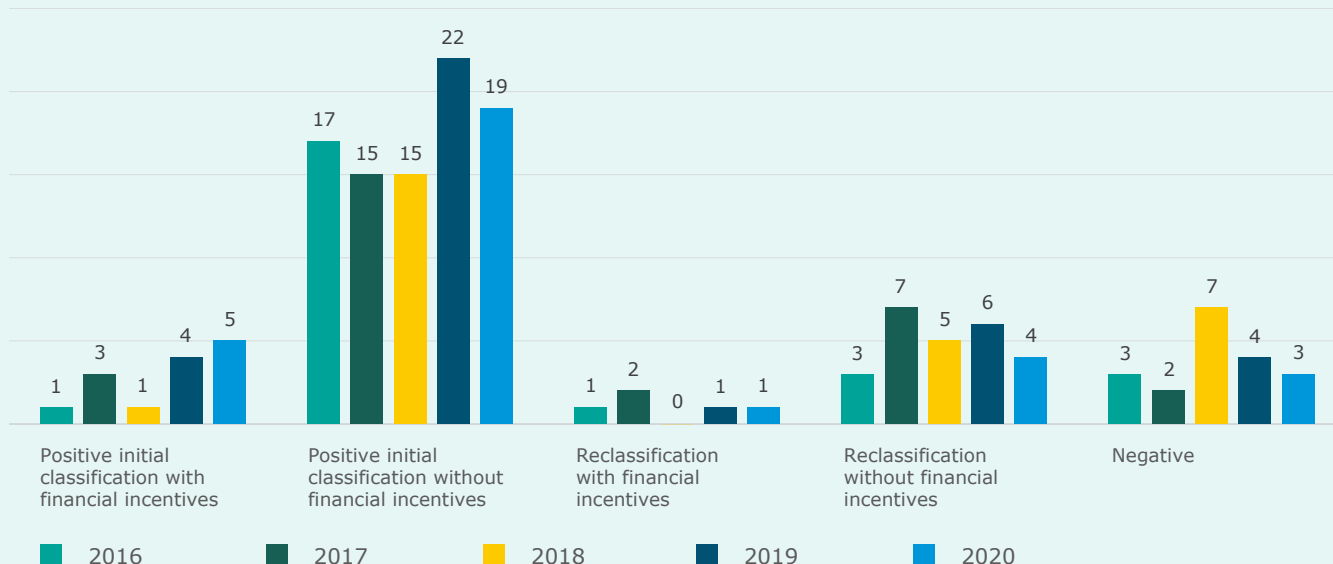
### Minor use minor species

The Agency’s minor use minor species (MUMS)/ limited market policy aims to assist companies with the submission of applications for products for limited markets. The goal is to stimulate the development of veterinary medicines for minor species, and for rare diseases in major species, which would otherwise not be developed in the current market environment. In 2020, the Agency received a total of 29 new requests for the (re) classification of veterinary medicines intended

for MUMS/limited market, showing stable interest from medicine developers in developing products for minor use or minor species. Among the 32 outcomes in 2020, 23 were classified or reclassified as MUMS, and benefited from reduced data requirements. Financial incentives, such as access to free scientific advice and reduced application fees, were granted in response to six requests.

### MUMS/limited market (re)classification requests outcome

Total 2020: 32



### Support to SMEs

EMA put the SME initiative in place in 2005 to promote innovation and development of medicines by SMEs. EMA’s SME office provides active regulatory, financial and administrative incentives to SMEs in the development of their medicines. Support takes the form of individual guidance and more general advice through the SME user guide, topical workshops and a dedicated newsletter. Of the 1,904 SMEs registered with EMA at the end

of 2020, 65 were developing veterinary products and 85 both human and veterinary products. SMEs submitted 4 of the 14 applications (29%) for marketing authorisation for veterinary medicines in 2020. The Agency received 12 new requests for scientific advice relating to the quality, safety or efficacy of medicines for veterinary use submitted by SME applicants, which represent 39% of the total.

## Innovation Task Force

The ITF is a multidisciplinary group that includes scientific, regulatory and legal expertise from across the EU. It provides a forum for early dialogue with applicants, in particular SMEs, to proactively identify scientific, legal and regulatory issues related to emerging therapies

and technologies. Three ITF meetings were held in 2020 concerning the development of veterinary medicines, showing a stable interest in this activity.

## Key scientific guidelines

The Agency develops scientific guidelines to provide advice to applicants or MAHs, competent authorities and other interested parties on the most appropriate way to test and monitor the safety, efficacy and quality of medicines. This is a key activity to support medicine development and ensure that they are safe, effective and of high quality. Guidelines are drafted by EMA working parties comprising experts from across Europe.

EMA issues new guidelines and revises existing ones every year to reflect the latest scientific developments and experience gained through scientific advice and the evaluation and monitoring of medicines.

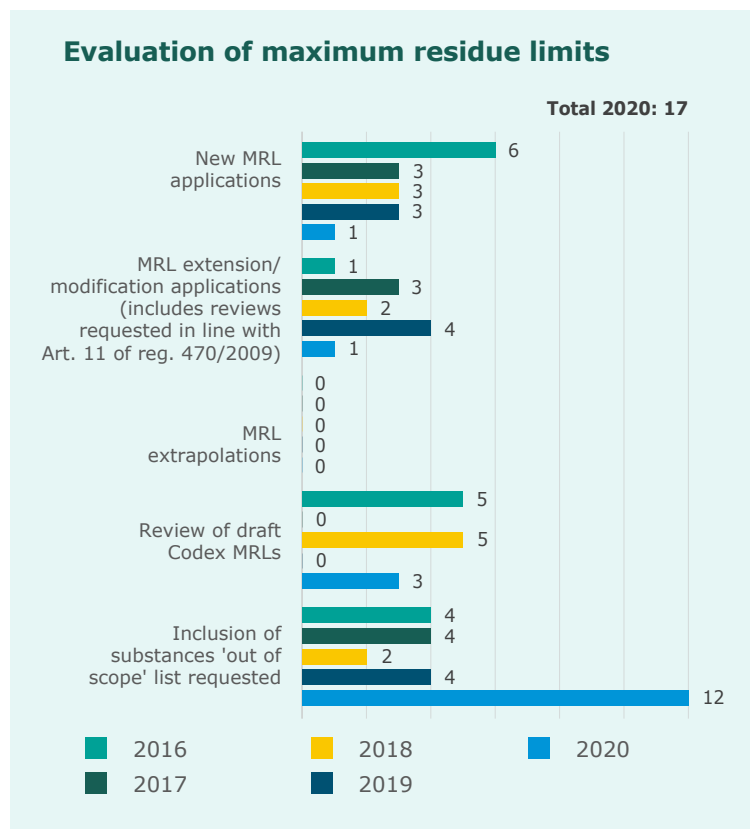
A selection of reflection papers and guidance issued or revised in 2020 is listed below:

Topics	Content
Antimicrobial resistance	<a href="#">Reflection paper on dose review and adjustment of established veterinary antibiotics in the context of SPC harmonisation</a>
Antimicrobial resistance	<a href="#">CVMP strategy</a> on antimicrobials 2021-2025.
Environmental risk assessment for veterinary products	<a href="#">Concept paper</a> for the development of a reflection paper on the environmental risk assessment for parasiticide veterinary medicinal products used in companion animals.
Immunologicals	<a href="#">Questions and answers on management of extraneous agents in immunological veterinary medicinal products</a>
Novel therapies	<a href="#">Questions and Answers</a> on stem cell-based products for veterinary use: specific question on target animal safety to be addressed by ADVENT.
Pharmacovigilance	<a href="#">Update to questions and answers on adverse event reporting</a>
Quality of veterinary medicines	<a href="#">Guideline</a> on the quality of water for pharmaceutical use.
Quality of veterinary medicines	<a href="#">Reflection paper</a> on risk management requirements for elemental impurities in veterinary medicinal products.

## Maximum residue limits

The use of veterinary medicines in food-producing animals may result in the presence of residues in foodstuffs obtained from treated animals. The Agency assesses and recommends MRLs for pharmacologically active substances in veterinary medicinal products used to treat food-producing animals. The objective is to ensure the safety of foodstuffs of animal origin, such as meat, fish, milk, eggs and honey. EMA has a parallel responsibility for recommending MRLs for pharmacologically active substances in biocidal products used in animal husbandry. MRLs are formally established by the EC on the basis of a recommendation from the CVMP. One application for the establishment of MRLs for new substances was received in 2020. The CVMP also received an application for the extension or modification of existing MRL classifications for one substance. While the number of applications for the establishment of MRLs has declined compared to previous years, the overall number of applications for MRLs indicates the continued interest of the animal health industry to develop new products for food-producing animals.

Non-active ingredients considered not to exert pharmacological effects, including many excipients, are considered to fall outside the scope of the MRL Regulation. The CVMP determines on a case-by-case basis whether a non-active ingredient exhibits pharmacological effects and poses a risk to the consumer. If the CVMP concludes that no MRL evaluation is required, EMA includes the substance in the list of [substances considered as not falling within the scope of Regulation \(EC\) No 470/2009 with regard to residues of veterinary medicinal products in foodstuffs of animal origin](#). In 2020, the CVMP reviewed 12 requests for the inclusion of substances in the list of substances considered as not falling within the scope of Regulation (EC) No 470/2009, a threefold increase compared to 2019.

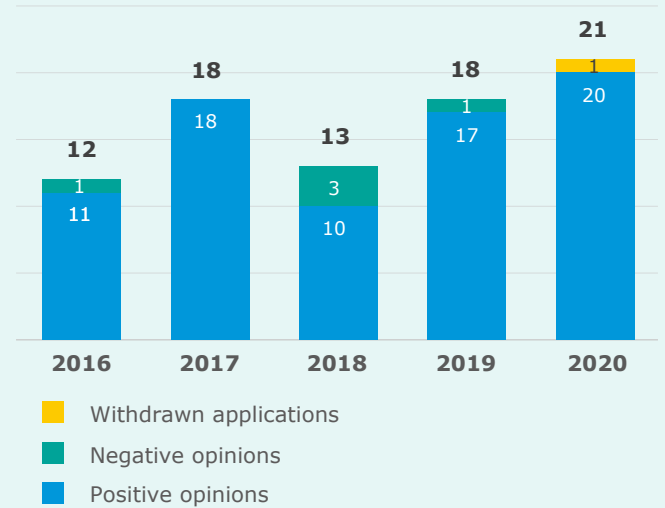


# Recommendations for marketing authorisations

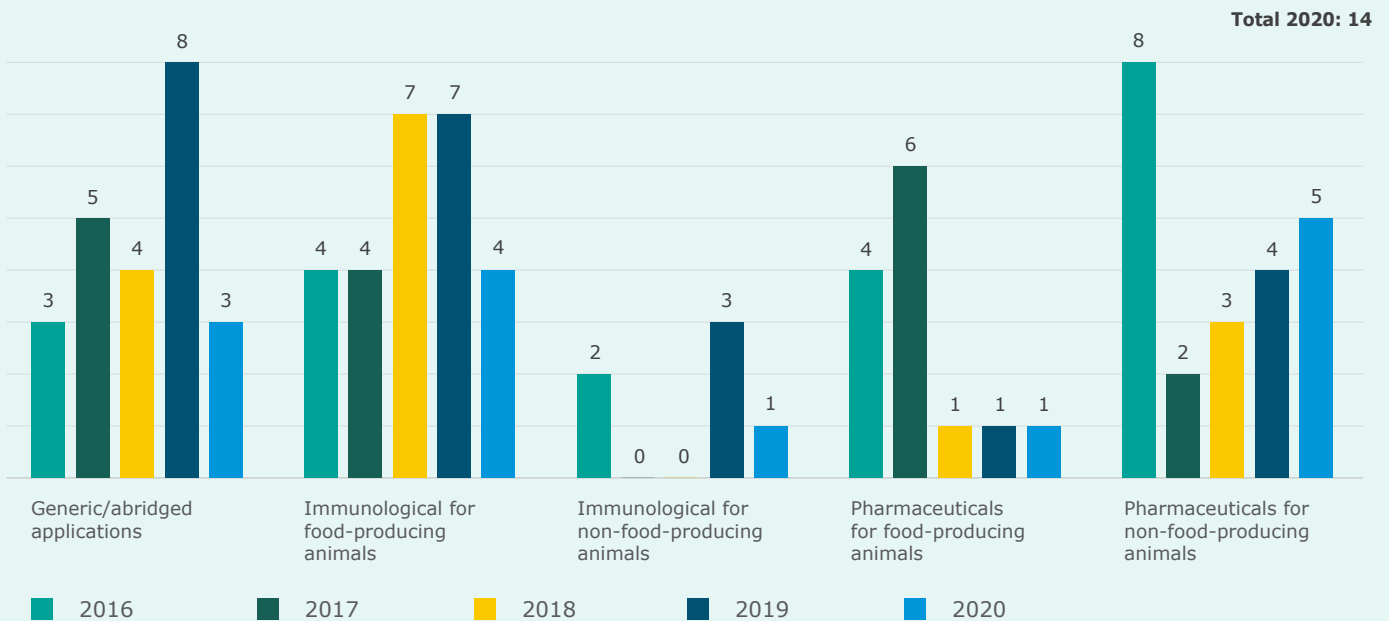
## Applications for initial evaluation

The initial evaluation phase covers activities relating to the processing of marketing authorisations for veterinary medicines, ranging from pre-submission meetings with future applicants, through evaluation by the CVMP to the granting of marketing authorisation by the EC. A total of 14 applications were received in 2020. More than a third of the applications were submitted for immunologicals. Four applications were for immunological products for food-producing animals.

