EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

ANNUAL REPORT 2022

The European Medicines Agency's contribution to science, medicines and health in 2022

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I FOREWORD

by Lorraine Nolan

Chair of EMA Management Board

Welcome to EMA's annual report for 2022. In here you will find details about EMA's achievements and milestones during another transformative year for the Agency, the regulatory network and European healthcare systems as a whole.

This is my first year as Chair of the Management Board, a role I took over from Christa Wirthumer-Hoche in March. I would like to start by thanking Christa for her valuable support. Her tenure as EMA Chair coincided with a series of crises and organisational challenges – Brexit, EMA's move to Amsterdam and the COVID-19 emergency. Throughout this challenging period, Christa's steadfast advocacy, commitment and dedication as chair of EMA's Management Board was exemplary.

In 2022, people began to live with COVID-19 in the community. The pandemic did not end, but it did evolve during the year with different phases requiring new vaccination campaigns for Member States. A key focus for EMA was on the approval of new and the development of existing vaccines and therapeutics to support this public health response collaborating across the regulatory network to pool the best scientific expertise from across the EU.

In March, EMA started operating under a new extended mandate which recognised the role the Agency played during the pandemic. One of my responsibilities as Chair of the Management Board is to ensure that the Agency has the resources to deliver efficiently on this new mandate.

During the course of the year, we also saw significant enhancements to the medicines regulatory system with the implementation of two new regulations, which are transforming human and animal medicines regulation in the EU – the Clinical Trials Regulation, which includes the Clinical Trials Information System, for which EMA is responsible, and the Veterinary Medicines Products Regulation. These regulatory changes will strengthen our system and provide better outcomes for patients and animal health and health system delivery.

I would like to acknowledge the forward steps we have been making to bring data and analytics into our work in 2022 more specifically. Digital innovation has disrupted all industries, and the work of a medicines regulator is not beyond its influence. By embracing new technologies, we can further develop new approaches to the way we assess and approve treatments and therapies in the EU. For example, the Data Analysis and Real World Interrogation Network (DARWIN EU) will deliver timely and reliable evidence from across Europe on diseases, populations and the uses and performance of medicines.

At the organisational level, the Management Board saw the benefits of continued investment in IT to improve processes and efficiency in EMA. Our organisation has to make sure that our ways of working meet the needs of the European medicines regulatory network in a fashion that is streamlined, efficient and reliable. We will continue to ensure that EMA's processes, systems and approaches are progressive and fit for a world leading public health agency.

Our achievements, as outlined in this report, give multiple examples of the true value of partnership across the EU regulatory network. Most of EMA's work relies heavily on collaboration between regulators, organisations, people and Member States. Looking ahead, as Chair of the Management Board I would like to see continued investment in the sustainability of our network to ensure we have the resourcing and capacity to meet the regulatory needs of the EU population, both in normal times, and in a crisis.

Finally, I would like to thank my fellow Board members for putting their trust in me as Chair, and to all of my colleagues across the regulatory network and the European Commission. I would also like to express my deep gratitude to EMA's staff whose scientific excellence in the evaluation and supervision of medicines supports all European citizens and animals alike. As we continue to navigate our way out of the pandemic, let us all continue to work closely together, share our ideas and expertise and make sure the medicines regulatory network that emerges from this crisis is stronger, bolder and ready for current and emerging challenges.

I INTRODUCTION

by Emer Cooke

EMA Executive Director

As the Executive Director of EMA, I look back on 2022 with a sense of pride and satisfaction in how we tackled new phases of the pandemic, negotiated a new health crisis and expanded on our mission.

Although we saw some return to more routine activities, largely thanks to the speed of scientific progress and the roll-out of effective vaccination campaigns across the EU, the COVID-19 virus continued to force us to pivot, innovate and adapt.

In 2022, new variants of concern emerged requiring appropriate counter measures by Member States to protect the health of citizens. We invested additional efforts into being an authoritative, reliable source of information for EU citizens and our experts continued to work around the clock to ensure the review of the safety and effectiveness of much-needed vaccines and therapeutics.

As a result, we have many more options to prevent serious hospitalisation and death now than we did in 2021. By the end of the year, we had a total of seven COVID-19 vaccines authorised for use in the EU. Two of these, the mRNA vaccines, were further developed and tailored to specific strains of the SARS-CoV-2 virus. This gave Member States the flexibility they needed to adapt when it came to launching their own vaccination campaigns.

In March, we started to operate under our extended mandate, which was shaped by the extensive role we had played through this health crisis. This mandate gives us added responsibilities in the area of crisis co-ordination and response. As well as formalising some of our ad hoc procedures, it gives us new tools to respond effectively to future public health crises and tackle medicine shortages.

The first real test of our extended mandate came in mid-2022 through the mpox (monkeypox) public health emergency. This crisis put our new responsibilities to the test. EMA played a central role in co-ordinating actions and providing scientific recommendations on critical medicines and vaccines as well as putting measures in place to avoid shortages.

Our extended mandate also set the framework for the establishment of DARWIN EU – a federated model for collecting real-world evidence from across the EU on diseases, populations and the uses and performance of medicines and vaccines right through their lifecycle. Potentially, this is a sea change for medicines regulation, feeding into a future European health data space.

Despite the ongoing focus on crises, our regulatory approvals continued with 89 human medicines recommended for approval by the Committee for human medicines. This included the first authorised product worldwide for the prevention of respiratory syncytial virus (RSV) disease in newborns and infants, as well as six advanced therapy medicines, notably the first gene therapy for severe and moderately severe haemophilia B. Under the EU Medicines for all (EU-M4All) procedure, EMA evaluated a new vaccine against dengue and two diabetes treatments that address important public health issues outside the EU. In the veterinary area, we recommended 10 new medicines for approval, including the first DNA vaccine for dogs.

Just as important has been the progress made in the implementation of two new major pieces of legislation, bringing profound changes to the way clinical trials are regulated and veterinary medicines are supervised in the EU.

In January, the Clinical Trials Regulation and the Clinical Trials Information System, or CTIS, came into force setting the building blocks to reinvigorate and facilitate clinical research in the EU. This is a major change, a move from entirely national approaches to a system with a single EU submission, coordinated assessment between the Member States and high levels of transparency never seen before for clinical trials.

The Veterinary Medicines Products Regulation, which came into force in January, also helps to foster product innovation as well as facilitating wider access to information about medicines for animals, better monitoring of suspected side effects, and new measures to limit the development of antimicrobial resistance.
As part of the intense implementation efforts, EMA successfully launched the Veterinary Medicines information website at the beginning of the year.

The last three years have brought untold change and put new pressure on our healthcare systems. One of the key things we have learned during this crisis is how to quickly adapt to a dynamic new world.

As we look ahead, EMA will continue to develop, adapt and streamline our regulatory processes while maintaining the highest standards for quality, safety and efficacy of medicines. We will further strengthen scientific collaboration between regulators, governments, industry and patients and step up our communication to EU citizens. And along with all of the incredible EMA staff and experts from the national authorities in our committees and working parties, I look forward to continuing the important work we do with our partners and stakeholders to further promote public and animal health in the EU.

CHAPTER 1

KEY ACHIEVEMENTS IN 2022

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 2022, EMA recommended 89 medicines for marketing authorisation, 41 of which had a new active substance. Below is a selection of medicines approved in 2022 that represent significant progress in their therapeutic areas:

Beyfortus, the first medicine for the prevention of respiratory syncytial virus (RSV) lower respiratory tract disease in newborns and infants during their first RSV season (when there is a risk of RSV infection in the community).

Breyanzi, a gene therapy for the treatment of adult patients with three subtypes of non-Hodgkin lymphoma (diffuse large B-cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B)), whose cancer has come back or who have not responded to treatment after two or more lines of systemic therapy.

Carvykti, for the treatment of adults with relapsed and refractory multiple myeloma who have received at least three prior therapies and whose cancer has worsened since they received their last treatment.

Ebvallo, for the treatment of Epstein-Barr virus positive post-transplant lymphoproliferative disease. This somatic cell therapy is intended for adult and paediatric patients who develop this malignancy after transplantation as a result of the immunosuppression caused by the medication required to reduce the possibility of rejection of the transplanted organ or bone marrow.

Hemgenix, the first gene therapy for the treatment of severe and moderately severe Haemophilia B in adults, an inherited disorder characterised by an increased bleeding tendency due to a partial or complete deficiency in the activity of factor IX.

Kimmtrak, a monotherapy for treatment of adult patients with a form of eye cancer called uveal melanoma.

Mounjaro, a first-in-class medicine that activates both the GLP-1 and GIP receptors, which leads to improved blood sugar control in adults with type-2 diabetes mellitus.

Roctavian, for the treatment of severe haemophilia A in adults who do not have factor VIII inhibitors (auto-antibodies produced by the immune system which make factor VIII medicines less effective) and no antibodies to adeno-associated virus serotype 5 (AAV5).

Upstaza, the first treatment for adult and paediatric patients with aromatic L-amino acid decarboxylase (AADC) deficiency, an ultra-rare genetic disorder affecting the nervous system.

Xenpozyme, the first therapy for the treatment of adult and paediatric patients with acid sphingomyelinase deficiency (ASMD), a rare genetic condition, historically known as Niemann-Pick disease type A, A/B and B.

Zokinvy, the first treatment for children with progeroid syndromes, an ultra-rare genetic disease which causes premature aging and death.

COVID-19 Vaccine Valneva and **VidPrevtyn Beta**, two vaccines for preventing COVID-19 in adults.

Paxlovid (for adults) and **Evusheld** (for adults and adolescents aged 12 years and older), two treatments for COVID-19.

EARLY ACCESS TO MEDICINES THAT ADDRESS PUBLIC HEALTH NEEDS

In 2022, **five medicines** received a recommendation for marketing authorisation following an **accelerated assessment: Beyfortus, Kimmtrak, Lunsumio, Tecvayli** and **Xenpozyme**. 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).

The **two vaccines and two treatments for COVID-19** recommended for authorisation by EMA in 2022 were assessed under a rolling review. EMA can use this regulatory pathway during a pandemic to speed up the evaluation of medicines by assessing data as they become available from ongoing studies.

Nine medicines received a recommendation for a **conditional marketing authorisation**, one of the possibilities in the EU to give patients early access to new medicines: **Carvykti, Hemgenix, Kinpeygo, Lunsumio, Paxlovid, Roctavian, Spevigo, Tecvayli** and **Zynlonta**.

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), because the benefit of earlier patient access outweighs the potential risks of limited data. These authorisations are subject to specific post-authorisation obligations to generate complete data on the medicines.

Five medicines (Ebvallo, Livmarli, Nulibry, Upstaza and **Zokinvy**) 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, either because there are only very few patients with the disease, or the collection of complete information on the efficacy and safety of the medicine would be unethical, comprehensive data cannot be obtained even after authorisation. These medicines are subject to specific post-authorisation obligations and monitoring.

The enhanced development support provided by EMA's PRIority MEdicines (PRIME) 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 medicines** with **PRIME designation** were recommended for approval (**Beyfortus, Breyanzi, Carvykti, Ebvallo, Hemgenix, Roctavian, Tecvayli, Xenpozyme**).

13 medicines under development were accepted in the scheme in 2022 pertaining to the following disease areas: endocrinology-gynaecology-fertility-metabolism (2), neurology (2), oncology (2), vaccines (2), haematology – haemostaseology (1), infectious diseases (1), musculoskeletal and connective tissue disorders (1), ophthalmology (1), and uro-nephrology (1).