Outcome of initial-evaluation applications



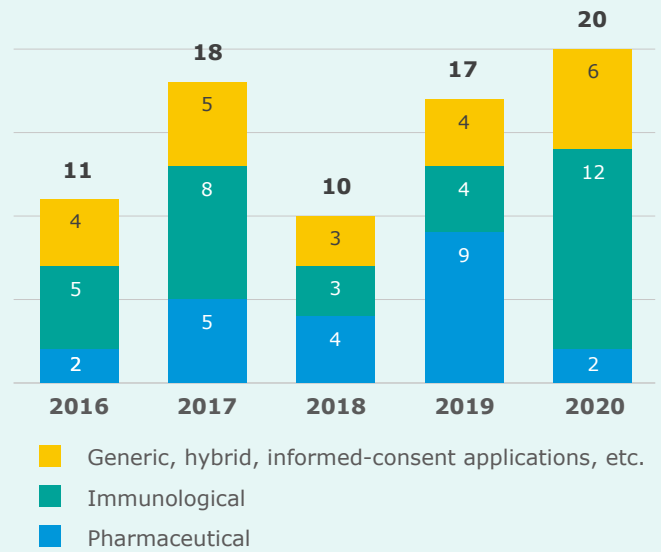
Applications for initial evaluations received



### RECOMMENDATIONS FOR AUTHORISATION



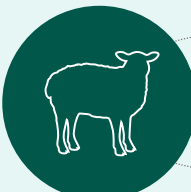
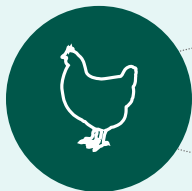


In 2020, 20 new veterinary medicines were granted a positive opinion, including 13 with a new active substance. Twelve of these were for immunologicals. Ten were vaccines, more than double the number of vaccines authorised in the previous year. Of these, eight were biotechnological vaccines. This demonstrates the animal health industry’s continued strong interest in developing vaccines. Vaccines are an alternative option for combating infectious diseases and by reducing the need for antimicrobials they also indirectly reduce the risk of AMR in food-producing animals.

Positive opinions for veterinary medicines



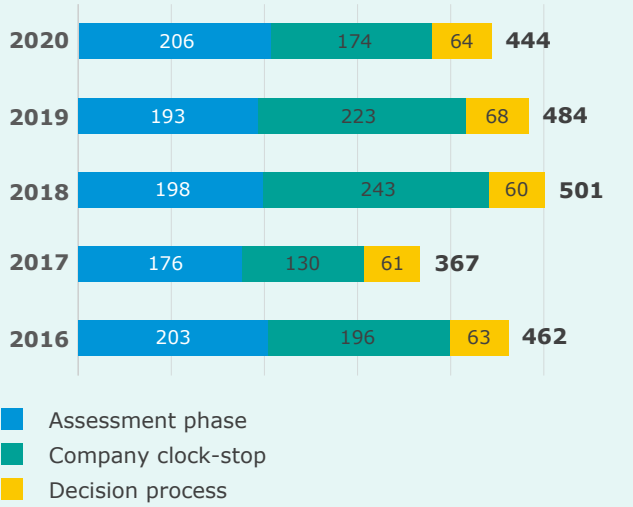
### Medicines recommended for approval in 2020

#### New veterinary medicines

<p><b>Pigs</b></p>  <ul style="list-style-type: none"> <li><b>CircoMax Myco</b></li> <li><b>Enteroporc Coli</b></li> <li><b>Enteroporc Coli AC</b></li> <li>Increxxa</li> <li>Lydaxx</li> <li><b>Mhyosphere PCV ID</b></li> <li><b>OvuGel</b></li> <li>Rexxolide</li> <li>Tulaven</li> <li>Tulinovet</li> <li>Tulissin</li> </ul>	<p><b>Cattle</b></p>  <ul style="list-style-type: none"> <li>Increxxa</li> <li>Lydaxx</li> <li>Rexxolide</li> <li>Tulaven</li> <li>Tulinovet</li> <li>Tulissin</li> </ul>	<p><b>Sheep</b></p>  <ul style="list-style-type: none"> <li>Increxxa</li> <li>Lydaxx</li> <li>Rexxolide</li> <li>Tulaven</li> <li>Tulinovet</li> <li>Tulissin</li> </ul>
<p><b>Chickens</b></p>  <ul style="list-style-type: none"> <li><b>Innovax-ND-ILT</b></li> <li><b>Prevexxion RN</b></li> <li><b>Prevexxion RN+HVT+IBD</b></li> <li><b>Vectormune FP ILT</b></li> <li><b>Vectormune FP ILT+AE</b></li> </ul>	<p><b>Dogs</b></p>  <ul style="list-style-type: none"> <li><b>Librela</b></li> <li><b>Nobivac DP Plus</b></li> </ul>	<p><b>Cats</b></p>  <ul style="list-style-type: none"> <li>NexGard Combo</li> <li><b>Solensia</b></li> </ul>

Medicines that contain a new active substance are highlighted in **green**.

### Average number of days for initial authorisations

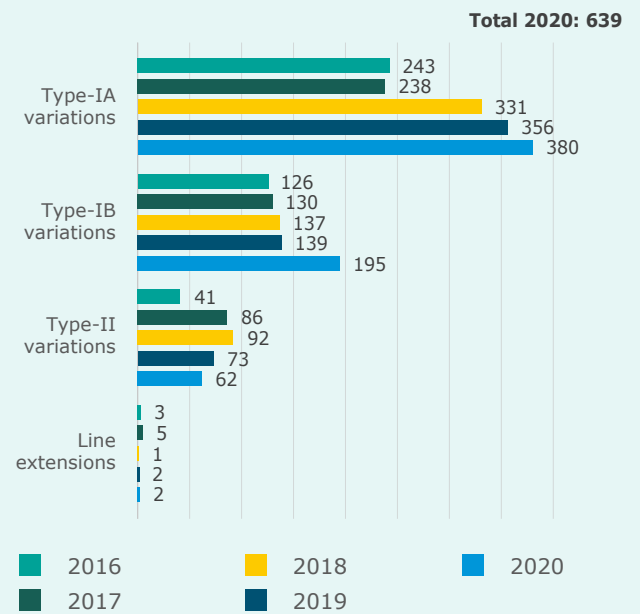


The average number of days taken for initial evaluations fell slightly compared to 2019, mainly due to shorter clock-stops.

### Post-authorisation activities

Post-authorisation activities relate to variations, extensions and transfers of marketing authorisations. The total number of post-authorisation procedures continues to increase year-on-year, broadly in line with the number of products authorised through the centralised procedure. In 2020, the overall number of post-authorisation applications increased by more than 10%. This is a combination of the high number of pharmacovigilance type-IB variations received and the natural annual increase due to the availability of more products on the market.

### Post-authorisation applications received



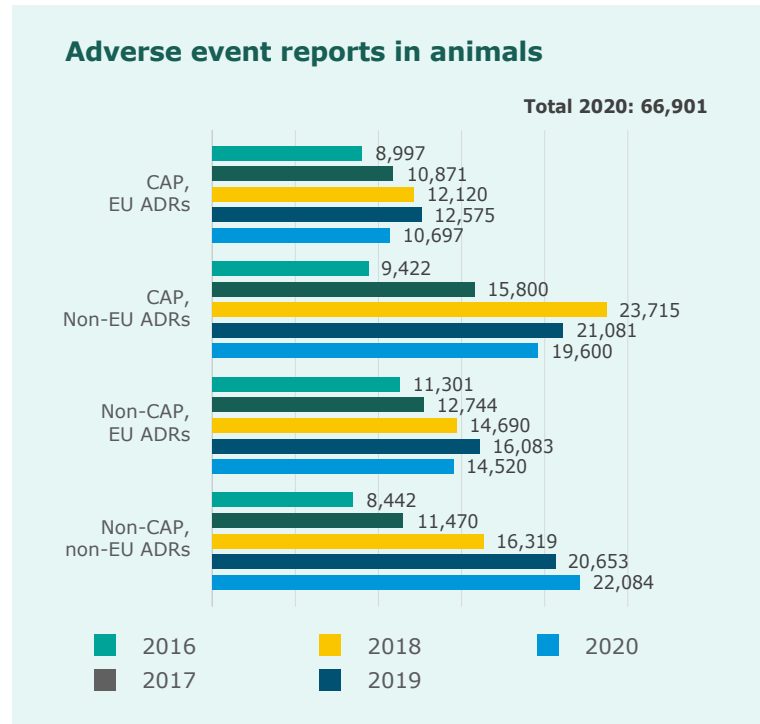


# Safety monitoring of medicines

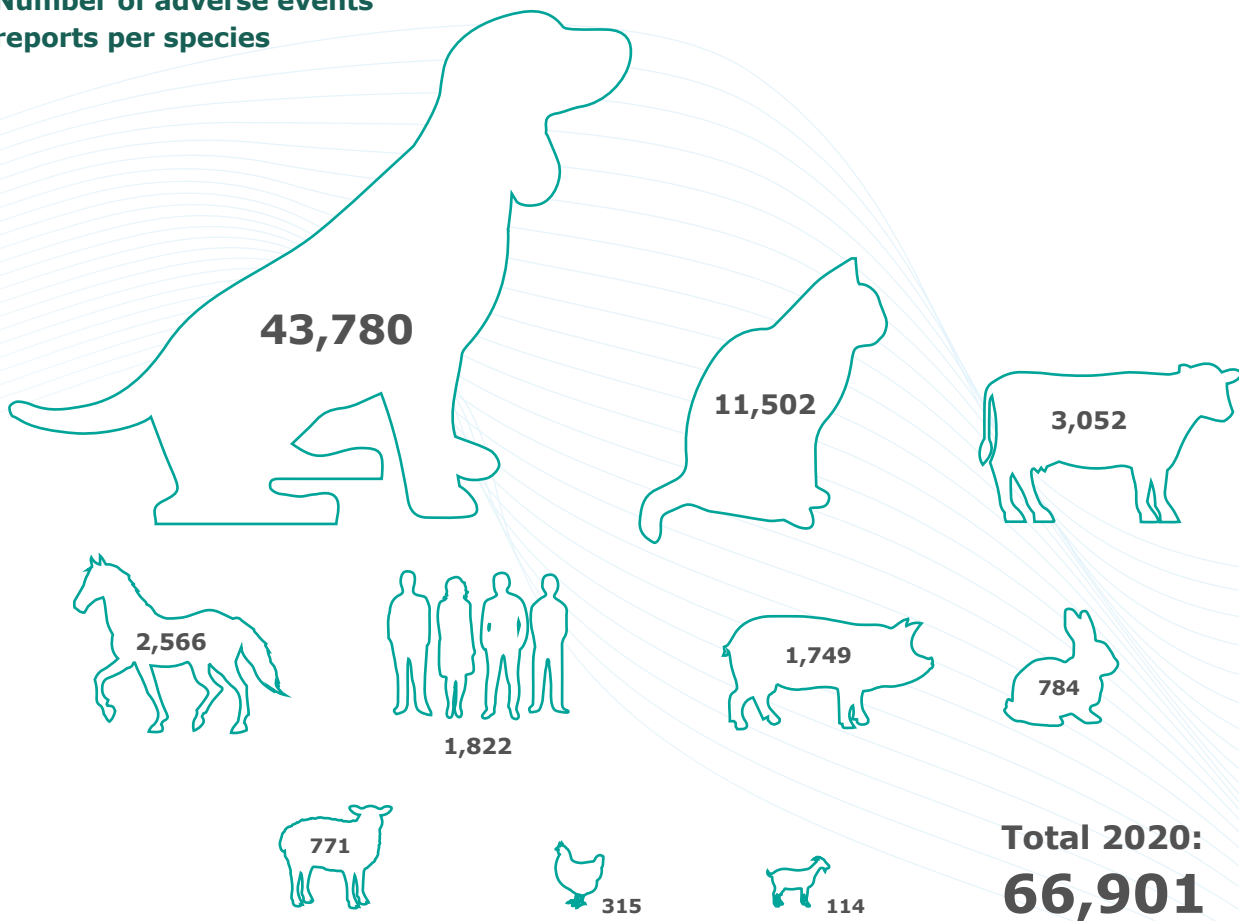
Pharmacovigilance covers activities relating to the detection, reporting, assessment, understanding and prevention of adverse events (AEs) following the administration of veterinary medicines. It aims to ensure the monitoring of the safety of veterinary medicines and the effective management of risks throughout the EU.

## EudraVigilance

In 2020, the overall number of AE reports received in the EudraVigilance system was slightly lower than in 2019. This indicates that after a significant increase over the past few years, the number of reports received is now stabilising, following the full implementation of the CVMP revised recommendation for the basic surveillance of EudraVigilance Veterinary (EVVet) data for CAPs.