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 89 medicines recommended for marketing authorisation in 2022, **21 had their orphan designation confirmed** by the end of the year.

Three medicines lost their orphan status before receiving a marketing authorisation, which means they were still authorised as medicinal products but not as orphan medicinal products. These are: **Breyanzi**, **Pepaxti** and **Tecvaily**.

NEW USES FOR EXISTING MEDICINES

In 2022, 90 extensions of indication were recommended, including 37 for paediatric use. The extension of the use of a medicine that is already authorised for marketing in the EU can also offer new treatment opportunities for patients. Extensions of indication included:

Adcirca, for the treatment of pulmonary arterial hypertension (PAH) in paediatric patients aged 2 years and above;

Dupixent, for the treatment of eosinophilic esophagitis (a rare, chronic, inflammatory disease of the esophagus) in adults and adolescents 12 years and older who cannot follow conventional medicinal therapy;

Jakavi, for the treatment of paediatric patients with acute and chronic Graft vs Host Disease (when white blood T cells in donated stem cells or bone marrow attack the host's body cells) from 12 years of age, who have inadequate response to corticosteroids or other systemic therapies;

Jardiance, for the treatment of all types of heart failure, including those with preserved ejection fraction;

Xydalba, for the treatment of acute bacterial skin and skin structure infections in adults and paediatric patients aged 3 months and older.

NEGATIVE OPINIONS

The Committee for Medical Products for Human Use (CHMP) adopted a **negative opinion for three medicines** in 2022: **Hervelous, Omblastys** and **Tuznue**.

98% of all opinions (positive and negative) were reached by consensus among the 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.

52% of applicants that were granted a positive opinion for their medicine had received scientific advice or protocol assistance from EMA during their product's development phase. The figure increases to 78% for applicants for medicines with new active substances. Early engagement with developers allows EMA to clarify what kind of evidence is required to later evaluate a medicine for authorisation. This encourages the 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 done 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 a recall of a limited number of batches.

The product information for 467 centrally authorised medicines was updated on the basis of new safety data in 2022. Every year, recommendations by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) on safety 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 make informed decisions when using or prescribing a specific medicine.

Important new safety advice issued in 2022 included:

- a recommendation to withdraw the marketing authorisations for **amfepramone obesity medicines** because risk management measures were not sufficiently effective to reduce the risk of serious side effects, such as pulmonary arterial hypertension (high blood pressure in the lung arteries) and dependency. In addition, there was evidence of use during pregnancy, which could pose risks to the unborn baby;
- an update of the product information of **dexmedetomidine** to highlight the increased risk of mortality when administering dexmedetomidine in intensive care unit (ICU) patients aged 65 years and less, compared with alternative sedatives;
- a recommendation to suspend marketing authorisations for **hydroxyethyl-starch (HES) solutions** for infusion across the EU to avoid their use outside the recommendations previously included in the product information to minimise the risk of kidney injury and death in certain patients (those critically ill, with burn injuries or with sepsis);
- an update of the product information of **infliximab** to include a recommendation to postpone the use of live vaccines in infants who are exposed to infliximab during pregnancy or via breastfeeding;
- a recommendation to only use **Janus-kinase (JAK) inhibitors** if no suitable treatment alternatives are available for people at increased risk of major cardiovascular problems, those who smoke / have smoked and those at increased risk of cancer. In addition, caution is advised for use in patients with risk factors for blood clots in the lungs and in deep veins (venous thromboembolism, VTE). The use of a lower dose is recommended in patients with risk factors;
- an update of the product information of **Mavenclad (cladribine)** to include the risk of serious liver injury and to conduct liver function tests during treatment. In case a patient develops liver injury, treatment with Mavenclad should be interrupted or discontinued, as appropriate;

- a recommendation to add new measures to use **medicines containing nomegestrol or chlormadinone** at the lowest effective dose and for the shortest duration possible, and only when other interventions are not appropriate, and not to use these medicines in patients who have, or have had, meningioma;

- a recommendation to withdraw marketing authorisations of **pholcodine-containing medicines** across the EU given the serious risk of anaphylactic reactions (sudden, severe and life-threatening allergic reactions) to certain medicines called neuromuscular blocking agents (NMBAs) used in anaesthesia in patients who have been previously treated with pholcodine;

- a recommendation to not use **Rubraca** (rucaparib) as third-line treatment for cancers of the ovary, fallopian tubes or peritoneum with a BRCA mutation in patients whose cancer has come back after at least two platinum-based chemotherapies and who cannot have further platinum-based therapy;

- a revised warning against the use of live vaccines in infants exposed to **Stelara** (ustekinumab) in utero for six months following birth or until the infant's serum levels of ustekinumab are undetectable;

- new recommendations to avoid or discontinue the use of **Stresam** (etifoxine) in patients with severe skin reactions or severe liver problems after taking etifoxine;

- a recommendation to update the product information for **terlipressin-containing medicines** with warnings to reduce the risk of respiratory failure and sepsis when using terlipressin to treat kidney problems in people with advanced liver disease;

- an update of the product information of **Xalkori** (crizotinib) to reflect the risk of ocular toxicity, severe visual loss and the need to monitor paediatric patients for vision disorders. In addition, a dose reduction of Xalkori should be considered in patients who develop Grade 2 ocular disorders and treatment should be permanently discontinued if Grade 3 and 4 ocular disorders occur, unless another cause is identified.

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.

The CHMP recommended the suspension of marketing authorisations for some 100 medicines which obtained approval on the basis of flawed bioequivalence studies conducted by the contract research organisation **Synchron Research Services**, located in Ahmedabad, India. For around 20 medicines included in this review, bioequivalence data from other sources are available and therefore the medicines concerned are allowed to remain on the EU market. To lift the suspension, companies relying on data from Synchron Research Services must provide alternative data demonstrating bioequivalence.

All marketing authorisation holders (MAHs) have continued to report on finished products at risk of **N-nitrosamine** presence in line with the requirements of the 'call for review' to MAHs. Competent authorities assessed notifications of products containing N-nitrosamines and, where necessary, took actions to protect patient safety whilst avoiding shortages of critical medicines. Some deadlines have been extended to allow companies more time to perform thorough investigations and establish required risk-mitigating actions in light of new scientific developments since 2020.

The Nitrosamine Implementation Oversight Group (NIOG) oversaw a harmonised implementation of the CHMP's Article 5(3) opinion on nitrosamines adopted in 2020. This involved engaging with industry to discuss challenges and solutions to the ongoing 'call for review' process and cooperating with other regulatory authorities to facilitate international alignment. Highlights of these interactions are available here[1].

The NIOG also issued guidance to facilitate compliance with the call for review, ensuring harmonisation of assessment and prioritisation, and approaches for temporary limits for nitrosamines to mitigate the risk of shortages of medicines while ensuring patient safety.

The EU Regulatory Network implemented measures to reduce potential risks associated with nitrosamines in medicines and ensure that regulators are better prepared to manage cases of unexpected impurities, as agreed in the implementation plan to address the lessons learnt on the presence of nitrosamines in sartan medicines.

1 https://www.ema.europa.eu/en/search/search/ema_editorial_content/ema_event?search_api_views_fulltext=%22Nitrosamine+Implementation+Oversight+Group%22

Veterinary medicines

New medicines to benefit animal health in Europe

In 2022, EMA recommended ten veterinary medicines for marketing authorisation. Of these, three had a new active substance, which had not previously been authorised in the EU. Among the ten medicines recommended for marketing authorisation, two were vaccines, one of which had been developed by means of a biotechnological process.

A SELECTION OF KEY RECOMMENDATIONS IN 2022:

DogStem, a new veterinary medicine for reduction of pain and lameness associated with osteoarthritis in dogs.

Neoleish, a plasmid DNA vaccine for the active immunisation of Leishmania-negative dogs from 6 months of age to reduce the risk of developing an active infection and/or clinical disease after exposure to *Leishmania infantum*.

RenuTend, a new veterinary medicine to improve healing of injuries of tendons and suspensory ligaments in horses.

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 2022

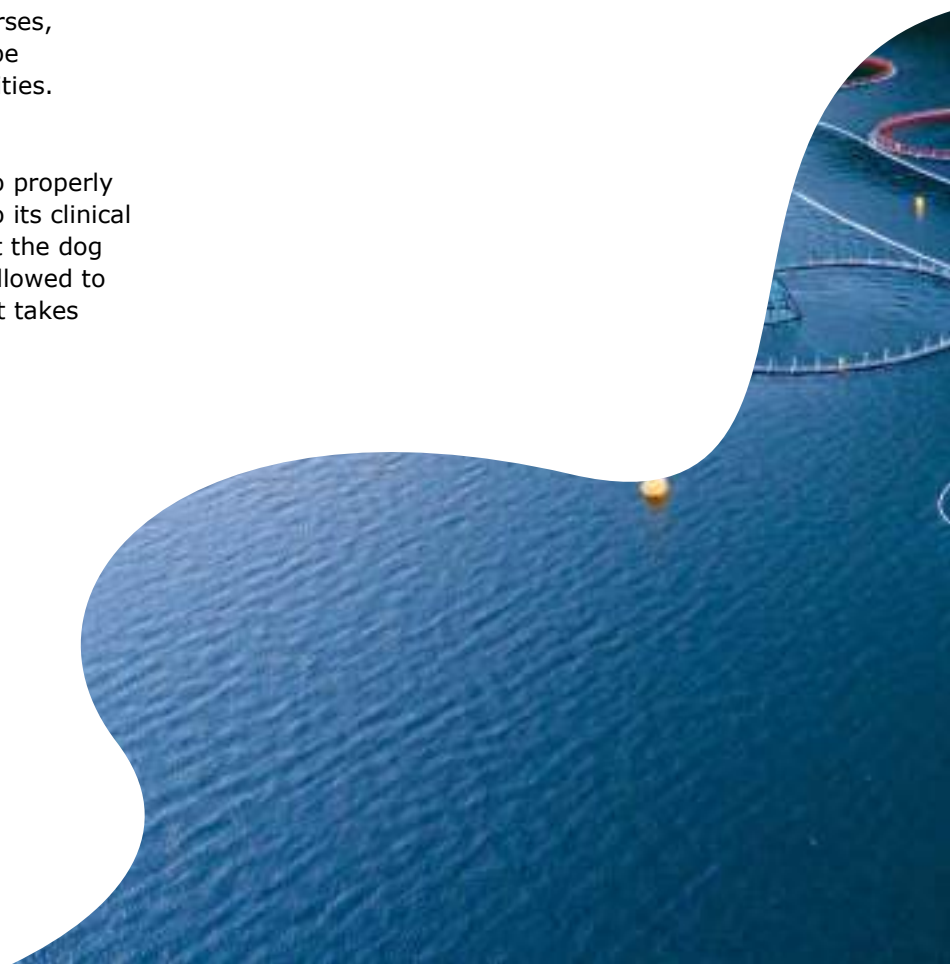
The product information for 24 medicines was updated on the basis of new safety data. The revised information is expected to help animal owners and healthcare professionals make informed decisions when using or prescribing a medicine. This included:

- Addition of further information in the package leaflet on potential side effects following the administration of:
  - **Bravecto spot-on solution for dogs**: muscle tremor (shaking); ataxia (incoordination); convulsion;
  - **BTVPUR**: hypersensitivity reactions;
  - **Cardalis**: lethargy (lack of energy); anorexia (loss of appetite); ataxia; incoordination or signs of fatigue. In dogs with chronic kidney disease, benazepril[2] may increase plasma creatinine concentrations at the start of therapy very rarely;
  - **Cerenia**: neurological disorders, such as ataxia, convulsion/seizure, or muscle tremor;
  - **Equilis Prequenza**: hypersensitivity reaction, including anaphylaxis (sometimes fatal);
  - **Equilis Prequenza Te**: hypersensitivity reaction, including anaphylaxis (sometimes fatal);
  - **Equilis Te**: hypersensitivity reaction, including anaphylaxis (sometimes fatal);
  - **Felpreva**: neurological disorders, such as ataxia (incoordination) and tremor;
  - **Hiprabovis IBR Marker Live**: hypersensitivity reactions, including anaphylaxis (sometimes fatal) (change of frequency from "very rare" to "rare" and addition of anaphylaxis);
  - **Librela**: polydipsia; polyuria (increase in urine production); addition of anaphylaxis, pruritus (itching) and facial swelling under hypersensitivity reactions; clinical signs of immune-mediated diseases, such as haemolytic anaemia or thrombocytopenia (low blood platelet counts, which can lead to bleeding and bruising);
  - **Mhyosphere PCV ID**: anaphylactic-type reactions (e.g. vomiting, circulatory disorders, dyspnoea), which might be life-threatening;
  - **Nasym**: anaphylactic-type reactions, which may be serious (including fatal);
  - **Neptra**: deafness or impaired hearing, mainly in elderly animals (dogs);
  - **Nobivac DP Plus**: hypersensitivity reaction, including anaphylaxis (sometimes fatal);
  - **Nobivac Myxo-RHD Plus**: anorexia; lethargy;
  - **Procox**: lethargy; muscle tremor; ataxia (incoordination); convulsion;
  - **Proteq West Nile**: injection site abscess;
  - **Solensia**: mild reactions at the injection site (e.g. pain and alopecia (hair loss));

2 Benazepril hydrochloride and Spironolactone are the active substances of Cardalis.

- **Stelfonta**: compromised circulation; loss of essential tissue;
- **Suprelorin**: epileptic seizures;
- **Zuprevo**: anaphylaxis (may be fatal).

- Addition of new special precautions for use of:
  - **Aservo EquiHaler**
    A European survey showed that 16 out of 84 horses could not be treated according to the product information due to horses not co-operating. In case a horse has a tendency towards defensive behavioural reactions, additional safety precautions could be considered (e.g. employ a second person to handle the horse). Acclimatising the horse with a training device prior to treatment start has in some cases shown to ease the administration of the veterinary medicine.
  - **Improvac**
    The safety and efficacy of the veterinary medicine in non-target species, such as horses, has not been evaluated. Adverse events have been observed in horses, including serious anaphylactic-type reactions, which have led to fatalities.
  - **Librela**
    Where a dog has not been able to properly exercise prior to treatment due to its clinical condition, it is recommended that the dog is gradually (over a few weeks) allowed to increase the amount of exercise it takes (to prevent overexercise).
  - **Stelfonta**
    Treating tumours at extremities may result in localised impairment of circulation due to a local inflammatory response at the treatment site. This can lead to tissue loss and can sometimes make an amputation necessary. Ingestion of tumour remnants should be prevented.
  - **Suvaxyn Circo**
    In case of accidental self-injection, the person administering the veterinary medicine should seek medical advice immediately and show the package leaflet or the label to the physician.
- Addition of new advice on correct administration of:
  - **Stelfonta**
    The site of application should be covered for the first day after treatment in order to prevent licking of residual or leaking product (in addition to the prevention of direct contact with the residual or leaking product).



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 and entered in the annex to Commission Regulation (EU) No 37/2010.

In 2022, positive opinions were adopted recommending the extension of MRLs for the following active substances:

- **ketoprofen**
  extension to chickens; this conclusion was extrapolated to poultry.

- **praziquantel**
  extension to fin fish; the entry for ovine species was extrapolated to all ruminants except cattle.

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

EUROPEAN MEDICINES REGULATORY NETWORK'S RESPONSE TO PUBLIC HEALTH EMERGENCIES

EMA and the European medicines regulatory network continued to focus their efforts on tackling public health emergencies. In 2022, the COVID-19 pandemic continued to evolve and present new challenges. Through EMA's recommendations, new vaccines and treatment options were added to the EU's arsenal in the fight against the disease. An outbreak of the mpox virus in July posed an additional challenge to public health. The crisis preparedness tools established in the context of the Agency's extended mandate were put to use, ensuring a joint EU response.

Response to the COVID-19 pandemic

Support to developers of COVID-19 vaccines and treatments

Providing scientific advice is EMA's primary instrument for supporting the sound development of medicines. Through the Emergency Task Force (ETF), which was formalised as part of the Agency's extended mandate, EMA continued to assist developers working on vaccines and treatments for COVID-19, providing them with advice on the best study designs and methodologies to generate reliable data for their marketing authorisation applications.

Expediting development and approval of safe COVID-19 vaccines and therapeutics

In 2022, two new vaccines were approved for use throughout the EU:

- **COVID-19 Vaccine Valneva** is authorised to protect people from 18 to 50 years who have not been immunised before against COVID-19;
- **VidPrevtyn Beta** is authorised as a booster to protect adults who have received at least a primary vaccination course against COVID-19.

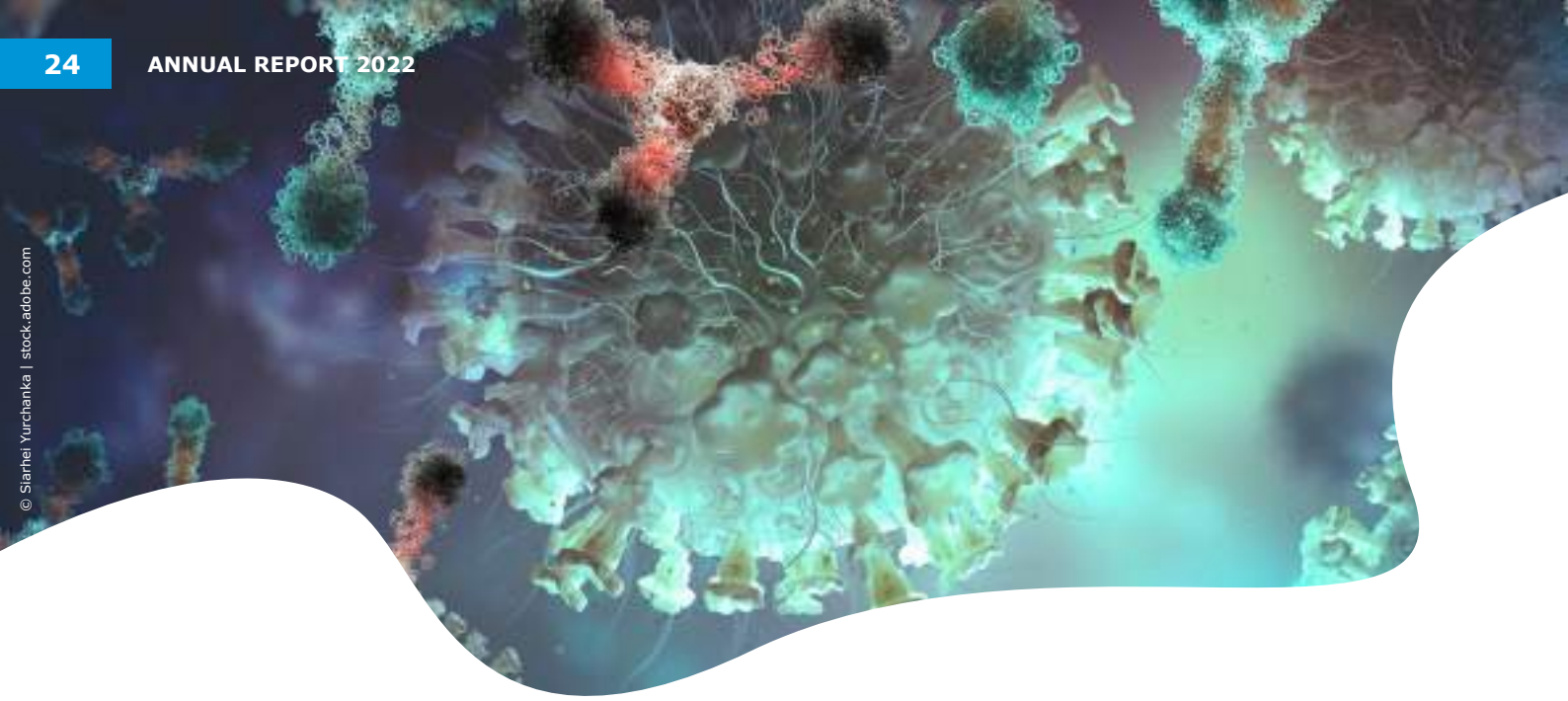
In 2022, adapted mRNA vaccines were developed to extend the immune response of vaccinated people against a wider range of the frequent mutations of the virus. Four bivalent vaccines, each of them targeting the original strain and a mutation of the Omicron variant, were recommended to be used in people who have received at least a primary vaccination course against COVID-19:

- **Comirnaty Original/Omicron BA.1** and **Comirnaty Original/Omicron BA.4-5** are adapted versions of Comirnaty containing an additional mRNA molecule with instructions for producing a protein from the Omicron BA.1 and BA.4/BA.5 subvariants of SARS-CoV-2, respectively.
- **Spikevax bivalent Original/Omicron BA.1** and **Spikevax bivalent Original/Omicron BA.4-5** are adapted versions of Spikevax containing an additional mRNA molecule with instructions for producing a protein from the Omicron BA.1 and BA.4/BA.5 subvariants of SARS-CoV-2, respectively.

Overview of authorised COVID-19 vaccines as of December 2022

In addition to the work on integrating new virus variants, EMA was also able to recommend the granting of several extensions of indications for the existing COVID-19 vaccines to increasingly younger populations, following a thorough assessment of the supporting evidence. The following table summarises the COVID-19 vaccines authorised in the EU as of 2022, including their characteristics and indications.

Vaccine	Platform*	Strain	Use	Population			
				≥6 months	≥5 years	≥12 years	≥18 years
Comirnaty (BioNTech)	mRNA	Original strain	Primary vaccination	✓ 6 months to 4 years	✓ 5-11 years	✓	✓
			Booster		✓ 5-11 years	✓	✓
		Original strain + Omicron BA.1 variant (adapted**)	Booster			✓	✓
		Original strain + Omicron BA.4-5 variants (adapted**)	Booster		✓ 5-11 years	✓	✓
Spikevax (Moderna)	mRNA	Original strain	Primary vaccination	✓ 6 months to 5 years	✓ 6-11 years	✓	✓
			Booster		✓ 6-11 years	✓	✓
		Original strain + Omicron BA.1 variant (adapted**)	Booster		✓ 6-11 years	✓	✓
		Original strain + Omicron BA.4-5 variants (adapted**)	Booster			✓	✓
Vaxzevria (AstraZeneca)	Adenoviral vector	Original strain	Primary vaccination				✓
			Booster				✓
Jcovden (Janssen)	Adenoviral vector	Original strain	Primary vaccination				✓
			Booster				✓
Nuvaxovid (Novavax)	Protein	Original strain	Primary vaccination			✓	✓
			Booster				✓
COVID-19 Vaccine Valneva (Valneva)	Inactivated	Original strain	Primary vaccination				✓ 18-50 years
VidPrevtyn Beta (Sanofi Pasteur)	Protein	Beta variant	Booster				✓



ECDC and EMA advice on the use of COVID-19 vaccines

Throughout the year, EMA and the European Centre for Disease Prevention and Control (ECDC) gave a number of joint recommendations to provide guidance and support to Member States in the roll-out of their vaccination campaigns.