## Number of adverse events reports per species



Total 2020:  
**66,901**

## Periodic safety update reports (PSURs)

A PSUR provides an evaluation of a medicine’s benefit-risk balance, which is submitted by MAHs at predefined times following a medicine’s authorisation. PSURs summarise data on the benefits and risks of a medicine and include the results of all related studies carried out

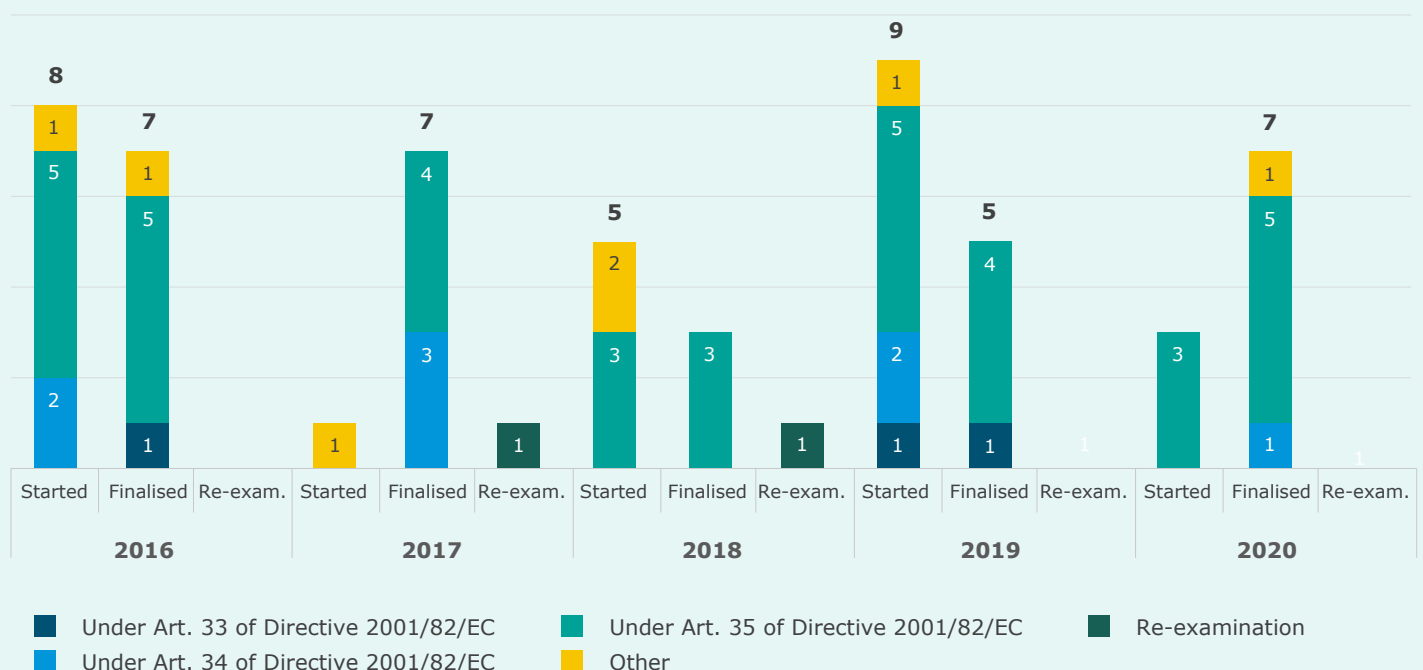
(in authorised and unauthorised indications). The CVMP started the assessment of 160 PSURs in 2020. This number of PSURs reflects the progressive accumulation of products authorised through the centralised procedure.

## Referral procedures

Referral procedures are used to address concerns over the quality, safety, efficacy or benefit-risk balance of a veterinary medicine, or disagreement among Member States on the use of a veterinary medicine. In a referral, the Agency is requested, on behalf of the EU, to conduct a scientific assessment of a particular veterinary medicine or class of veterinary medicines, and issues a cross-EU recommendation. The recommendation

subsequently results in a legally binding decision throughout the Union issued by the EC. Three referral and arbitration procedures related to veterinary medicinal products began in 2020 and seven procedures were finalised. Among these, five were safety- or efficacy-related (under Article 35 of Directive 2001/82/EC or under Article 45 of Regulation (EC) No 726/2004).

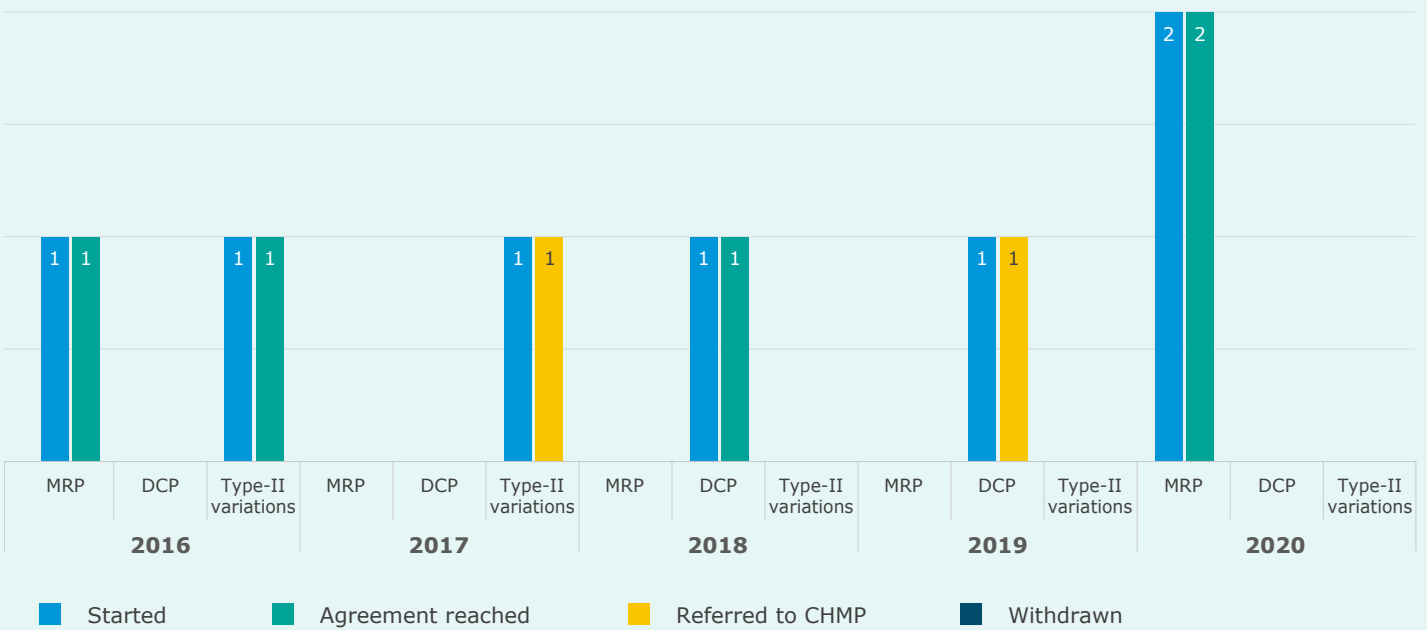
### Arbitration and referrals for veterinary medicines



# Mutual recognition and decentralised procedures

The Agency provides secretarial support to the Coordination Group for Mutual Recognition and Decentralised Procedures - Veterinary (CMDv) and its working groups, in accordance with the approved rules of procedure. The work of the CMDv is essential for the effective authorisation and maintenance of veterinary medicines entering the EU market via the MRP and the DCP, which constitute the primary routes for veterinary medicines entering the EU market.

Applications referred to the CMDv



# EUROPEAN MEDICINES REGULATORY NETWORK

The European medicines regulatory network – a partnership between EMA, the European Commission and 50 medicines regulatory authorities in the EU and the EEA – is the basis of the success of EMA.

The network gives the Agency access to a pool of over 4,000 experts, who provide the best available scientific expertise for the regulation of medicines in the EU. Experts participate in the work of the Agency as members of its committees, working parties, SAGs and a number of ad hoc advisory groups as well as members of the assessment teams carrying out the evaluation of medicines (see annex for further information on these groups).

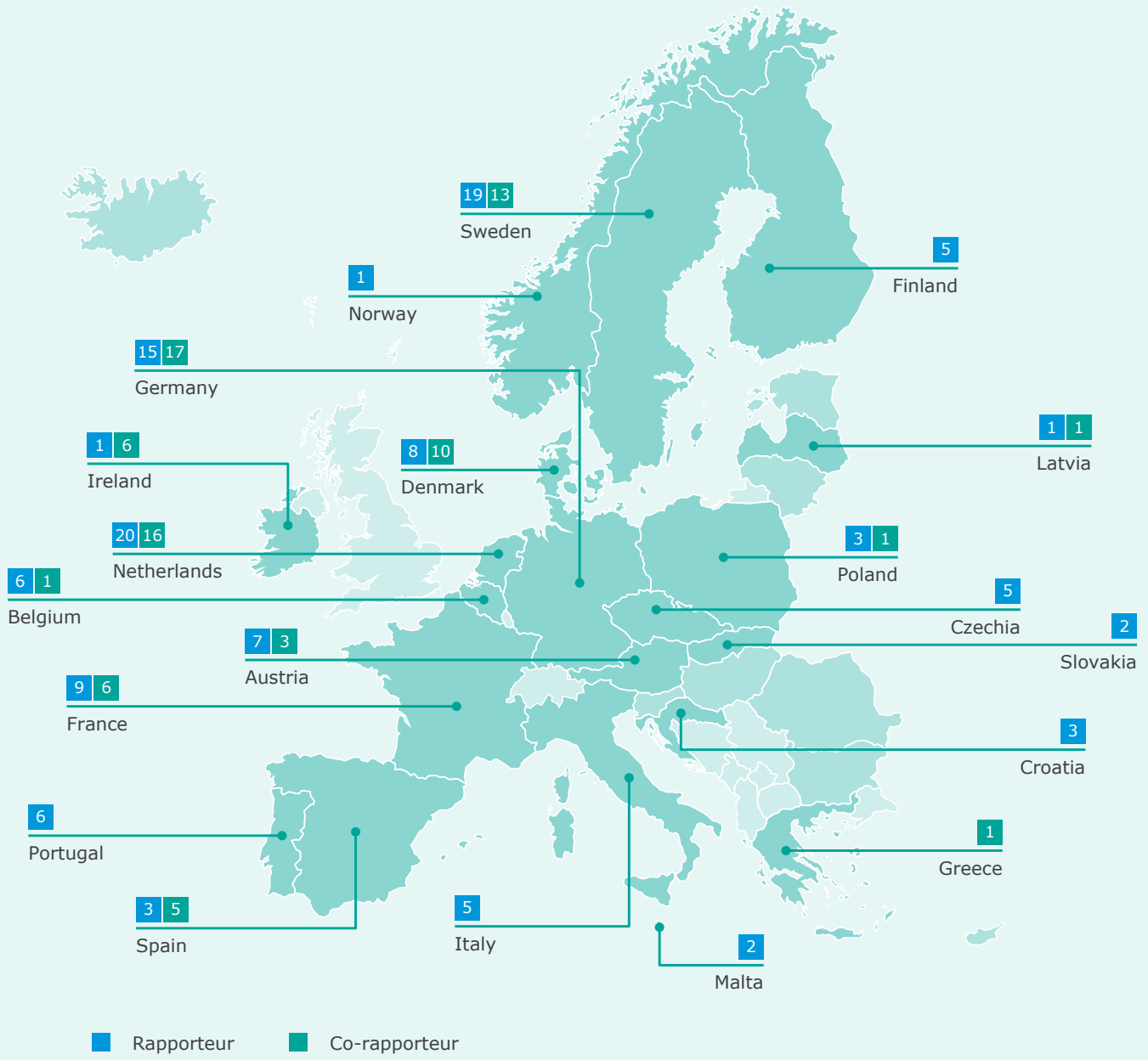
## Rapporteurships and co-rapporteurships

The assessment of a medicine by EMA's scientific committees is carried out by a rapporteur and a co-rapporteur, who prepare the assessment reports and lead the discussions in the committees. The appointment is made on the basis of the best possible expertise for the particular product. Rapporteurs work through assessment procedures and also take the lead in evaluating any new information on the medicine that may become available.



## PRAC rapporteurs/co-rapporteurs appointed in 2020

**PRAC rapporteurs/co-rapporteurs appointed in 2020**  
(for initial marketing authorisation applications)

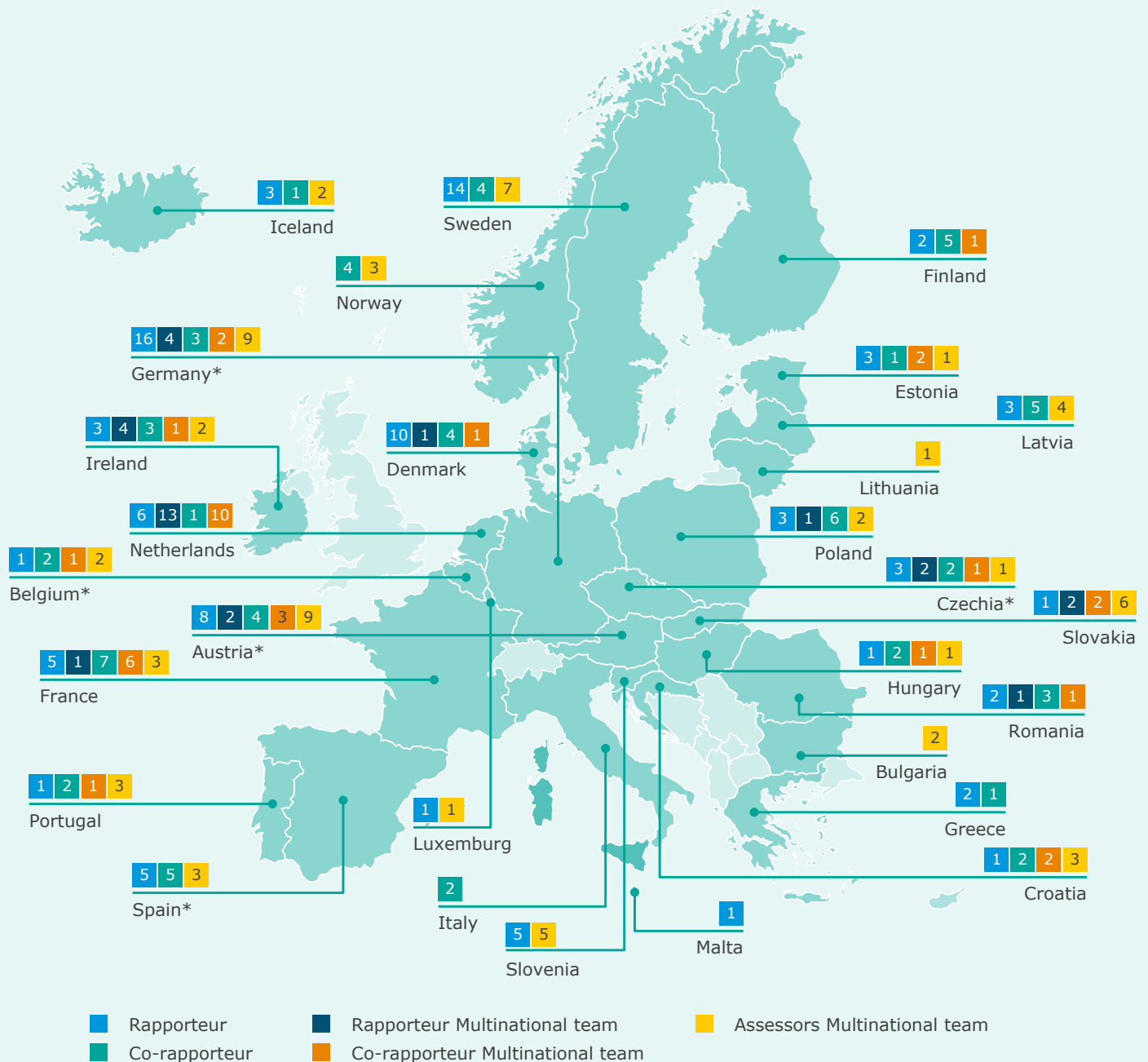


## CHMP rapporteurships/co-rapporteurships

CHMP rapporteurs and co-rapporteurs are able to create multinational teams for the initial assessment of marketing authorisation applications.

The table below presents the number of procedures in which each country was involved in 2020 either as a regular rapporteur or co-rapporteur, as a rapporteur or co-rapporteur leading a multinational team, or as an assessor of part of a multinational team.

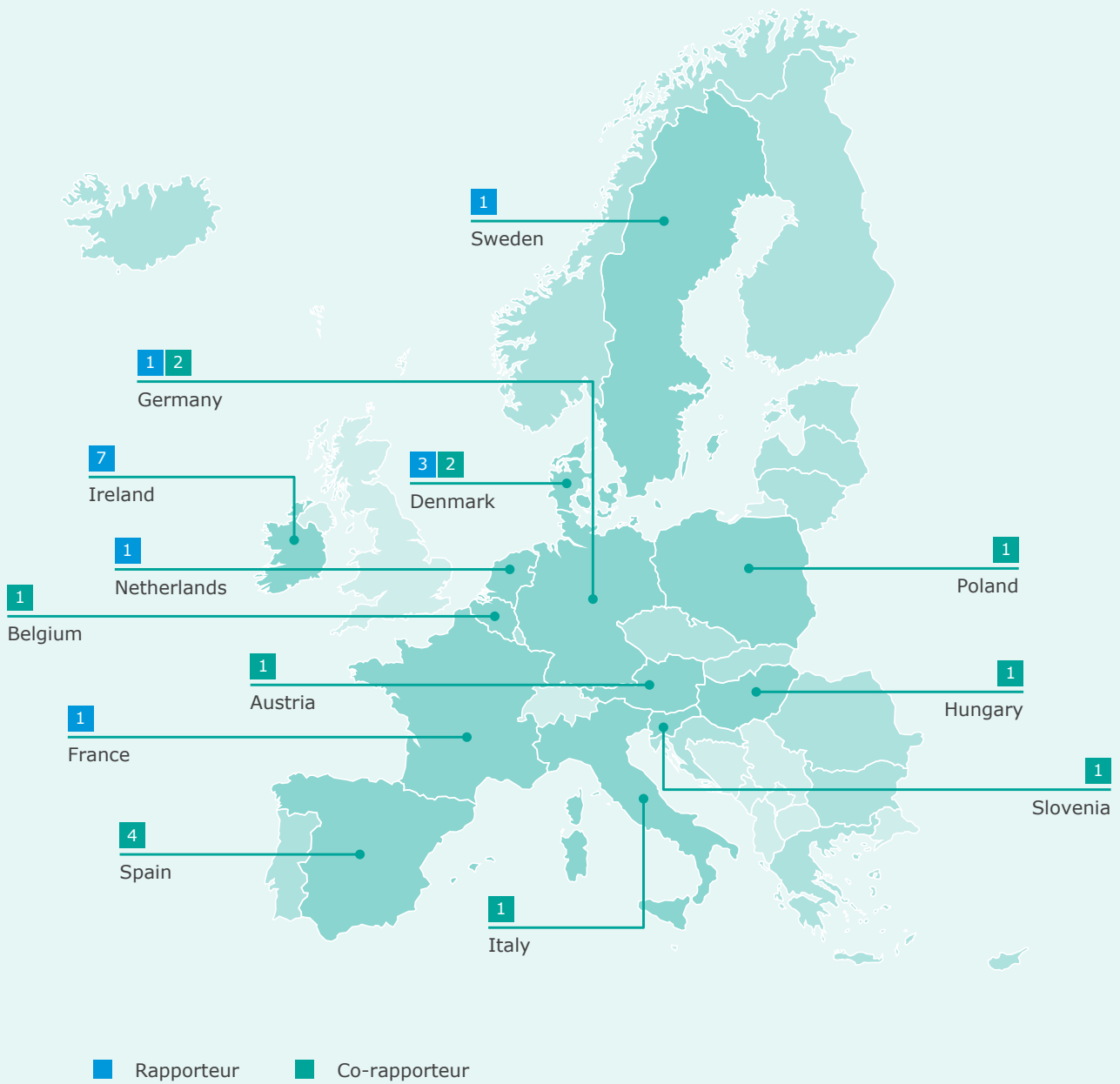
**CHMP rapporteurs/co-rapporteurs appointed in 2020**  
(for initial marketing autorisation applications, including generics)



\* co-opted members included under the country of affiliation/provenance

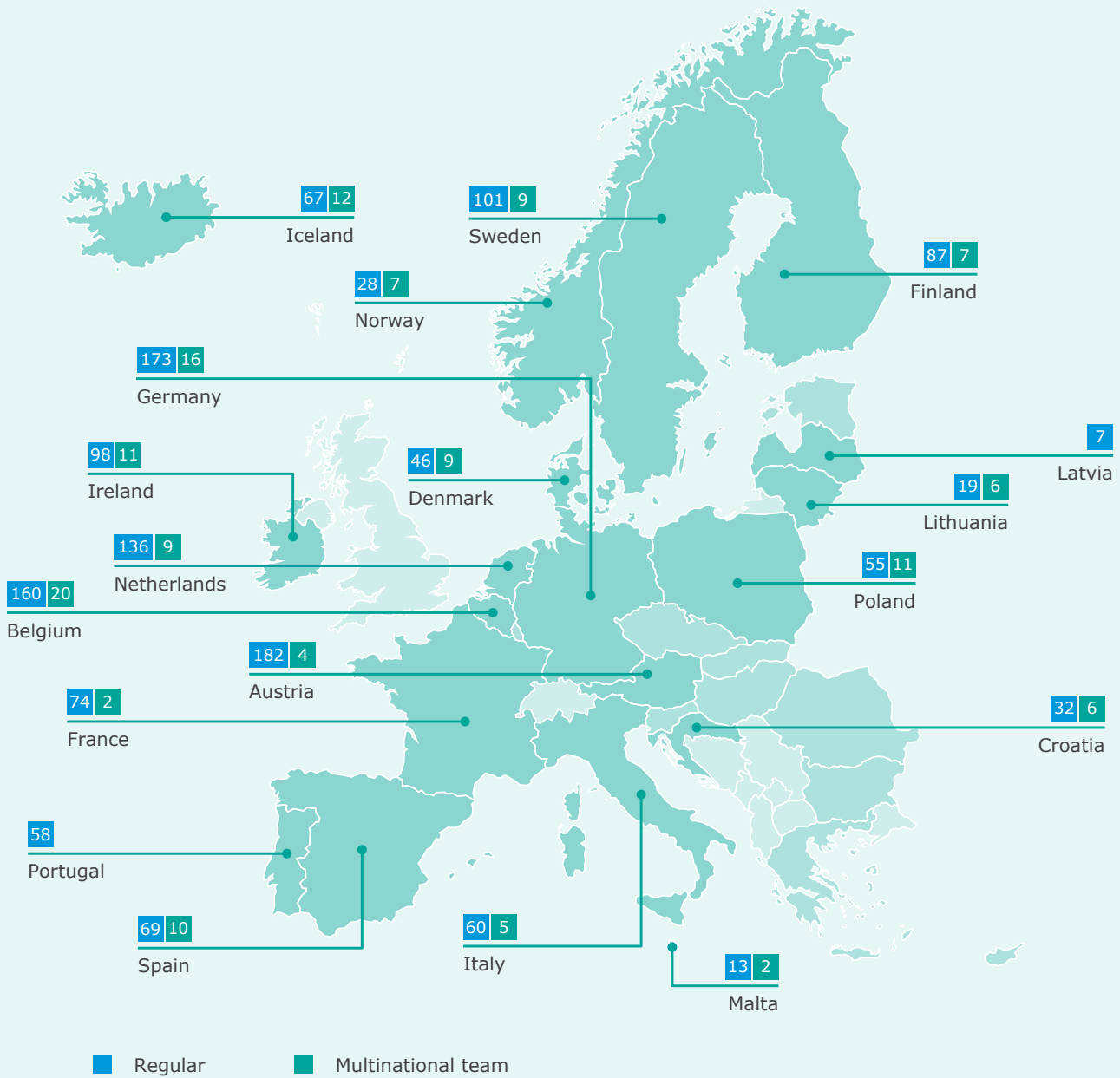
## CVMP rapporteurships/co-rapporteurships

**CVMP rapporteurs/co-rapporteurs appointed in 2020**  
 (for initial marketing authorisation applications, including generics)



## Scientific advice working party (SAWP)

### SAWP coordinators appointed in 2020







## EU Network Training Centre

The EU Network Training Centre (EU NTC) is a joint initiative of EMA and the NCAs. It is identified as a centralised resource for knowledge sharing and capacity building for the European medicines regulatory network, facilitating the development

of the network's capabilities, making best use of available resources and supporting the quality and efficiency of operations on both human and veterinary medicines. The table below highlights its key activities since its creation in 2015.

	2016	2017	2018	2019	2020
New scientific, regulatory and telematics curricula developed	8	0	2	2	2
Number of training events advertised to the EU Network	140	100	60	40	46
Number of reimbursed training events to the EU Network	25	20 (14 by EU NTC)	8 (5 by EU NTC)	12	1
Number of NCAs that have opened their training for inclusion in EU NTC Learning Management System	14	8	7	10	7
Number of users registered in the EU NTC Learning Management System	2,117	3,583	4,424	5,121	5,290
Number of NCA experts registered in the EU NTC Learning Management System	1,225	2,668	3,480	4,143	4,297

# I INSPECTIONS AND COMPLIANCE

EMA coordinates the verification of compliance with the principles of GMP<sup>2</sup>, GCP<sup>3</sup>, GLP<sup>4</sup>, GVP<sup>5</sup> and certain aspects of the supervision of authorised medicinal products in the EU. The main verification tool is inspection, which can either be carried out routinely or is requested by the CHMP or CVMP in the context of the assessment of marketing authorisation applications and/or matters referred to these committees in accordance with EU legislation.

The responsibility for carrying out inspections rests with EU NCAs but EMA plays a coordinating role.

EMA also coordinates the preparation and maintenance of risk-based inspection programmes to verify compliance with the principles of GMP, GCP and pharmacovigilance at the EU level in the following areas:

- a risk-based programme of GMP inspections based on the results of inspections by trusted authorities;
- a risk-based programme of routine GCP inspections of the clinical research organisations (CROs) most often used in the conduct of bioequivalence trials included in a marketing authorisation application in the mutual recognition and decentralised procedures (in collaboration with NCAs/CMDh);
- a risk-based programme of routine pharmacovigilance inspections in relation to CAPs (in collaboration with NCAs);
- a two-year programme of routine GCP inspections based on risk factors and a random element to ensure that a diverse range of applications, trials and sites and geographical locations are covered.

In the area of inspections, EMA ensures the best use of resources by promoting mutual reliance and work sharing with other international authorities. For GMP inspections, there are several mutual recognition agreements in place.

EMA and its European and international partners continued a pilot programme to increase their cooperation in the inspection of manufacturers of sterile medicines for human use as well as the international active pharmaceutical ingredients (APIs) inspection programme.

Through its inspectors' working groups, the Agency coordinates the development and setting of standards for GMP, GCP, GLP and GVP. This helps to harmonise standards within the EU and internationally, to strengthen global supply chains and improve access to authorised medicines. The delivery of training and capacity building on inspection-related activities for inspectors and assessors, including non-EU regulators, is a core activity of EMA. The Agency is the primary contact point for notification of suspected quality defects for centrally authorised medicines and coordinates their investigation, evaluation and follow-up. It also operates a sampling-and-testing programme to supervise the quality of centrally authorised medicines placed on the market and to check compliance of these products with their authorised specifications.

<sup>2</sup> Good manufacturing practice, a code of standards concerning the manufacture, processing, packing, release and holding of a medicine.

<sup>3</sup> Good clinical practice, a code of international standards concerning the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials.

<sup>4</sup> Good laboratory practice, a code of standards concerning the testing of medicines in laboratories during their development.

<sup>5</sup> Good pharmacovigilance practice, a set of measures drawn up to facilitate the performance of the safety monitoring of medicines in the European Union.



## Inspections

GMP, GCP, GLP and pharmacovigilance inspections requested by the CHMP or CVMP for medicines that are subject to centralised authorisation procedures take place worldwide. However, they represent just a small part of the total number of inspections performed by the EU/EEA inspectors, who also carry out inspections as part of their national programmes in the context of:

- the evaluation of marketing authorisation applications submitted to regulatory authorities across the EU;
- the oversight of manufacturers importing medicines into the EU;
- the oversight of the conduct of clinical trials in Europe;
- the oversight of compliance with pharmacovigilance obligations.

### GMP inspections

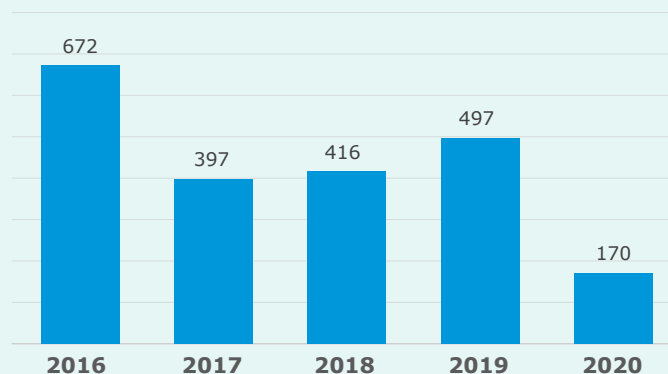
The number of GMP inspection requests within the context of the centralised authorisation procedure has decreased by 66% compared to 2019 owing to travel and safety restrictions during the pandemic.