The joint statements included topics such as the use of second booster doses in the elderly and vulnerable populations and the use of Omicron-adapted COVID-19 boosters to support the planning of the autumn and winter vaccination campaigns in the EU.

Manufacturing

EMA approved additional manufacturing capacity for COVID-19 vaccines, bringing the total of approved manufacturing sites to 68 (compared to 52 in 2021). This work ensures high-quality manufacturing processes and resulted in a steady supply of high-quality and safe vaccines.

COVID-19 therapeutics approved

Although vaccination was rolled out widely throughout the EU, there was a continued need for new and better treatments for people who contracted the disease.

Two new treatments for COVID-19 were approved in 2022:

- **Paxlovid**, to treat adults with COVID-19 who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19. Paxlovid was the first antiviral treatment for COVID-19 that is taken orally and can be used in the comfort of people's own homes. Subsequently, the use of this medicine was extended to adolescents.
- **Evusheld**, for the prevention of COVID-19 in adults and adolescents from 12 years of age weighing at least 40 kg before potential exposure to the SARS-CoV-2 virus. This medicine was later extended to include the treatment of adults and adolescents with COVID-19 who do not require supplemental oxygen. Updated information on the effectiveness of Evusheld and other monoclonal antibodies for COVID-19 is available in the next section.

The indication for **Veklury** was extended to include children at least 4 weeks old and weighing at least 3 kg with pneumonia requiring supplemental oxygen or other non-invasive ventilation at the start of treatment; and children weighing at least 40 kg who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19.

Effectiveness of monoclonal antibodies against emerging strains of SARS-CoV-2

The ETF issued a warning in December 2022 to inform healthcare professionals that monoclonal antibodies that attach to the spike protein of SARS-CoV-2 may not be effective against the emerging strains of the virus and to consider alternative treatment options. These included the authorised medicines **Evusheld**, **Regkirona**, **Ronapreve** and **Xevudy**, as well as the bamlanivimab/etesevimab combination assessed under Article 5(3) of Regulation 726/2004.

Use of medicines not authorised to treat COVID-19

EMA's ETF started a review of available data on the use of **sabizabulin** to treat hospitalised patients with moderate-to-severe COVID-19 who are at high risk of acute respiratory distress syndrome and death. The outcome of the review will be transmitted to CHMP in view of a possible recommendation.

The review is the first triggered under Article 18 of the new EU regulation (Reg 2022/123) that expanded the role of EMA during public health emergencies.

Safety monitoring of COVID-19 vaccines and therapeutics

The enhanced safety monitoring and supervision of all authorised COVID-19 vaccines continued throughout 2022. EMA issued monthly updates highlighting new safety signals assessed by the EMA's safety committee (PRAC) and the related changes to the product information of these medicines.

International collaboration

EMA collaborated with international regulators from Australia, Canada, Japan, Switzerland and the World Health Organization (WHO) in the review of all COVID-19 vaccines and therapeutics under the OPEN (Opening our Procedures at EMA to Non-EU authorities) framework. Each regulatory authority conducted their own assessment in parallel with EMA's evaluation while sharing scientific expertise and maintaining their scientific and regulatory independence.

EMA's assessments were also used to support WHO's Emergency Use Listing of COVID-19 vaccines, a risk-based procedure for assessing and listing vaccines to expedite their availability to people affected by a public health emergency. EMA is the regulatory authority of record for the following vaccines: **Comirnaty**, **Vaxzevria**, **Jcovden**, **Spikevax**, **Nuvaxovid**, **VidPrevtyn**, **HIPRA**, **Valneva** and **Curevac**.

mpox (monkeypox): the EU's response

EMA supported the EU's response to an atypical outbreak of mpox following reports of a number of cases in several Member States not linked to countries where the disease is endemic. The mpox outbreak was declared a Public Health Emergency of International Concern (PHEIC) by the WHO on 23 July 2022.

There was no authorised mpox vaccine in the EU when the PHEIC was declared. However, there was a smallpox vaccine, **Imvanex**, which had an equivalent in the US – **Jynneos** – that was already approved against mpox. EMA's ETF recommended – as a temporary measure – the use of the US-approved mpox vaccine Jynneos to support vaccination efforts by national authorities in the EU. In parallel, EMA also recommended an extension of the use of **Imvanex** to also protect adults from mpox.

The ETF also provided advice on the intradermal use of Imvanex / Jynneos against mpox based on a study of people who had received the vaccine intradermally at a lower dose as dose-sparing measure. The ETF's advice supported the temporary use of **Imvanex** as an intradermal injection at a lower dose by the national authorities to protect at-risk individuals. This helped to rapidly increase the number of people who could be protected from the virus.

EMA's ETF also interacted with developers of vaccines and therapeutics for mpox, providing scientific advice and reviewing the available scientific data on medicinal products that have the potential to address this public health emergency.

Real-world evidence (RWE) studies in public health emergencies

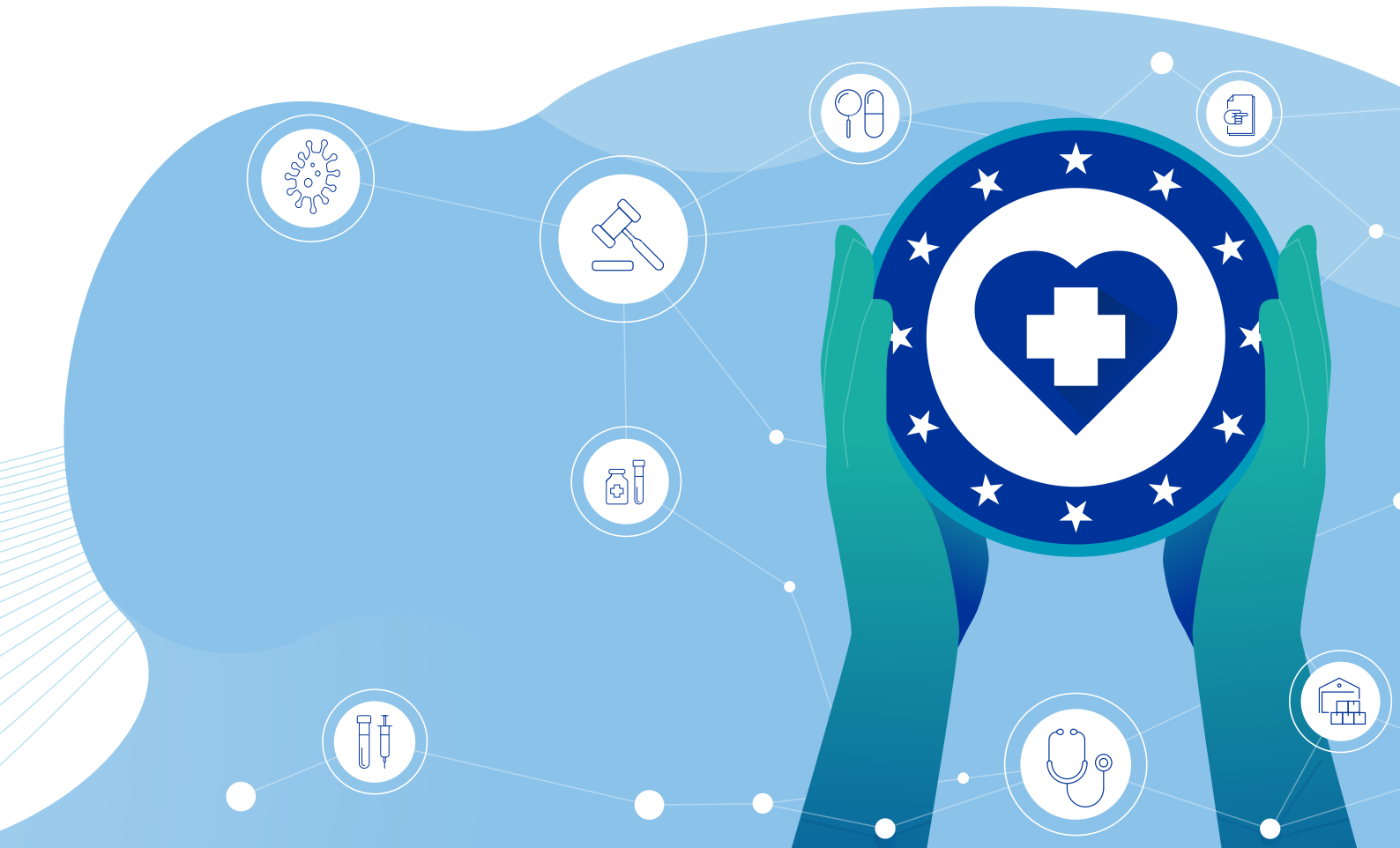
Building on the work in 2020 and 2021 to leverage collaborations with academics in observational research, EMA used real-world data from routine clinical practice to monitor the safety and effectiveness of COVID-19 and mpox vaccines to generate timely RWE supporting the response to both outbreaks. Building on this experience, a process for the rapid procurement of studies in emergency situations, where rapid evidence is required to support public health and regulatory actions, has been developed in line with EMA's extended mandate (see next section).

EMA'S EXTENDED MANDATE

On 1 March 2022, EMA's mandate was extended with the entry into force of the regulation reinforcing EMA's role in crisis preparedness and management of medicinal products and medical devices.

Throughout 2022, the extension of EMA's mandate led to the creation of new structures and mechanisms to fulfil this new role.

> 'The Agency became stronger thanks to the European Commission's decision to extend our mandate. This is a recognition of the Agency's efforts and successes during the pandemic. The extended mandate formalises some of our existing procedures, but also provides us with new tools to respond effectively to future public health crises, tackle medicine shortages and improve the monitoring of medical devices and their authorisation.'
>
> **Emer Cooke**, EMA's Executive Director



The Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG)

With the extended mandate, a new executive body, the Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG), was established, comprising representatives from EMA, EU Members States, the European Commission and patient and healthcare professional representatives. The group's role is to respond to medicine supply issues caused by major events or public health emergencies, and to coordinate swift actions within the EU.

Lists of critical medicines

One of the key responsibilities of the MSSG is to establish lists of critical medicines needed during a major event or a public health emergency that require close monitoring of supply and demand, with a view to identifying any actual or potential shortages of those medicinal products. In 2022, EMA published lists of critical medicines for COVID-19 and monkeypox (mpox).

Medicines Shortages Single Point of Contact (SPOC) Working Party

The Medicines Shortages Single Point of Contact (SPOC) Working Party was formally established in May 2022. It is responsible for monitoring and reporting events that could affect the supply of medicines in the EU. The SPOC Working Party provides recommendations to the MSSG on all matters related to the monitoring and management of medicines shortages.

Industry Single Point of Contact network (iSPOC)

The extended mandate also comes with new obligations for companies. Since September 2022, every marketing authorisation holder in the EU has to register an iSPOC to enable rapid communication between EMA and companies to detect, report, and prevent or manage supply and availability issues of medicines included in a list of critical medicines for a 'public health emergency' or a 'major event'.

Companies have to submit their information via IRIS, EMA's secure online platform for handling product-related scientific and regulatory procedures.

The Emergency Task Force (ETF)

The Emergency Task Force (ETF) was formalised in April 2022, as part of the extended mandate. This is a recognition of the pivotal role the task force played throughout the COVID-19 public health emergency. The ETF provides scientific advice and reviews evidence on medicines that could be used for prevention or treatment during a public health emergency. It also offers scientific guidance to facilitate clinical trials and supports EMA's scientific committees with the authorisation and safety monitoring of medicines and with recommendations on the use of medicines before authorisation.