One GMP inspection conducted by EEA authorities led to the issuing of a non-compliance statement. Medicines manufactured at a site with such a non-compliance statement cannot be sold in the EU.

When inspections lead to findings, companies have to implement corrective action plans agreed with the inspectors.

EEA authorities issued one statement of non-compliance relating to CAPs either in relation to the active substance or the finished product, which resulted in stopping the distribution of the medicines. The statement was withdrawn following the successful outcome of the company's distant assessment.

#### GMP inspections



### GMP certificates and non-compliance statements issued by EEA authorities

	2016		2017		2018		2019		2020	
	GMP certificate	GMP non-compliance statement	GMP certificate	GMP non-compliance statement	GMP certificate	GMP non-compliance statement	GMP certificate	GMP non-compliance statement	GMP certificate	GMP non-compliance statement
EEA/EU	1,951	5	2,115	7	2,213	6	2,235	11	1,695	1
China	55	4	39	1	66	4	51	4	11	0
India	96	12	119	7	112	5	105	1	64	0
USA	86	3	106	0	27	0	127	0	35	0
Rest of the world	81	0	97	2	84	1	108	0	38	0
<b>Total</b>	<b>2,269</b>	<b>24</b>	<b>2,476</b>	<b>17</b>	<b>2,502</b>	<b>16</b>	<b>2,626</b>	<b>16</b>	<b>1,843</b>	<b>1</b>

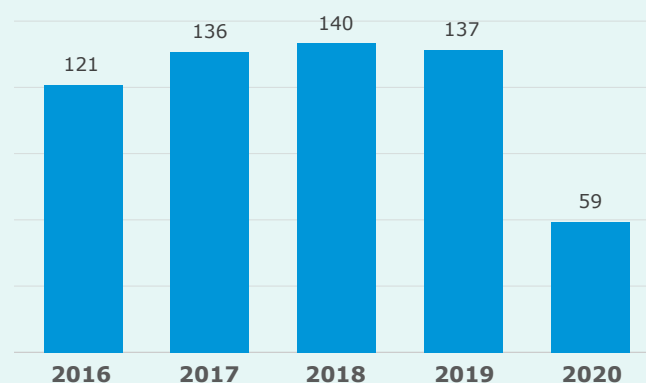
Note: This table shows the number of GMP certificates and non-compliance statements issued by EEA authorities as an outcome of GMP inspections conducted between 2016 and 2020. It includes GMP inspections requested by the CHMP or the CVMP.

### GCP inspections

The number of GCP inspections decreased significantly last year, from 137 GCP inspections in 2019 to 59 in 2020 owing to travel and safety restrictions due to the pandemic.

In 2020, the highest number of GCP inspections requested by the CHMP was conducted in the EU/EEA/EFTA, followed by the Middle East/Asia/Pacific regions and the US, which have the highest number of patients, investigator sites and pivotal clinical trials included in marketing authorisation applications for CAPs.

#### GCP inspections



Where GCP inspections report critical and/or major findings on the conduct of studies forming the basis for an application for marketing authorisation or for the extension of indication of a medicine already authorised, the CHMP evaluates the impact of the inspection findings on the medicine’s benefit-risk balance and on the rights, safety and well-being of clinical trial subjects.

Following this evaluation, the committee can request analyses of the data, excluding affected patients and/or sites. When the findings affect the overall evaluation of the clinical development programme, the approval of the medicine is likely to be compromised.

Applications for three centralised marketing authorisations and one type-II variation were withdrawn due to non-compliance with **good clinical practice (GCP)**. The CHMP adopted one negative opinion (refusing the granting of the marketing authorisation) for a medicine for which there were GCP-related non-compliance issues in the clinical study submitted by the applicant.

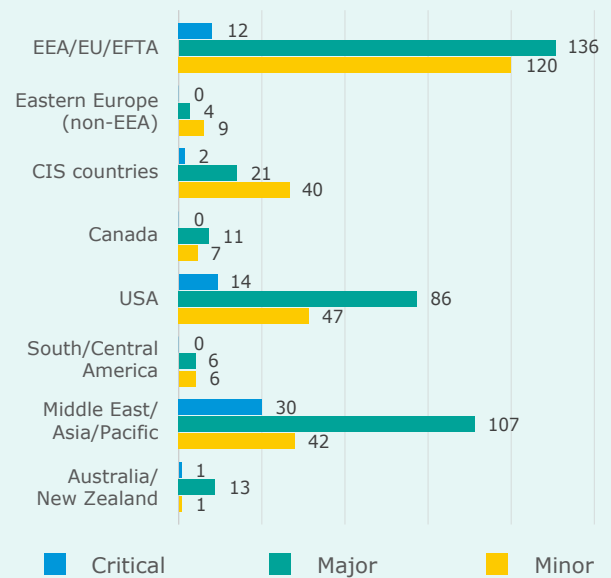
### Pharmacovigilance inspections

EMA, in cooperation with competent authorities in the Member States, maintains a risk-based programme for routine pharmacovigilance inspections of MAHs of CAPs and ensures its implementation. It also plays a key role in the coordination of pharmacovigilance inspections specifically triggered by the CHMP or CVMP and in inspection follow-up.

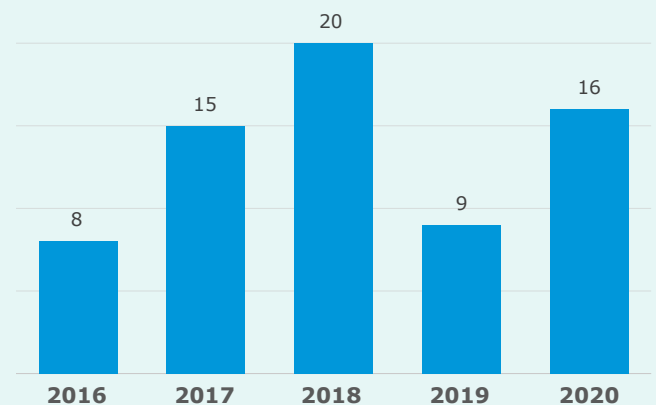
In 2020, 16 pharmacovigilance inspections were requested by the CHMP or CVMP, which is a significant increase compared to the number of pharmacovigilance inspections requested in 2019.

Most of the EU/EEA pharmacovigilance inspections (over 90%) are conducted under national pharmacovigilance inspection programmes which relate to MAHs with product authorisations of all types (including CAPs).

Type of findings of CHMP-requested GCP inspections finalised by EEA authorities (2020)



Number of pharmacovigilance inspections



## Market surveillance and quality defects

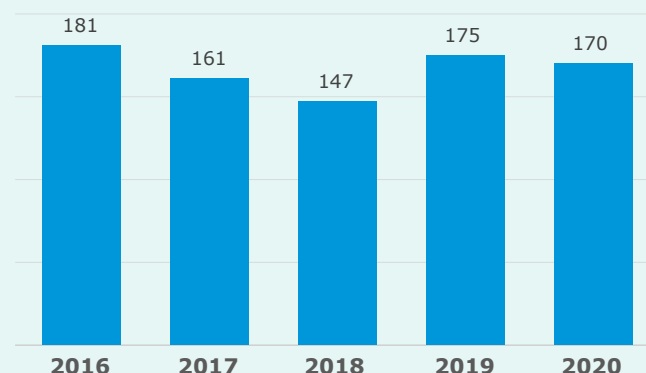
Manufacturers are required to inform authorities of quality defects in batches of a manufactured product. This can lead to a recall of batches from the market or prevention of their release by the manufacturer.

Where a defect is considered to pose a risk to public or animal health, the MAH is requested to withdraw the affected batches of the centrally authorised product from the EU market and the supervisory authority issues a rapid alert. The alert is classified from 1 to 3, depending on the expected risk to public or animal health arising from the defective product:

- Class 1 recall: the defect presents a life-threatening or serious risk to health.
- Class 2 recall: the defect may cause mistreatment or harm to the patient or animal but is not life-threatening or serious.
- Class 3 recall: the defect is unlikely to cause harm to the patient, and the recall is carried out for other reasons, such as non-compliance with the marketing authorisation or specification.

In 2020, the Agency received 170 suspected quality defect notifications. Of these, 157 cases were confirmed quality defects and led to batch recalls of 17 centrally authorised medicines.

**Number of quality defect notifications received**



### Recalls due to reported quality defects

	2016	2017	2018	2019	2020
Recalls	16	17	27	15	17
Class 1	3	2	3	3	0
Class 2	9	8	17	3	9
Class 3	4	7	7	9	8

The main reasons for recall of CAPs in 2020 are summarised in the following table:

	Manufacturing laboratory control issues	Product contamination and sterility issues	Product label issues	Product packaging issues	Product physical issues
Class 1	0	0	0	0	0
Class 2	2	0	2	3	3
Class 3	1	0	2	5	0

**Manufacturing laboratory control issues** include out-of-specification results obtained during quality control testing.

**Product contamination and sterility issues** include chemical, microbiological or physical contamination of the medicinal product.

**Product label issues** include issues related to labelling of the medicinal products (e.g. missing or incorrect batch number).

**Product packaging issues** relate to physical issues (e.g. a mix-up or a damaged container).

**Product physical issues** relate to incorrect product physical properties (e.g. friability, size/shape, leakage).

## Parallel distribution

EMA checks that the parallel distribution of centrally authorised medicines from one Member State to another by a company independent of the MAH is compliant with the rules.

Parallel distribution notifications received					
	2016	2017	2018	2019	2020
Initial notifications	2,850	2,639	2,304	2,468	3,172
Notifications of change	1,847	1,975	2,184	2,103	
Notifications of bulk change	8	6	11	12	10
Annual updates	5,138	5,843	5,245	4,270	11,624
<b>Total</b>	<b>9,843</b>	<b>10,463</b>	<b>9,744</b>	<b>8,853</b>	<b>14,806</b>

## Certificates

EMA also issues certificates to confirm the marketing authorisation status of medicines that have either been authorised or for which an application for marketing authorisation has been submitted to the Agency.



### Requests for certificates

	2016		2017		2018		2019		2020	
	re-ceived	fin-a-lised	re-ceived	fin-a-lised	re-ceived	fin-a-lised	re-ceived	fin-a-lised	re-ceived	fin-a-lised
Standard certificates requests	3,787	3,776	4,023	3,717	3,703	3,471	2,565	2,401	3,115	3,528
Urgent certificates requests	487	517	531	488	1,069	795	2,399	2,371	1,647	1,594
<b>Total</b>	<b>4,274</b>	<b>4,293</b>	<b>4,554</b>	<b>4,205</b>	<b>4,772</b>	<b>4,266</b>	<b>4,964</b>	<b>4,772</b>	<b>4,762</b>	<b>5,122</b>



# COMMUNICATION AND STAKEHOLDERS

## External communication

EMA's response to the COVID-19 pandemic was of significant interest to the media in 2020.

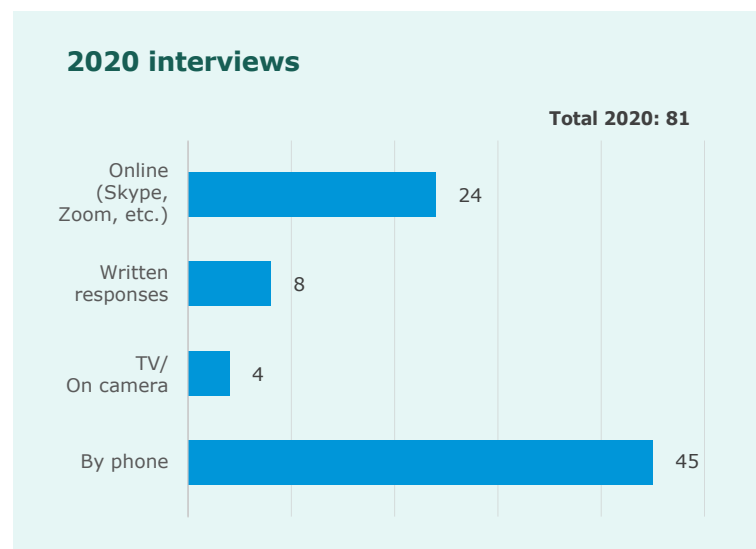
Overall, in 2020, EMA organised 81 media interviews – 63 of which were related to COVID-19. These interviews appeared in media outlets across Europe, including Euronews TV, Politico, *Die Zeit* in Germany, Bulgarian National Radio and *De Standaard* in Belgium.

EMA held two virtual press briefings in 2020.

The first briefing took place in May. At the briefing, EMA experts provided details on the Agency's response to the COVID-19 pandemic and explained how EMA is actively supporting the development and approval of medicines and vaccines.

EMA held a second press briefing in December following the CHMP's recommendation to grant a marketing authorisation in the EU for the vaccine developed by Pfizer/BioNTech (Comirnaty). The press briefing was attended by 106 journalists from across the EU and further afield.

Another topic that attracted substantial media interest in 2020 was the appointment of Emer Cooke as EMA's new Executive Director in



November. In the first months of her leadership, Emer Cooke was interviewed by several media outlets, including Bloomberg, Politico and *The Irish Times*.

## Social media

By the end of December, EMA had over 60,000 followers on Twitter (a 33% increase compared to 2019) and nearly 155,100 followers on LinkedIn (a 41% increase compared to 2019).

Throughout the year, the Agency ran several social media campaigns to highlight various topics, including campaigns for European Antibiotic Awareness Day (EAAD) and World Antimicrobial Awareness Week (WAAW) in November.