The EU Vaccine Monitoring Platform (VMP)

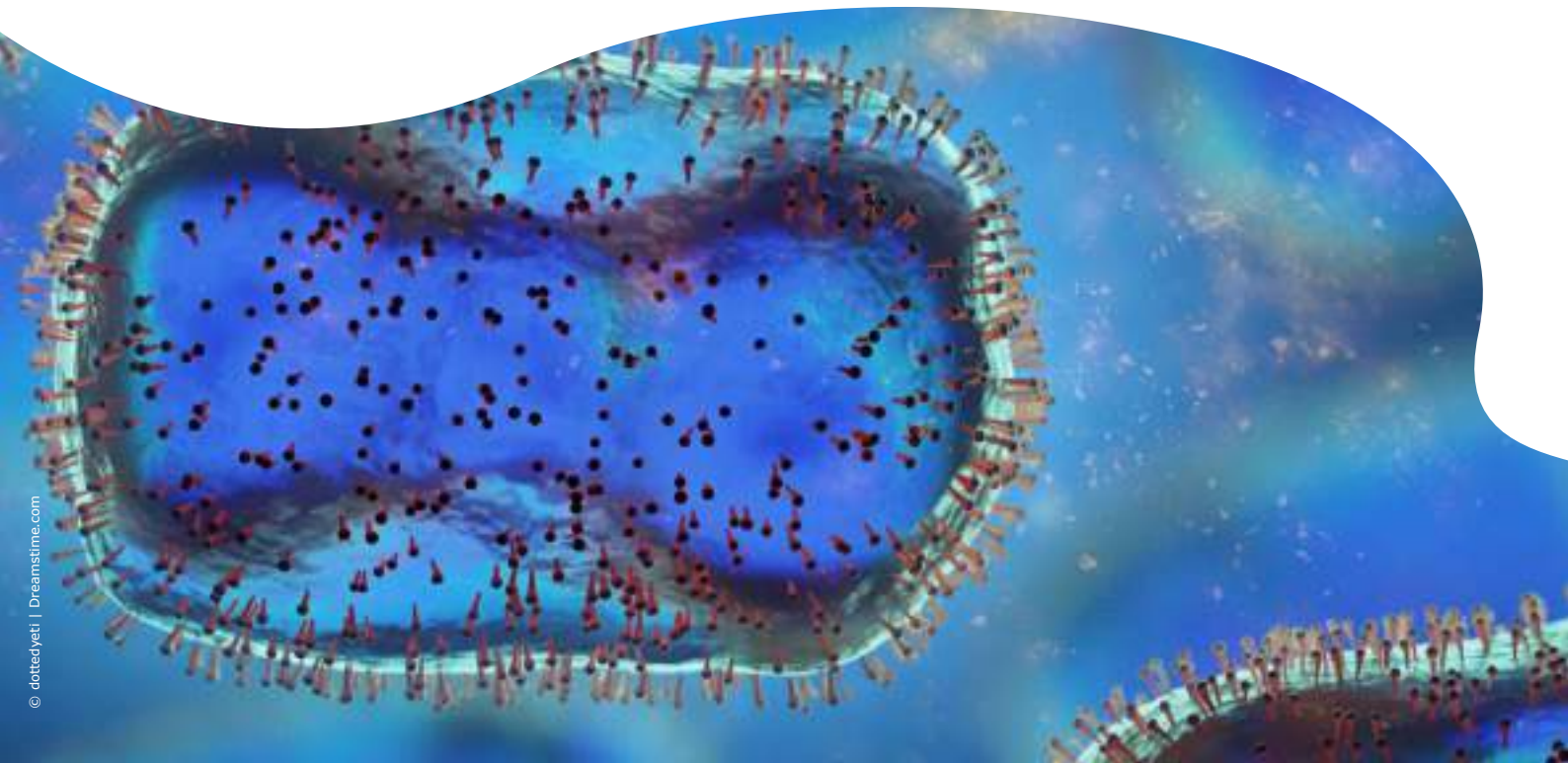
The EU Vaccine Monitoring Platform (VMP) was established in May 2022 as a collaboration between EMA and the European Centre for Disease Prevention and Control (ECDC), with the goal to generate real-word evidence (RWE) through EU-funded post-authorisation studies on vaccine use, safety, and effectiveness. As an important milestone for the European Health Union initiative, the VMP ensures the prioritisation, design, and implementation of studies, and interprets and communicates the results. The Immunisation and Vaccine Monitoring Advisory Board (IVMAB), a multidisciplinary panel with representatives from the European Commission, ECDC's National Focal Points, EMA's Emergency Task Force (ETF), and EMA's committees on human medicines (CHMP) and safety of medicines (PRAC), advises EMA and ECDC on the VMP research agenda.

'With the new VMP we have an instrument in place through which we will prioritise research, fund independent studies and complement our knowledge of how vaccines work in real life. The additional evidence generated through these independent studies will enhance our ability to continuously monitor the safety and effectiveness of vaccines. This will improve the robustness of our decision making, which is essential to build and maintain people's trust in these key products.'

Emer Cooke, EMA's Executive Director

Medical devices expert panels

The new mandate transferred the coordination of 12 medical device expert panels from the European Commission to EMA. The objective of the panels is to improve the safety of certain high-risk medical devices marketed in the EU and the European Economic Area (EEA).



IMPLEMENTING THE VETERINARY MEDICINAL PRODUCTS REGULATION

On 28 January 2022, the Veterinary Medicinal Products Regulation became applicable, bringing in a new era in the regulation of medicines for animals. The new legislation aims to reduce administrative burden and introduce better incentives for developers to stimulate innovation and increase the access to safe and high-quality medicines for veterinarians, farmers and pet owners to treat and prevent animal diseases. It also introduces new rules for the prudent and responsible use of antimicrobials in animals to help fight antimicrobial resistance (AMR) in the EU.

By the time the new Regulation became applicable, EMA had revised its procedures and key regulatory and scientific guidance documents to reflect these changes.

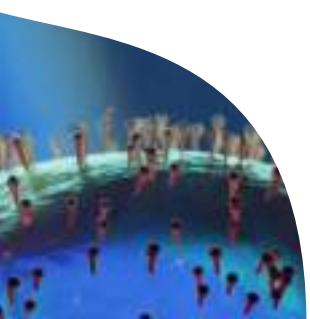
Commissioning of three IT systems to manage safe and high-quality medicines for animals

The new Regulation is underpinned by three IT systems, developed by EMA in close collaboration with Member States and stakeholders, that enable the simplification of processes and ensure wider access to information on medicines for animals for all stakeholders: the **Union Product Database (UPD)**, the **Union Pharmacovigilance Database (EVV)**, and the **Manufacturing and Wholesale Distribution Database (MWD)**. These systems went live on the day the Regulation became applicable.

‘A critical success factor in the timely delivery of the IT systems which stem from the new Regulation was the consistent collaboration with the European Commission, the regulatory network and our stakeholders.’

Ivo Claassen, Head of EMA’s Veterinary Medicines Division

IT development for the **Collection of Antimicrobials Sales and Use Data (ASU)** project started in January 2022. Over the following months, ASU project activities progressed as planned, with the aim that the first data will be submitted to the system in 2024.



Throughout the year, EMA provided intense support to facilitate the transition of users from pharmaceutical companies to these new platforms. The Agency established a dedicated support service for users of the new systems and continued to run refresher webinars and change information sessions. In September 2022, EMA established the Veterinary System Improvement Advisory Group (VSIAG) which helps to prioritise new or improved functionalities in the UPD and EVV systems. The group includes representatives from national competent authorities, the pharmaceutical industry, the European Commission, veterinary healthcare professionals and EMA.

Due to the strong collaboration between national competent authorities and EMA throughout the year the uploading of data held in the Member States into the UPD was almost complete by December 2022.

A single source of up-to-date information on all EU veterinary medicines

A key part of the new Regulation in terms of transparency is the Veterinary Medicines information website, which provides public access to the UPD data. It is the first central multilingual website that gives details on all veterinary medicines authorised in the EU and the EEA. The website enables veterinary healthcare professionals and all interested users to find out in which EU Member States and EEA countries a specific veterinary medicine is available, or to find information that could help identify potential treatment alternatives.

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IMPROVING THE ENVIRONMENT FOR CLINICAL RESEARCH IN THE EU

2022 was an important year for clinical research in the EU.

Clinical Trials Regulation

On 31 January 2022, the Clinical Trials Regulation (CTR) entered into application, harmonising the submission, assessment, and supervision processes for clinical trials in the EU.

The changes brought about by the CTR are supported by the Clinical Trials Information System (CTIS), which went live on 31 January 2022, serving as a single-entry point for sponsors and regulators of clinical trials for the submission and assessment of clinical trial data. The system includes a public searchable database for healthcare professionals, patients, and the public at large.

Although the use of CTIS remained voluntary in 2022, over 200 initial clinical trial applications were authorised and more than 200 were under evaluation with the new system at the end of the year. EMA collaborated with clinical trial sponsors and Member States to identify and resolve technical issues, provide proactive hands-on support to the CTIS user community and strengthen the system ahead of its compulsory use for initial clinical trial applications on 31 January 2023.

EMA's activities to ensure stakeholder readiness and facilitate the transition to CTIS included:

- an extensive revision of the online modular training programme taking into account user feedback;
- three large information events for stakeholders and three targeted training sessions for SMEs and academia;
- 23 regular training webinars with sponsors;
- a multi-stakeholder workshop in December 2022, to allow for the sharing of experiences and feedback.

In addition, draft guidance on the protection of personal data and commercially confidential information contained in documents uploaded in CTIS was published for public consultation in 2022.

ACT EU – towards more and better clinical trials in the EU

In parallel with the implementation of the Clinical Trials Regulation, in January 2022 EMA, together with the European Commission (EC) and the Heads of Medicines Agencies (HMA), launched the Accelerating Clinical Trials in the EU (ACT EU) initiative to transform how clinical trials are initiated, designed and run. ACT EU aims to further develop the EU as a focal point for clinical research and to better integrate clinical research in the European health system for the benefit of patients.

This initiative will help to achieve the ambitious goals for clinical trials and innovation as set out in the European medicines agencies network strategy to 2025 and the European Commission's Pharmaceutical Strategy, and uses the momentum of the CTR to further promote the development of high-quality, safe and effective medicines.

An ACT EU steering group was established, and thematic teams were formed from across the three organisations. In August 2022, the steering group adopted the ACT EU 2022 – 2026 multi-annual workplan, introducing key deliverables for each of the initiative's ten priority actions, which among others, will facilitate innovation in clinical trials, enable stakeholder engagement through the establishment of a multi-stakeholder platform and enhance regulatory network collaboration.

One of the focus areas of ACT EU in 2022 was the implementation of the CTR and to understand how it is transforming the clinical trials environment. To do so, since April 2022 monthly statistics on the authorisation of clinical trials in the EU have been published. ACT EU also published a survey to understand the issues faced by sponsors submitting trials under the CTR. A report summarising the findings and subsequent actions taken by key Network groups has been published.

ACT EU made progress in developing methodology to support innovation in clinical trials. In June 2022, guidance was published on planning and conducting complex clinical trials for clinical trial sponsors and marketing authorisation applicants. Later in the year, following a multi-stakeholder event, a recommendation paper on the use of decentralised elements in clinical trials was published.

The key actors in clinical trials scientific advice in the EU came together under ACT EU to clarify the scope of scientific advice activities by providing a mapping of voluntary procedures available within the European medicines regulatory network. The EU Innovation Network (EU IN) collaborated with ACT EU to launch the second phase of its pilot on simultaneous national scientific advice (SNSA), which focuses specifically on scientific advice to facilitate clinical trials within the EU.

DATA ANALYTICS AND METHODS

In 2022, EMA continued its transformation towards a data-driven organisation that supports decision-making in the EU medicines regulatory network by building capability and capacity in the analysis of data.

Significant progress was made in enabling the use and establishing the value of Big Data in the development, authorisation and supervision of medicines in Europe.

EMA data governance

As part of its transformation and to strengthen its data governance, in 2022 EMA established an internal Data Board to steer the organisation on data matters. Its initial workplan foresees a data strategy and an improved data governance framework to connect with network data governance.

Big Data Steering Group workplan 2022-25

Last year, the Big Data Steering Group (BDSG), which was set up in 2020 by EMA and the Heads of Medicines Agencies (HMA), endorsed its third workplan that detailed key actions to be delivered between 2022–25. Its aim was to further enhance the integration of data analysis into the evaluation of medicinal products by regulators. The workplan laid out deliverables and timelines including for areas like DARWIN EU®, data quality, data discoverability, and EU network skills. A synchronised review of its mandate and the EU Network Data Board terms of reference was launched aimed at improved network data governance.

The BDSG 2022 report provides a summary of the key activities and achievements of the BDSG in 2022 and shows that significant progress in the transformation to data-driven regulation continued during the year.

Raw data analysis

One of the initiatives in the work plan was the launch of a pilot project to assess whether the analysis of 'raw data' from clinical trials by regulatory authorities improves the evaluation of marketing authorisation applications for new medicines and therefore holds promise for faster and better medicines access for patients. There are several potential benefits the analysis of raw data might bring, including faster evaluation through fewer questions being put to applicants and a better definition of the target treatment population.

The pilot, launched in July 2022, will run for up to two years and will include approximately ten regulatory procedures submitted to EMA. Since its launch, EMA received a first submission of an initial marketing authorisation application including individual patient data from clinical studies and numerous applicants have indicated their interest for 2023 and beyond.

Learnings from the pilot will help the EU medicines regulatory network take an informed decision on the optimal place of raw data in regulatory assessment and decision-making.

Discoverability and quality of data – key to data-driven regulation

Data quality is critical to realise the full potential of data-driven regulation and supports the trust of patients and healthcare professionals. Two guidance documents were released in 2022.

- The draft Data Quality Framework for EU medicine regulation aims to set out quality criteria for data used in medicine regulation to ensure they are fit for purpose to support benefit-risk decisions. The public consultation was open until 18 November 2022.
- Following a public workshop, a list of metadata describing real-world data sources and studies has been finalised and published to help pharmaceutical companies and researchers identify and use such data when investigating the use, safety and effectiveness of medicines.
- The draft good practice guide for the use of the planned EU metadata catalogue of real-world data sources was the first regulatory guide produced worldwide to focus on the discoverability of real-world data, supporting systematic integration of real-world evidence in medicines regulation. The public consultation was open until 16 November 2022.

DARWIN EU® becomes operational

In February 2022, EMA started working with Erasmus University Medical Center Rotterdam to establish the Coordination Centre for the Data Analysis and Real World Interrogation Network (DARWIN EU®). The vision of DARWIN EU® is to give EMA and national competent authorities in EU Member States access to trustworthy real-world evidence – for example on diseases, patient populations, and the use, safety and effectiveness of medicines, including vaccines – throughout the lifecycle of medicinal products.

The role of the Coordination Centre is to develop and manage the network of real-world healthcare data sources across the EU and to conduct scientific studies requested by medicines regulators and other stakeholders.

The first set of data partners to collaborate with DARWIN EU® was selected in October 2022. The data available to these partners will be used for studies to generate real-world evidence that will support scientific evaluations and regulatory decision making on medicines. The Big Data Steering Group workplan foresees more than 140 DARWIN EU® studies per year by 2025.

Big data in veterinary medicines

When it comes to veterinary medicine, EMA and the HMA adopted a Veterinary Big Data strategy to 2027 outlining their vision for fostering data-driven, digital innovations in the veterinary medicines' domain in the EU.

Building upon key objectives of the recently implemented Veterinary Medicinal Products Regulation (Regulation (EU) 2019/6), the strategy aims to converge traditional regulatory practice with innovative digital solutions. The strategy proposes to identify relevant use cases, existing and additional data sources, critical infrastructure and methods to enable an environment that encourages innovation in the development of new veterinary medicines for the benefit of animal and human health and welfare. The new strategy impacts different business areas, such as pharmacovigilance, the fight against antimicrobial resistance (AMR), environmental risk assessment, regulatory submission, innovation of veterinary medicinal products development and demonstration of efficacy/effectiveness.

KEY EVENTS IN 2022

JANUARY 2022

JANUARY 11, 2022
EMA continues to monitor emerging data on the effectiveness of vaccines against COVID-19, including disease caused by the Omicron variant.

JANUARY 13, 2022
The European Commission (EC), the Heads of Medicines Agencies (HMA) and EMA launch the initiative Accelerating Clinical Trials in the EU (ACT EU).

JANUARY 21, 2022
International regulators publish a report highlighting their discussions on the effectiveness of current vaccines against the COVID-19 Omicron variant, regulatory requirements for a variant vaccine and considerations on clinical study design.

JANUARY 18, 2022
EMA's COVID-19 task force (ETF) highlights the growing evidence indicating that mRNA COVID-19 vaccines do not cause pregnancy complications for expectant mothers and their babies.

JANUARY 24, 2022
EMA's human medicines committee (CHMP) approves a scale up of manufacturing of Vaxzevria (previously COVID-19 Vaccine AstraZeneca).

FEBRUARY 09, 2022
EMA initiates the establishment of the Coordination Centre for the Data Analysis and Real World Interrogation Network (DARWIN EU®).

FEBRUARY 22, 2022
The European medicines regulatory network adopts a Common Standard for the electronic public information (ePI) for medicines in the EU.

FEBRUARY 08, 2022
EMA starts the evaluation of an application for the use of a booster dose of Comirnaty (BioNTech/Pfizer's vaccine) in adolescents aged 12 to 15 years.

FEBRUARY 2022

JANUARY 31, 2022
The Clinical Trials Regulation enters into application and the new Clinical Trials Information System (CTIS), a single-entry point for sponsors and regulators of clinical trials for the submission and assessment of clinical trial data, is launched.

JANUARY 27, 2022
The CHMP recommends granting a conditional marketing authorisation for the oral antiviral medicine Paxlovid to treat COVID-19.

JANUARY 28, 2022
The Veterinary Medicinal Products Regulation becomes applicable. It contains new measures for stimulating innovation and increasing the availability and access to safe and high-quality veterinary medicines and also supports the EU action against antimicrobial resistance (AMR).

FEBRUARY 24, 2022
The CHMP recommends that a booster dose of the COVID-19 vaccine Comirnaty may be given where appropriate to adolescents from 12 years of age.

FEBRUARY 24, 2022
The CHMP recommends granting an extension of indication for the COVID-19 vaccine Spikevax to include use in children aged 6 to 11.

MARCH 03, 2022
A report presents the positive impact on the authorisation of new medicines in the first five years of PRIME.

MARCH 2022

MARCH 01, 2022
The regulation reinforcing EMA's role in crisis preparedness and management of medicinal products and medical devices becomes applicable as of 1 March 2022.

MARCH 24, 2022
The CHMP recommends granting a marketing authorisation for Evusheld, a new COVID-19 treatment.

MARCH 29, 2022
The CHMP starts a rolling review of COVID-19 Vaccine HIPRA (also known as PHH-1V).

MAY 11, 2022
The EMA Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG) officially meets for the first time.

MAY 17, 2022
EMA endorses a statement jointly developed by ICMRA and WHO to help healthcare professionals answer questions about the role of regulators in the oversight of COVID-19 vaccines.

MAY 2022

APRIL 2022

APRIL 25, 2022
EMA publishes a statement by Executive Director Emer Cooke to mark European Immunization Week, which takes place every year between 24 and 30 April.

APRIL 12, 2022
EMA and the European Network for Health Technology Assessment (EUnetHTA) 21 consortium publish a joint work plan until 2023.

MARCH 30, 2022
The EC, EMA and HMA issue initial advice for sponsors on how to manage the conduct of clinical trials in the context of the Russian invasion of Ukraine.

MARCH 31, 2022
EMA, in collaboration with the European Organisation for Research and Treatment of Cancer (EORTC), launches the Cancer Medicines Forum.

JUNE 2022

MAY 24, 2022
EMA publishes the final revised guideline on the evaluation of human medicines for the treatment of bacterial infections.

JUNE 01, 2022
Steffen Thirstrup is appointed as Chief Medical Officer of EMA.

JUNE 13, 2022
EMA and HMA adopt a Veterinary Big Data Strategy to 2027 outlining their vision for fostering data-driven, digital innovations in the veterinary medicines' domain.

JUNE 15, 2022
EMA starts a rolling review for a version of Comirnaty adapted to provide better protection against a specific variant or variants of SARS-CoV-2.

JUNE 08, 2022
EMA adopts first list of critical medicines for the COVID-19 public health emergency.

JUNE 17, 2022
EMA starts a rolling review for a version of Spikevax adapted to provide better protection against specific variants of SARS-CoV-2.

JUNE 23, 2022
EMA recommends granting a marketing authorisation for COVID-19 Vaccine Valneva for use in the primary vaccination of people from 18 to 50 years of age.

JULY 08, 2022
The MSSG adopts a list of the main therapeutic groups of medicines used in emergency care, surgery, and intensive care.

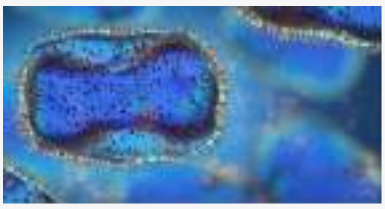
JULY 11, 2022
ECDC and EMA update recommendations on booster doses of mRNA COVID-19 vaccines, namely for people between 60 and 79 years old.

JUNE 30, 2022
Regulators from around the world discuss emerging evidence to support adaptation of COVID-19 vaccines during a workshop co-chaired by EMA and the US FDA under the umbrella of ICMRA.

JULY 2022

JUNE 30, 2022
EMA and EFSA publish a report on the development of a harmonised approach to the assessment of the dietary exposure of people to residues of veterinary medicines, feed additives and pesticides in food of animal origin.

JUNE 27, 2022
The CHMP recommends granting an extension of indication for the COVID-19 vaccine Nuvaxovid to include use in adolescents aged 12 to 17 years.

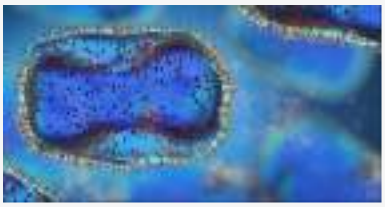


JUNE 28, 2022
The CHMP starts a review of data to extend the use of the smallpox vaccine Imvanex to include protecting people from mpox (monkeypox) disease.

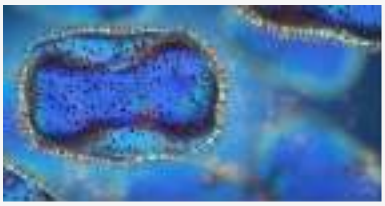
JULY 13, 2022
ICMRA elects EMA's Executive Director Emer Cooke as chair for the next mandate, which starts in October 2022.