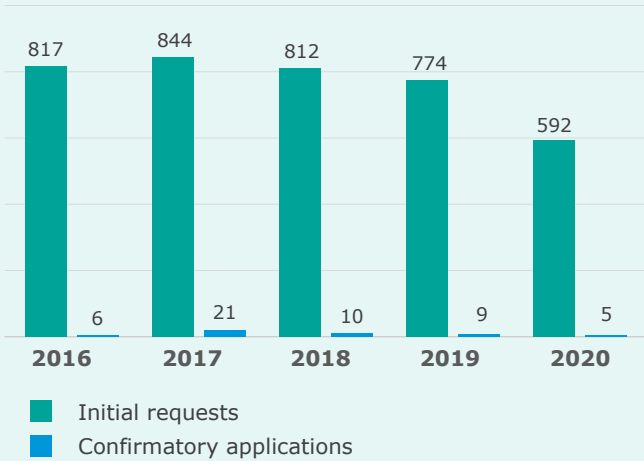
## Requests for access to documents

EU citizens have the right of access to documents held by EU institutions, bodies, offices and agencies. EMA grants this access according to the

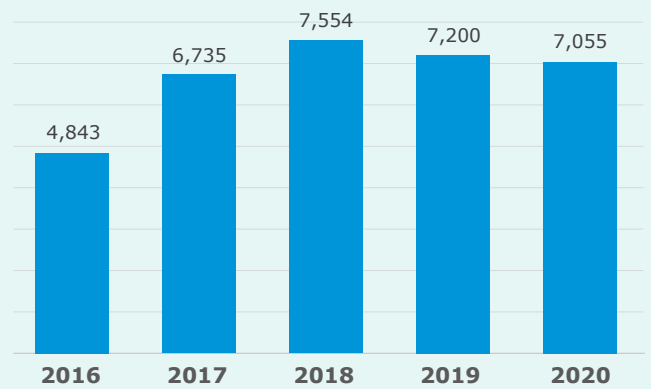
principles and further conditions as defined by Regulation (EC) No 1049/2001 and its policy on access to documents.

Requests received for access to documents

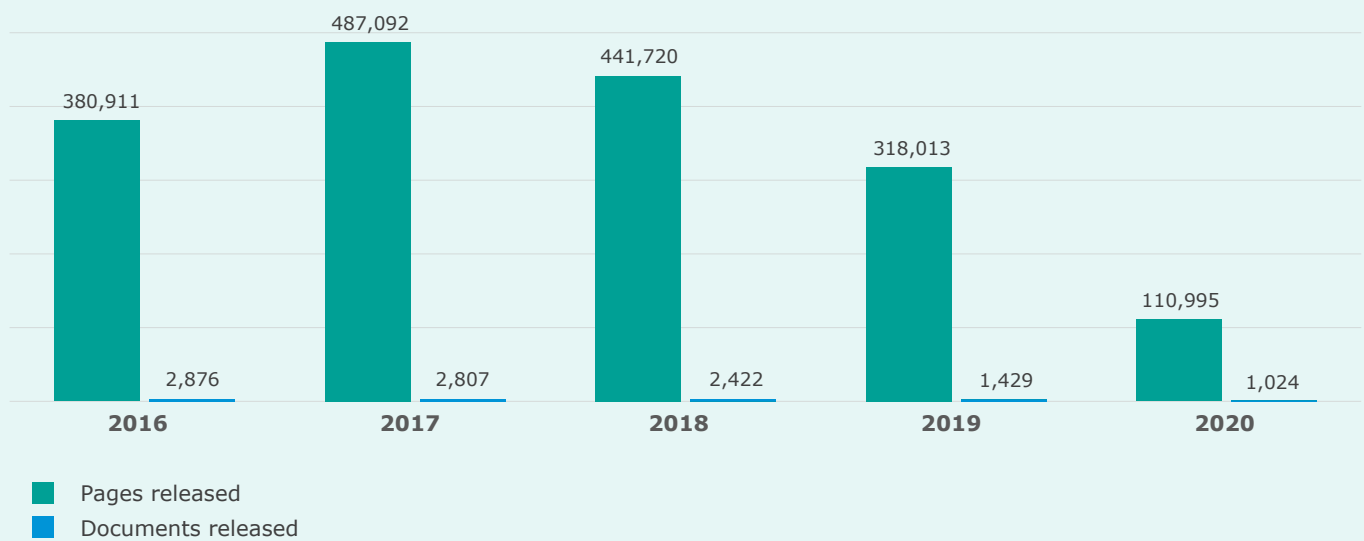
Total 2020: 597



Requests for information received



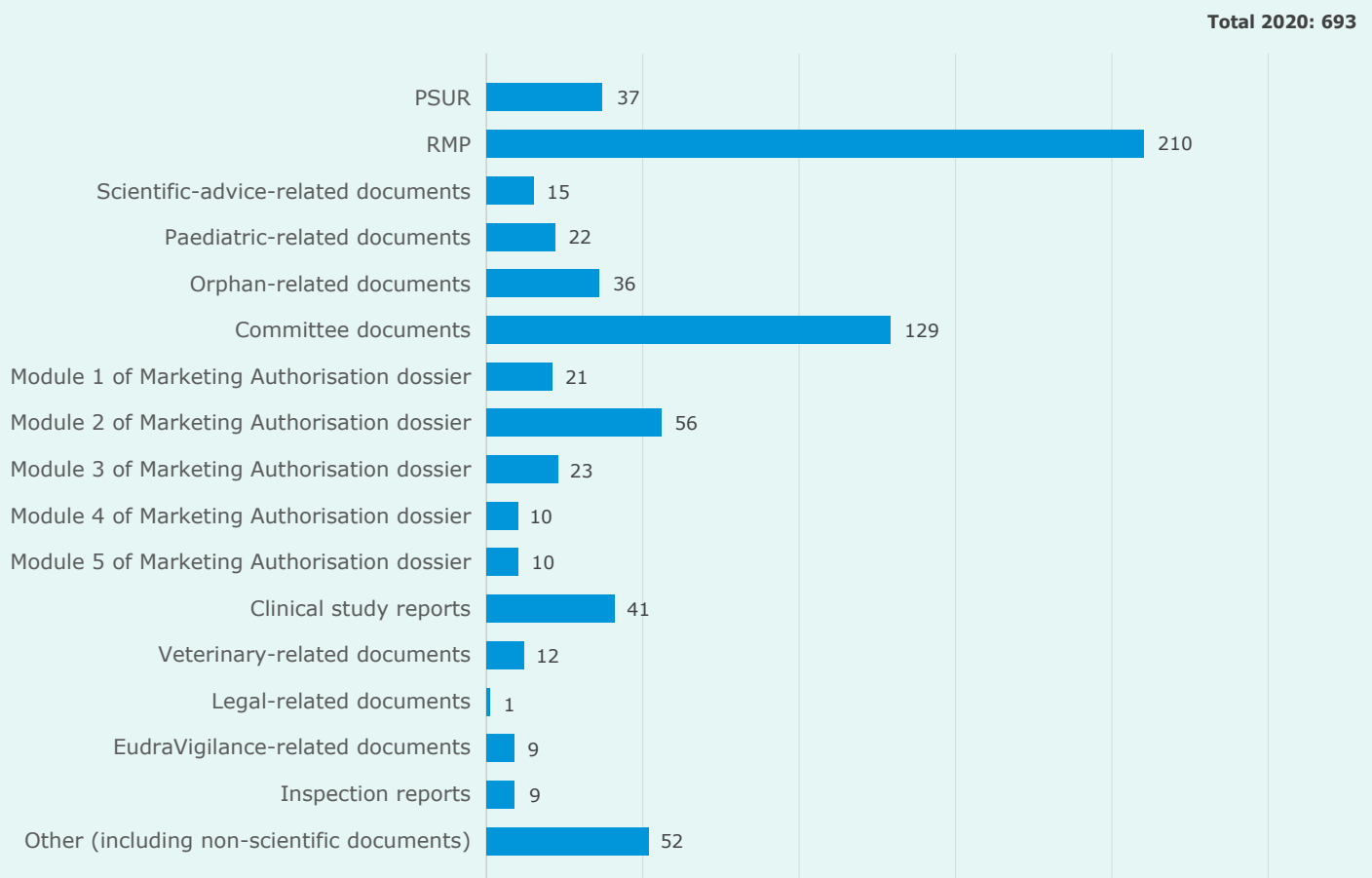
### Documents and pages released following access to document requests



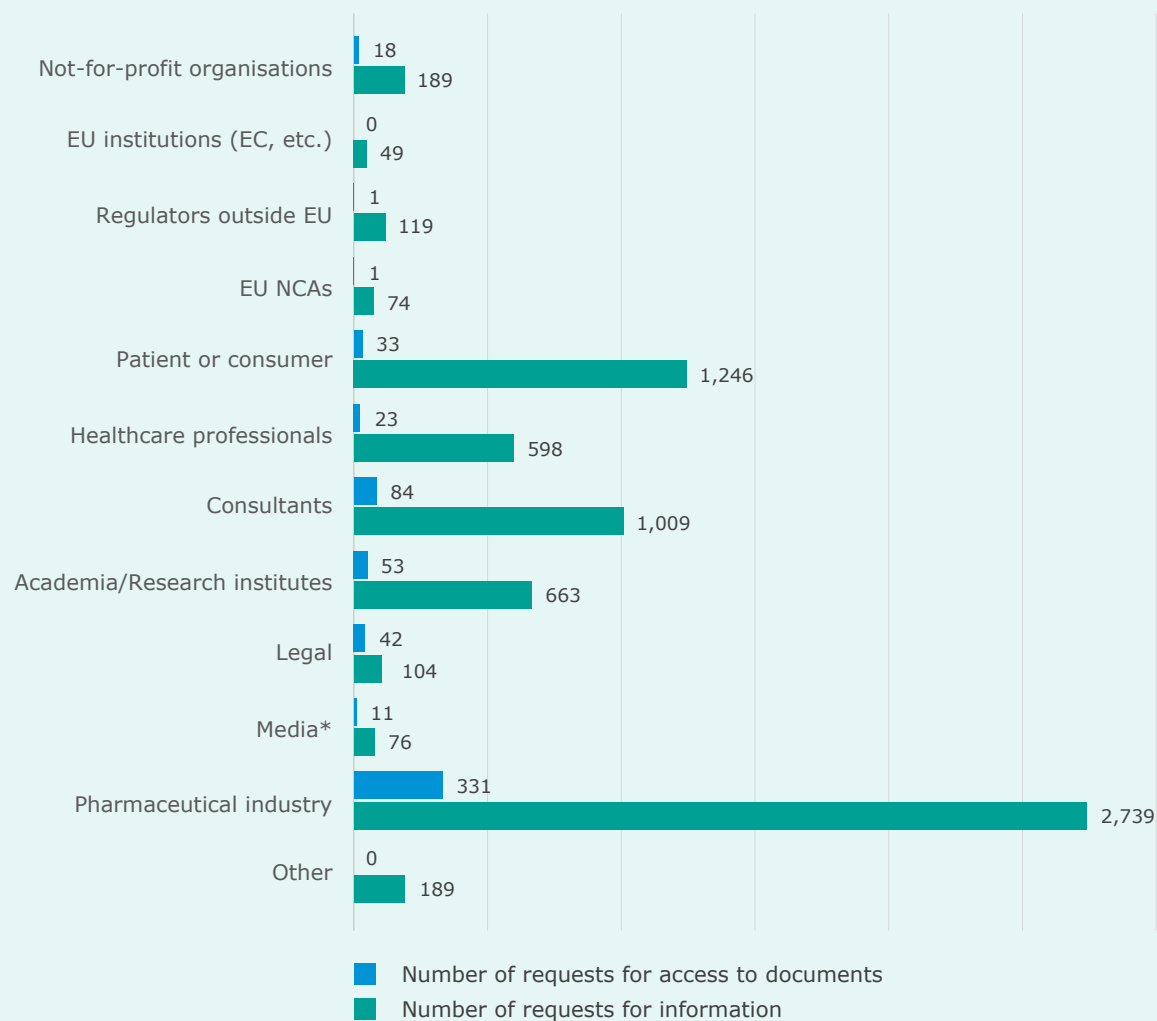
The fall in documents and pages released in 2020 was due in part to the implementation of new data protection rules (EUDPR) in the protection of personal data assessment methodology for

all access to document requests and to resource issues related to relocation of the Agency to the Netherlands following Brexit.

### Access to documents by type of document (2020)



### Affiliation of requestors of access to documents and of information (2020)



\* Requests from media submitted via EMA's online form; does not include requests sent directly to the EMA press office.

### Requests for access to document closed

Decision	2016		2017		2018		2019		2020	
	Initial re-quests	Confir-matory appl.	Initial re-quests	Confir-matory appl.	Initial re-quests	Confir-matory appl.	Initial re-quests	Confir-matory appl.	Initial re-quests	Confir-matory appl.
Fully granted	542	3	580	5	562	5	436	1	294	2
Partially granted (with redactions)	17	1	14	0	18	0	7	0	14	0
Refused	44	4	43	3	40	2	27	6	13	3
<b>Total</b>	<b>603</b>	<b>8</b>	<b>637</b>	<b>8</b>	<b>620</b>	<b>7</b>	<b>470</b>	<b>7</b>	<b>321</b>	<b>5</b>

## Publication of clinical data

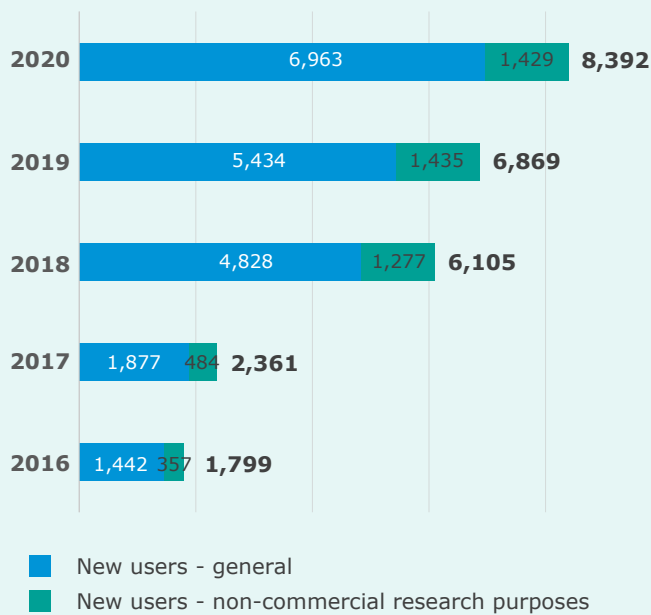
In October 2016, EMA became the first regulatory authority to give open access to clinical data submitted by companies in support of their marketing authorisation applications. The charts below capture the usage of the clinical data website from its launch in October 2016 to the end of 2020.