JULY 15, 2022
EMA publishes a guidance for patients' and healthcare professionals' organisations with key principles and examples of good practices to support them in preventing and managing shortages of human medicines.

JULY 22, 2022
EMA endorses a joint ICMRA statement calling for international collaboration to enable the generation and use of real-world evidence for regulatory decision-making.



JULY 22, 2022
The CHMP recommends extending the indication of the smallpox vaccine Imvanex to include protecting adults from mpox disease.



JULY 28, 2022
EMA initiates a series of actions to respond to the ongoing mpox outbreak, which was escalated by the WHO to a Public Health Emergency of International Concern (PHEIC) on 23 July.

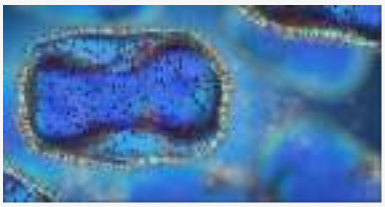
JULY 28, 2022
The ETF starts a review of data on the use of sabizabulin for treating COVID-19.

SEPTEMBER 2022

SEPTEMBER 01, 2022
The CHMP recommends authorising two vaccines adapted to provide broader protection against COVID-19: Comirnaty Original/Omicron BA.1 and Spikevax bivalent Original/Omicron BA.1.

SEPTEMBER 01, 2022
EMA launches a communication perception survey to collect feedback on its external communication.

AUGUST 30, 2022
EC, HMA and EMA publish the 2022-2026 workplan of the initiative ACT EU.

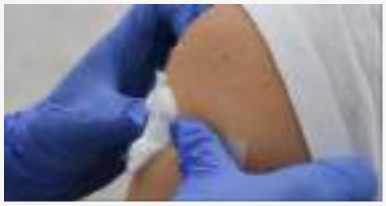


AUGUST 19, 2022
The ETF reviews data on the mpox vaccine Imvanex used as an intradermal injection.

JULY 28, 2022
The Big Data Steering Group set up by EMA and HMA publishes its third workplan that sets key actions to be delivered between 2022–25.

AUGUST 18, 2022
The CHMP starts evaluating an application for conditional marketing authorisation for Skycovion, a vaccine for protecting against COVID-19.

AUGUST 2022



SEPTEMBER 06, 2022
The European Centre for Disease Prevention and Control (ECDC) and EMA issue a joint statement on the use of the newly authorised adapted COVID-19 vaccines to support the planning of the autumn and winter vaccination campaigns.

SEPTEMBER 12, 2022
EMA recommends authorising a new adapted COVID-19 booster vaccine targeting the Omicron subvariants BA.4 and BA.5 and is for use in vaccinated people aged 12 and over.

SEPTEMBER 29, 2022
EMA launches a pilot to support the translation of basic research developments into medicines that could make a difference in patients' lives in the EEA.

OCTOBER 2022

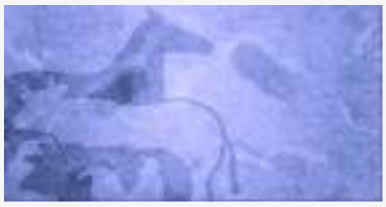
SEPTEMBER 19, 2022
EMA and HMA issue a joint statement confirming that biosimilar medicines approved in the EU are interchangeable with their reference medicine or with an equivalent biosimilar.

OCTOBER 10, 2022
The CHMP recommends granting The joint Big Data Steering Group set up by EMA and HMA endorses two documents for public consultation: one on the quality of all data types used in regulatory decision-making, the other on the discoverability of real-world data.

OCTOBER 14, 2022
The CHMP recommends Dengue Tetravalent Vaccine to prevent disease caused by dengue virus serotypes 1, 2, 3 and 4 in people from four years of age.

NOVEMBER 18, 2022
To mark European Antibiotic Awareness Day (EAAD) in 2022, EMA launches a social media campaign to highlight the importance of using antibiotics prudently.

NOVEMBER 21, 2022
EMA establishes a Quality Innovation Expert Group (QIG) to support innovative approaches for the development, manufacture, and quality control of medicines.



NOVEMBER 18, 2022
EMA's annual report on the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) shows that, since 2011, European countries have substantially reduced sales of antibiotics for animal use.

NOVEMBER 2022

NOVEMBER 10, 2022
The CHMP recommends authorising the COVID-19 vaccine VidPrevtyn Beta as a booster in adults previously vaccinated with an mRNA or adenoviral vector COVID-19 vaccine.

OCTOBER 19, 2022
EMA recommends authorising an adapted Spikevax COVID-19 vaccine targeting Omicron subvariants BA.4 and BA.5 and original strain of SARS-CoV-2.

OCTOBER 19, 2022
The CHMP recommends including the use in children aged 6 months to 4 years for Comirnaty and the use in children aged 6 months to 5 years for Spikevax.

NOVEMBER 21, 2022
In a new report ICMRA highlights successful regulatory and non-regulatory interventions used in different countries to address the growing public health problem of AMR.

NOVEMBER 23, 2022
EMA has selected the first set of data partners to collaborate with DARWIN EU, the Data Analysis and Real-World Interrogation Network.

DECEMBER 09, 2022
The ETF cautions that monoclonal antibodies currently authorised for COVID-19 are unlikely to be effective against emerging strains of SARS-CoV-2.

DECEMBER 2022

DECEMBER 08, 2022
EMA and ECDC convene on 6 and 7 December in Amsterdam the first meeting of the Immunisation and Vaccine Monitoring Advisory Board (IVMAB) of the Vaccine Monitoring Platform (VMP).

DECEMBER 19, 2022
EC, HMA and EMA publish recommendations that aim to facilitate the conduct of decentralised clinical trials.

DECEMBER 21, 2022
Emer Cooke looks back at 2022 and gives insights into the year ahead.

CHAPTER 2

KEY FIGURES IN 2022

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

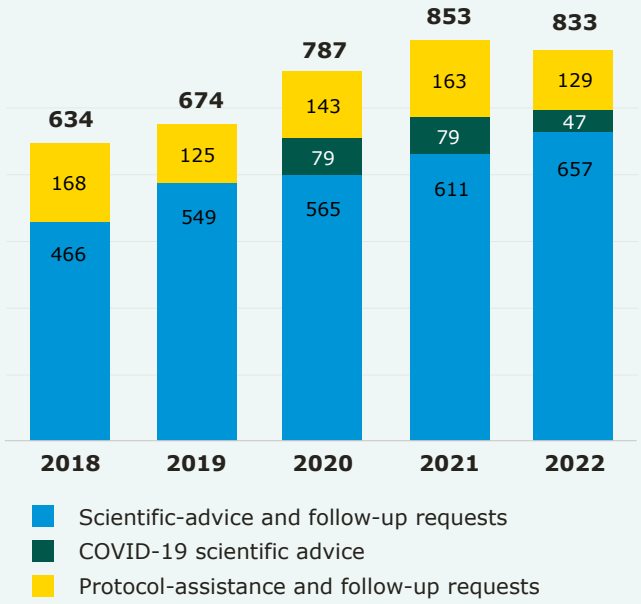
During a medicine's development, a developer can request guidance and direction from EMA on the best methods and study designs to generate robust information on how well a medicine works and how safe it is. This is known as scientific advice.

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.

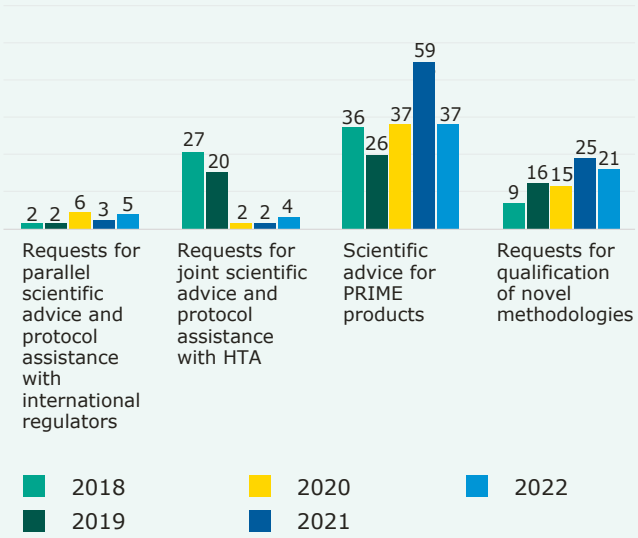
In 2022, EMA received 704 requests for scientific advice. Compared to 2021, the overall number was similar, but the proportion of COVID-19 related requests was lower.

Protocol assistance is the special form of scientific advice for developers of designated orphan medicines for rare diseases. The requests for protocol assistance decreased by 21%, from 163 requests in 2021 to 129 in 2022.