Due to business continuity planning (BCP) resource constraints, EMA temporarily suspended all new activities related to clinical data publication in 2018 to free up resources to safeguard and prioritise its core activities of medicines evaluation and supervision. While this suspension continued in 2020 due to the focus on COVID-19 activities

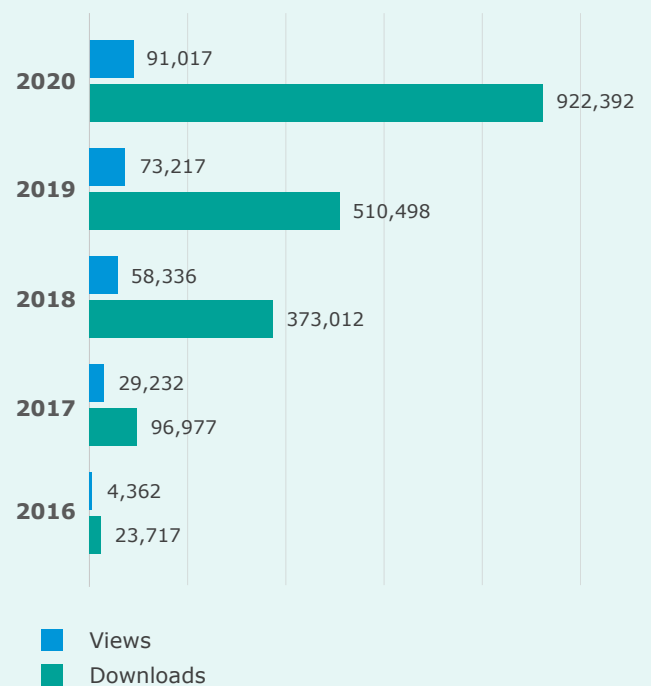
and human resource constraints, EMA decided to exceptionally publish clinical data for COVID-19 medicines, given the unprecedented public interest in this information. By the end of 2020, EMA had published the clinical data supporting the authorisation of Veklury.

Once the BCP is lifted, a strategy will be agreed by EMA for resourcing and relaunching the clinical data publication policy, with enhanced collaboration with other international partners.

Clinical data website - users



Clinical data website - usage

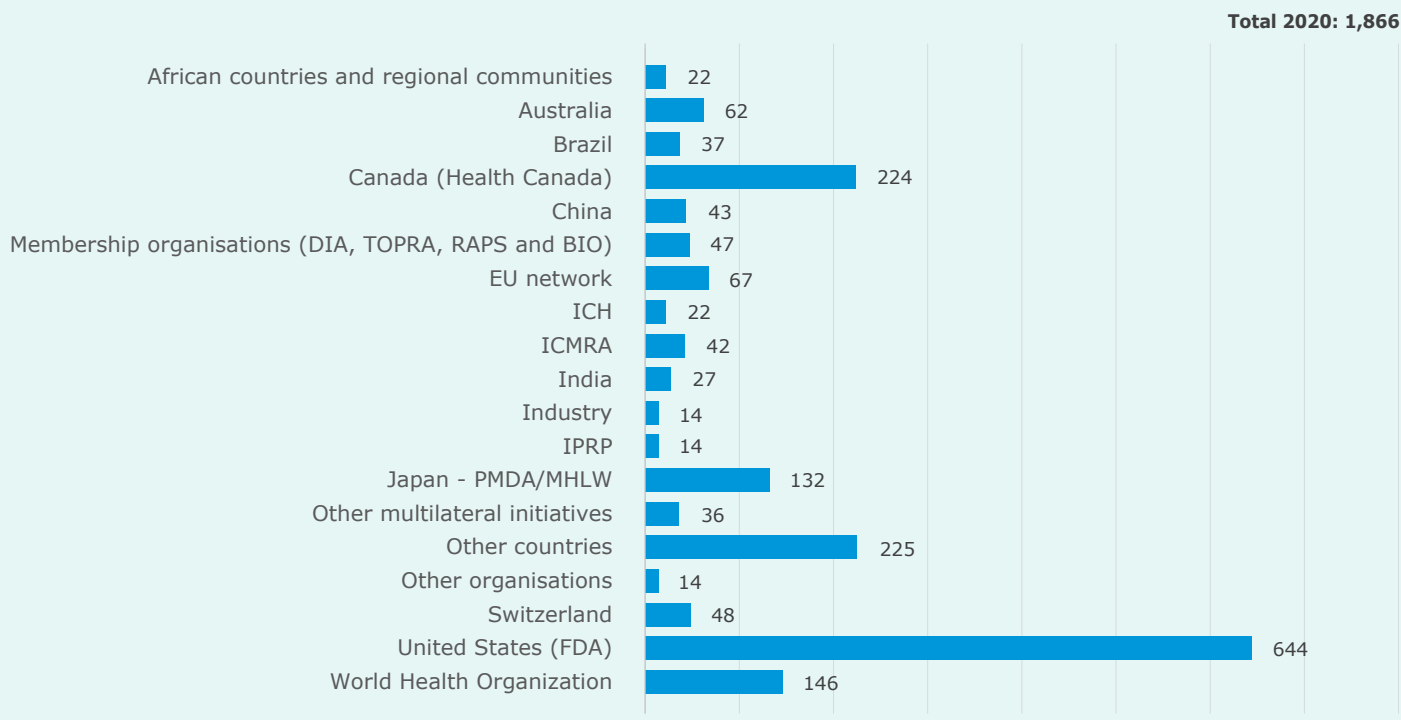


## Interaction with international stakeholders

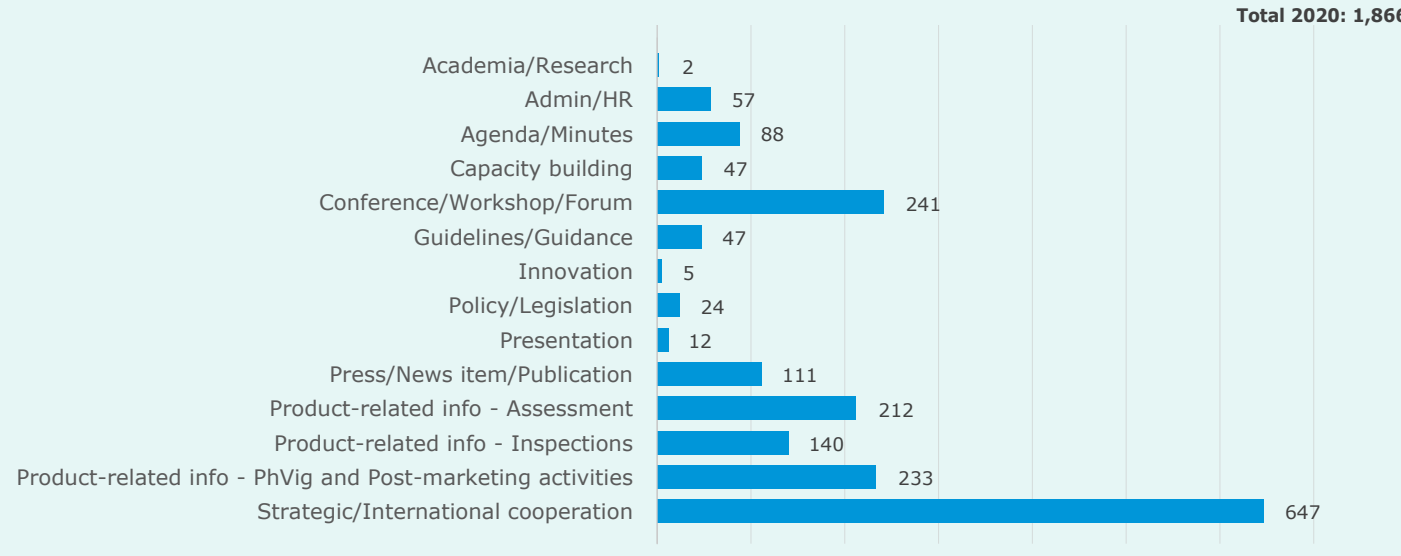
EMA has had an international role since its creation in 1995. Its founding regulation gives the Agency a specific responsibility to provide technical and scientific support for the evaluation of medicines. Today, international cooperation is moving from 'harmonisation' of technical requirements towards more mutual reliance and work-sharing through multilateral cooperation and coalitions.

In 2020, EMA had a total of 1,866 interactions with international stakeholders through its International Affairs department (AF-IA).

Number of interactions per stakeholder (2020)



Topics of interactions with international stakeholders (2020)



# I ADMINISTRATIVE ASPECTS

## Budget – total revenue

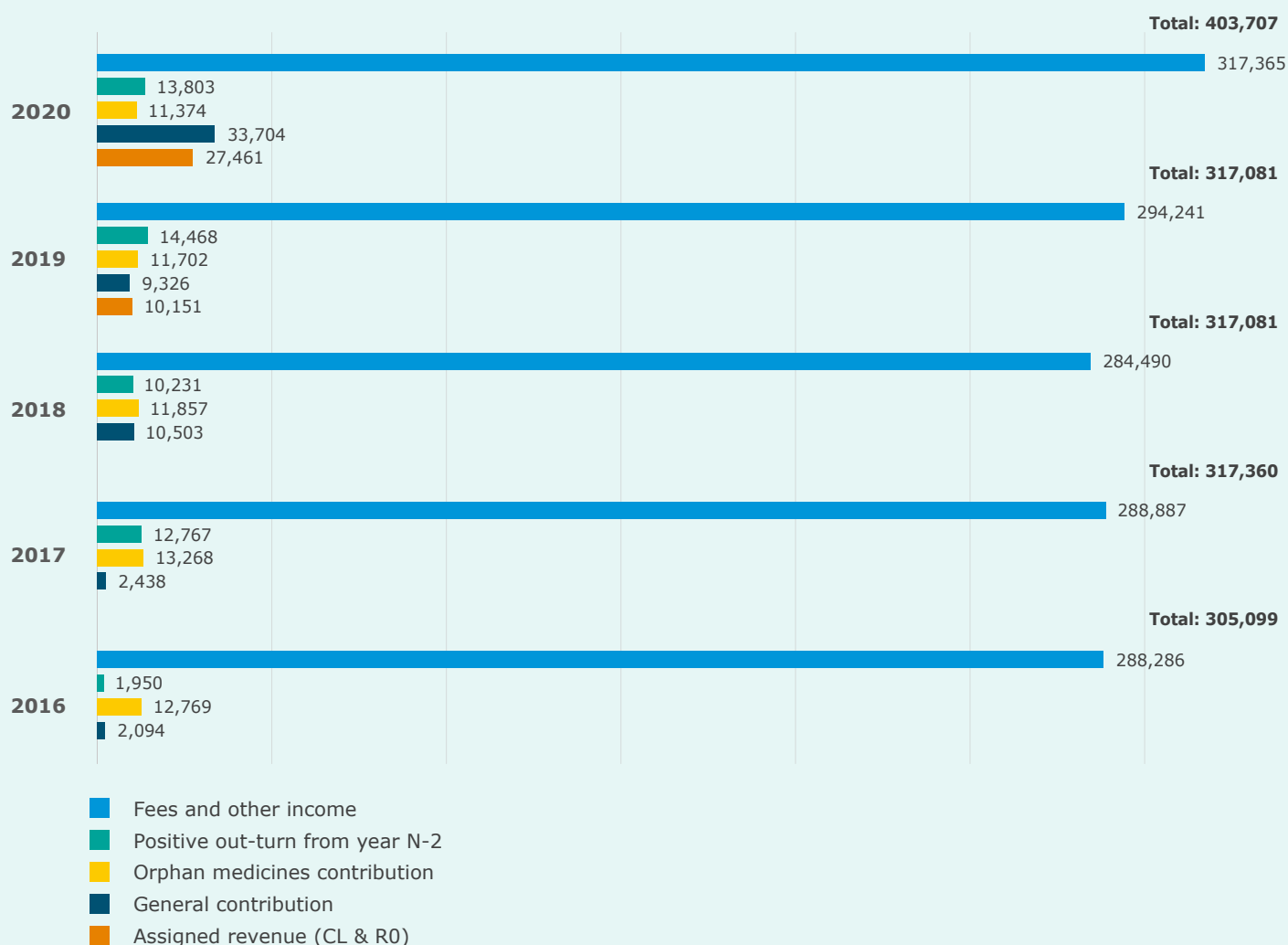
The Agency's total revenue in 2020 was €403.707 million compared to €339.889 million in 2019.

The revised Financial Regulation, which came into effect in 2019, introduced two new funding sources for handling assigned revenue: R0 for external assigned revenue (inducements related to the EMA building in Amsterdam) and CL for internal assigned revenue (rent and building charges received from the Agency's subtenant in London).

In view of the long-term nature of this revenue stream, it is now included as a separate category in the table below.

In 2020, the assigned revenue received amounted to approximately €27.461 million.

### Revenue (in € thousands)



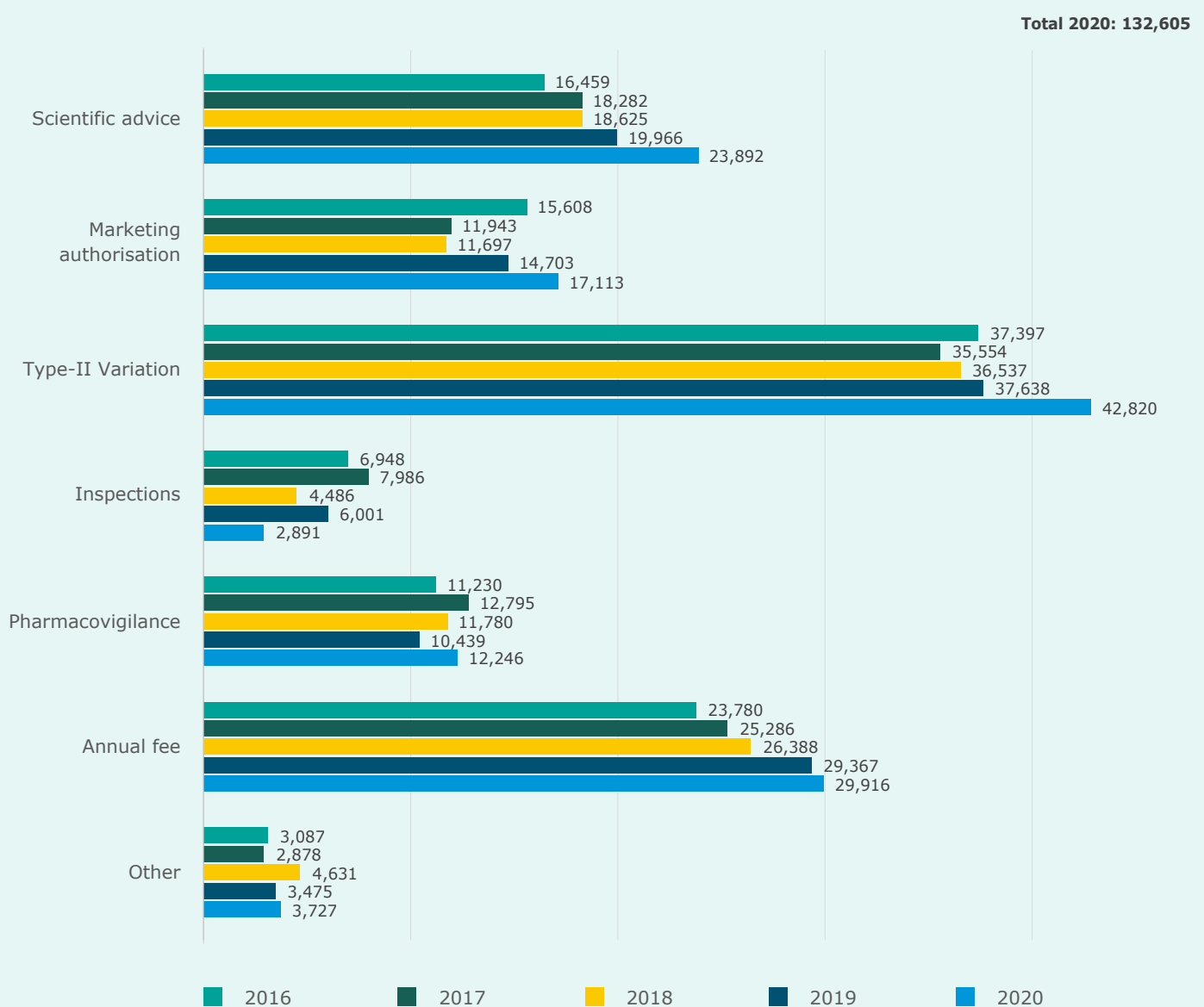
## Remuneration to national competent authorities

NCA's in the EU Member States receive a share of EMA's revenue from fees for the assessments they carry out on behalf of the Agency.

In 2020, EMA paid a total of €132.6 million to the NCA's, compared to €121.6 million in 2019.

This figure includes payment for pharmacovigilance procedures, including the assessment of PSURs, PASS protocols and study results, and of pharmacovigilance-related referrals. Fees are charged to companies whose medicines, whether authorised centrally or nationally, are included in these procedures.

Remuneration to NCA's per fiscal year (in € thousands)

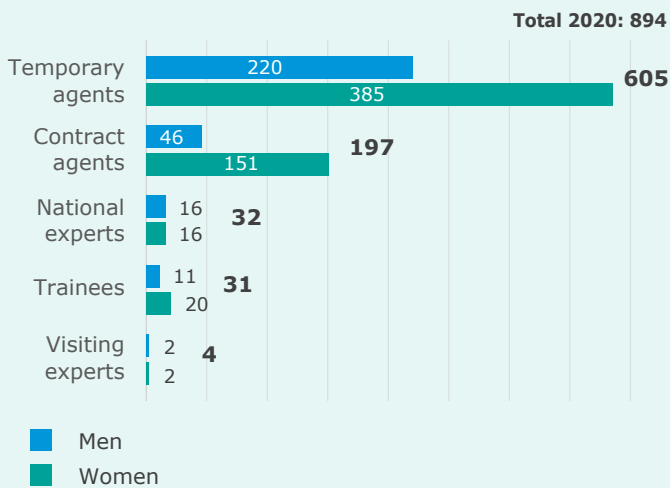




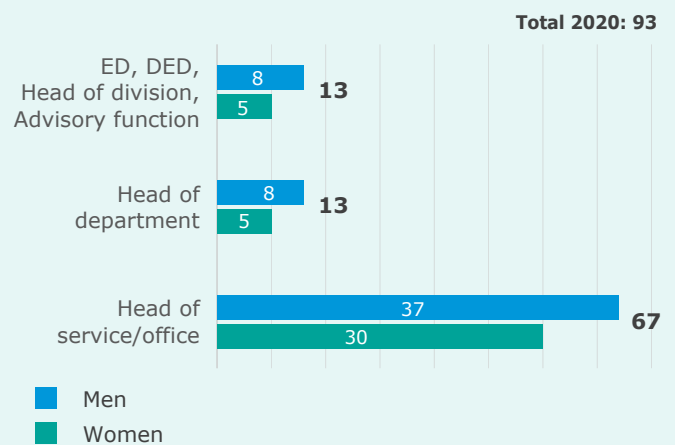
# Agency staff

As of December 2020, Agency staff numbered 894: 597 women and 297 men.

## Agency staff (as of 31 December 2020)



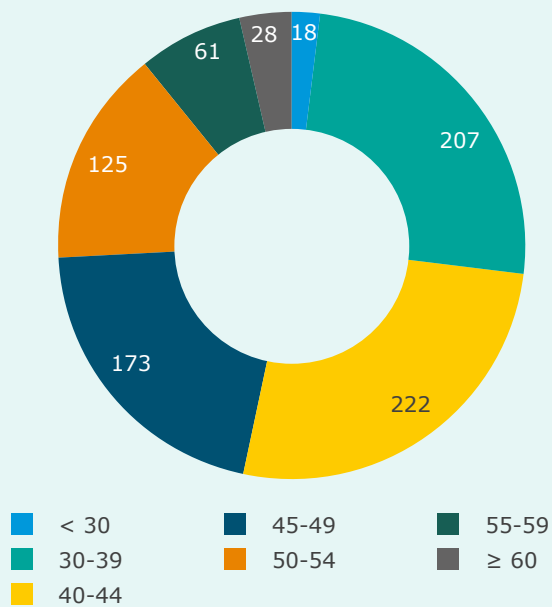
## Gender balance of Agency management (as of 31 December 2020)



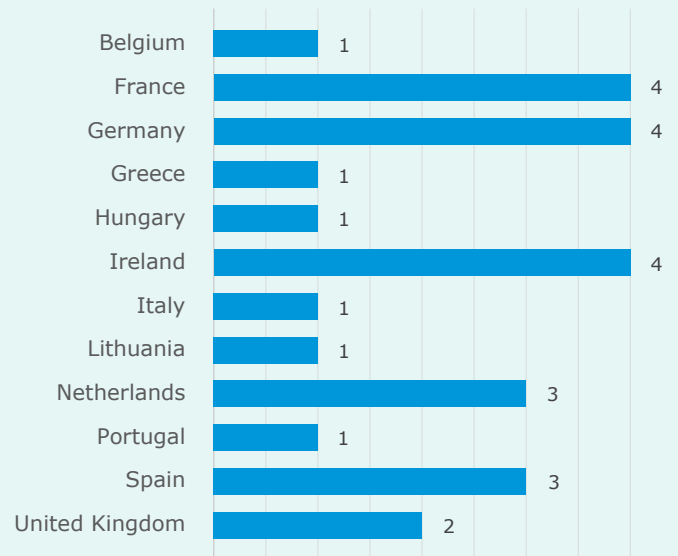
## Gender balance of Agency staff 2020

Status	Category AD (administrators)		Category AST (assistants)		TA/CA - all grades	
	Men	Women	Men	Women	Men	Women
Temporary agents	187	182	33	203	220	385
Contract agents	24	70	22	81	46	151
<b>Total</b>	<b>211</b>	<b>252</b>	<b>55</b>	<b>284</b>	<b>266</b>	<b>536</b>
<b>Total in %</b>	<b>46%</b>	<b>54%</b>	<b>16%</b>	<b>84%</b>	<b>33%</b>	<b>67%</b>

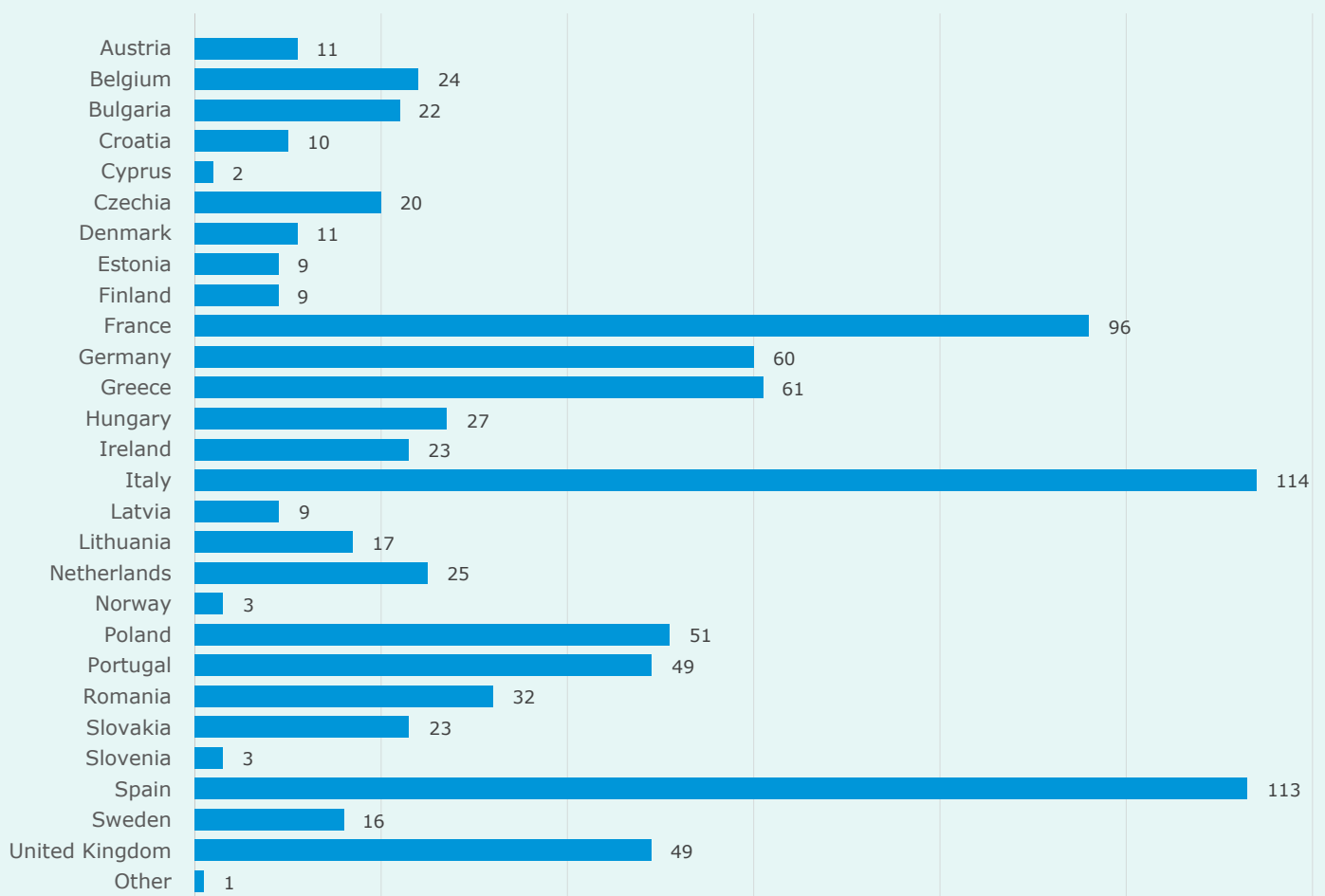
**Age-range statistics (31 December 2020)**



**National origins of Agency management (as of 31 December 2020)**



**National origins of Agency staff (as of 31 December 2020)**



# I ANNEXES

**Annex 1** – Members of the Management Board

**Annex 2** – Members of the Committee for Medicinal Products for Human Use

**Annex 3** – Members of the Pharmacovigilance Risk Assessment Committee

**Annex 4** – Members of the Committee for Medicinal Products for Veterinary Use

**Annex 5** – Members of the Committee on Orphan Medicinal Products

**Annex 6** – Members of the Committee on Herbal Medicinal Products

**Annex 7** – Committee for Advanced Therapies

**Annex 8** – Members of the Paediatric Committee

**Annex 9** – Working parties and working groups

**Annex 10** – CHMP opinions on initial evaluations and extensions of therapeutic indication in 2020

**Annex 11** – Guidelines and concept papers adopted by CHMP

**Annex 12** – CVMP opinions on medicinal products for veterinary use in 2020

**Annex 13** – Guidelines and concept papers adopted by CVMP in 2020

**Annex 14** – COMP opinions on designation of orphan medicinal products in 2020

**Annex 15** – HMPC European Union herbal monographs in 2020

**Annex 16** – PDCO opinions and EMA decisions on paediatric investigation plans and waivers in 2020

**Annex 17** – Referral procedures overview 2020 – human medicines

**Annex 18** – Arbitrations and referrals in 2020 – veterinary medicines

**Annex 19** – Budget summaries 2019–2020

**Annex 20** – European Medicines Agency establishment plan

**Annex 21** – Access to documents requests in 2020

**Annex 22** – Publications by Agency staff members and experts in 2020

The annexes are available on EMA's [website](#).



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**Annual report 2020**

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