Scientific-advice and protocol-assistance requests received - total

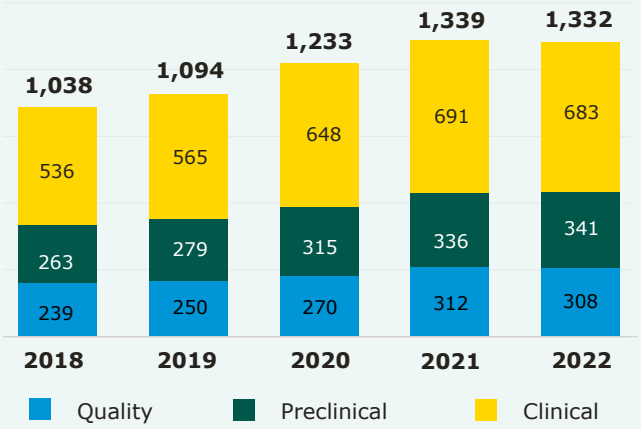


Scientific-advice and protocol-assistance requests received - special programmes



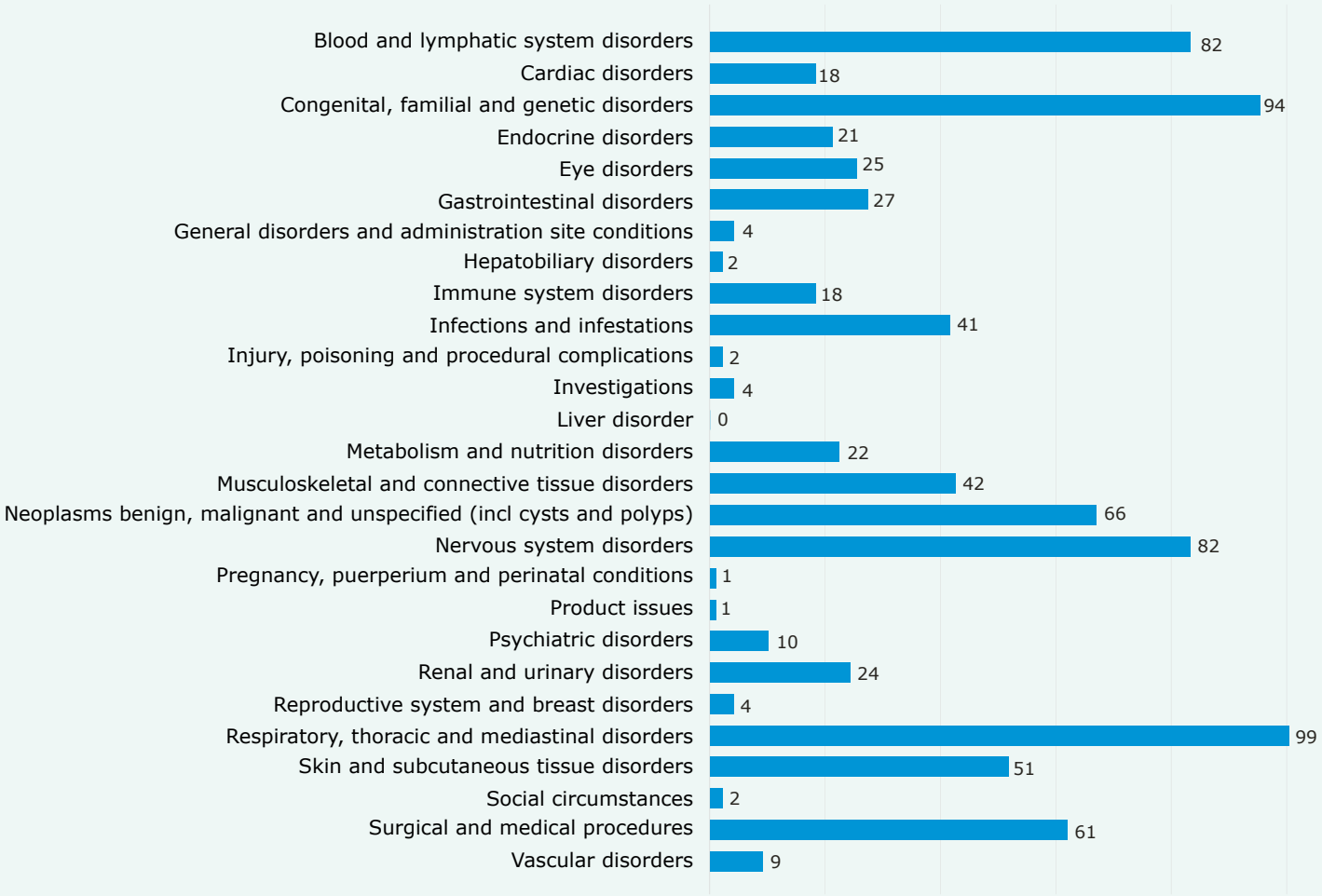
Scientific advice is the core of many of EMA's special programmes to encourage development and availability of new and innovative medicines.

Scientific-advice requests by topic



As in previous years, 51% of the requests for scientific advice included questions related to clinical issues, 26% to preclinical issues and 23% to quality issues. In terms of development stage, 61% of requests related to medicines in phase III, 23% to medicines in phase II, 14% to medicines in phase I and 2% to medicines in phase IV of their clinical development.

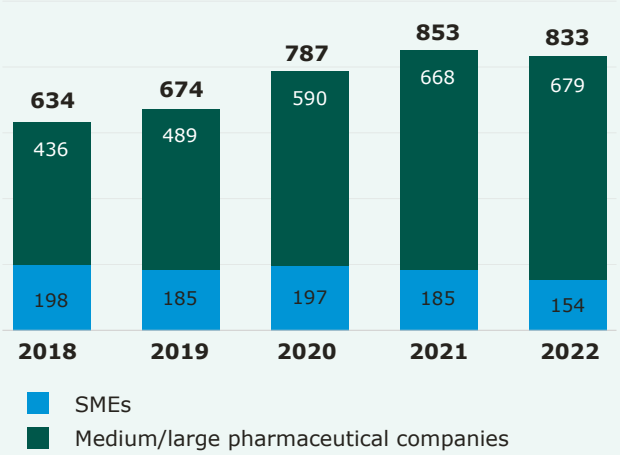
Scientific-advice requests by therapeutic area* (2022)



*excludes biomarkers

18% of the total number of requests came from small and medium-sized enterprises (SMEs).

Scientific-advice requests by affiliation of requester



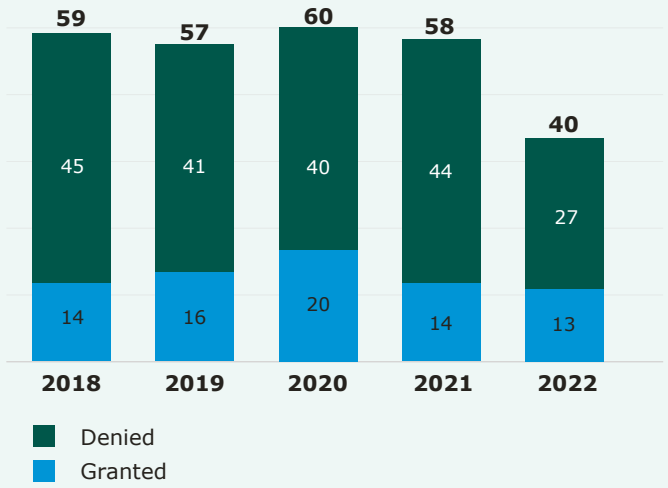
PRIME

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 2022, EMA received 45 PRIME eligibility requests, 13% less than in 2021, and adopted 40 recommendations, 31% less than in 2021. The drop in the number of PRIME applications and recommendations in 2022 may be explained by the global pandemic and its effect on priorities and resources of developers.

PRIME is meant 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, based on PRIME criteria, only a limited number of applications (13 out of 40 in 2021) are accepted into the scheme.

Eight PRIME-designated medicines were recommended for approval: Beyfortus, Breyanzi, Carvykti, Ebvallo, Hemgenix, Roctavian, Tecvayli, Xenpozyme.

PRIME - eligibility recommendations



Support for SMEs

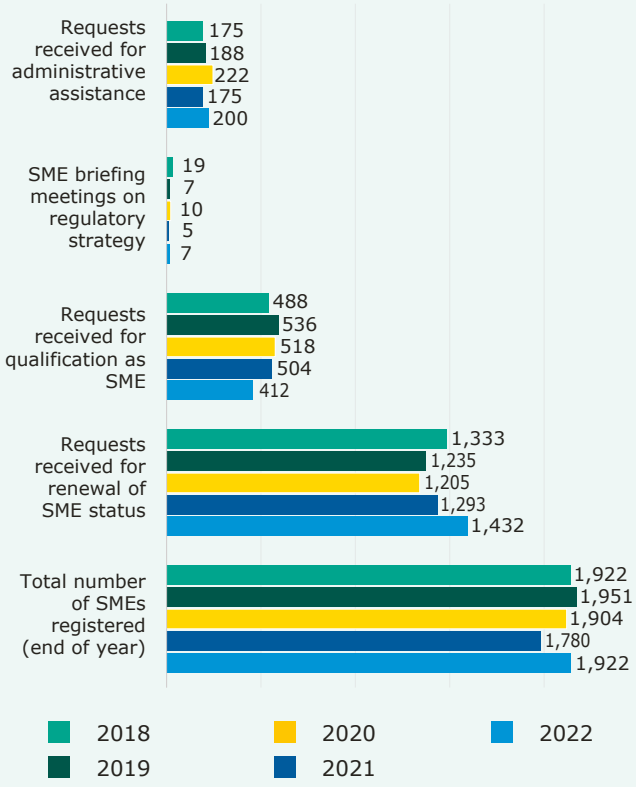
SMEs are recognised as a driver of innovation in the EU. The Agency promotes innovation and the development of medicines by SMEs through regulatory and administrative support to these companies. The Agency's SME office provides advice and guidance, organises topical workshops and produces a dedicated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

In 2022, the SME office received 200 requests for direct assistance on administrative or regulatory aspects and organised seven briefing meetings to assist SMEs that were unfamiliar with the EU regulatory system. A total of 1,922 SMEs were registered at the Agency by the end of 2022.

In 2022, SMEs submitted 13 marketing authorisation applications, a similar number to 2021. This represents 10% of all applications received in 2022. Out of the 13 applications, five were for orphan designated medicines.

The CHMP gave a positive opinion for five medicines developed by SMEs, 55% less than in 2021. This represents 6% of all positive opinions in 2022. One of the medicines developed by SMEs had a new active substance.

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



Initial evaluation application and SMEs (human medicines)

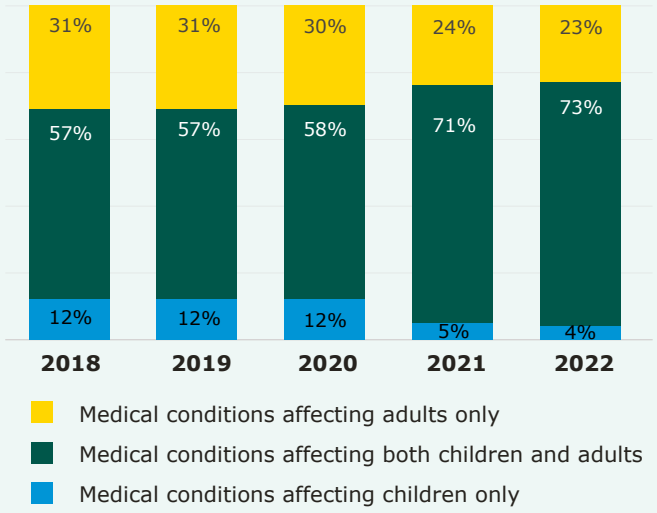
	2018	2019	2020	2021	2022
Initial marketing authorisation applications submitted by SMEs	15	24	23	10	13
Positive opinions	13	8	16	11	5
Negative opinions	5	1	1	0	4
Withdrawals	5	3	1	4	3

Orphan medicine designation

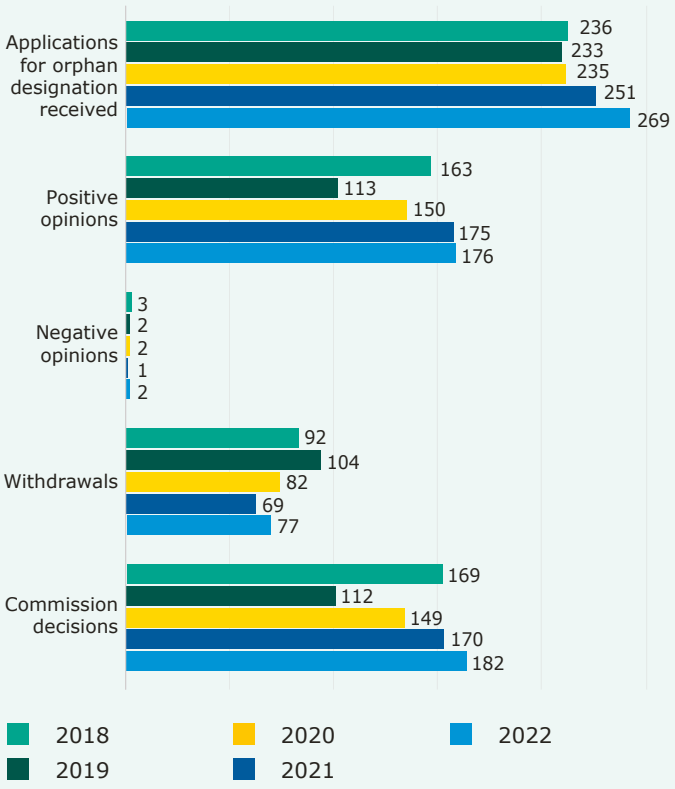
The EU framework for orphan medicines aims to encourage the development and marketing of medicines for patients with rare diseases by providing incentives for developers.

Medicines with an EU orphan designation benefit from ten years of market exclusivity if they are granted a marketing authorisation and continue to fulfil the criteria for orphan designation. 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 Committee for Orphan Medicines (COMP) is responsible for assessing orphan designation applications.

Designated orphan medicines for the treatment of children and adults



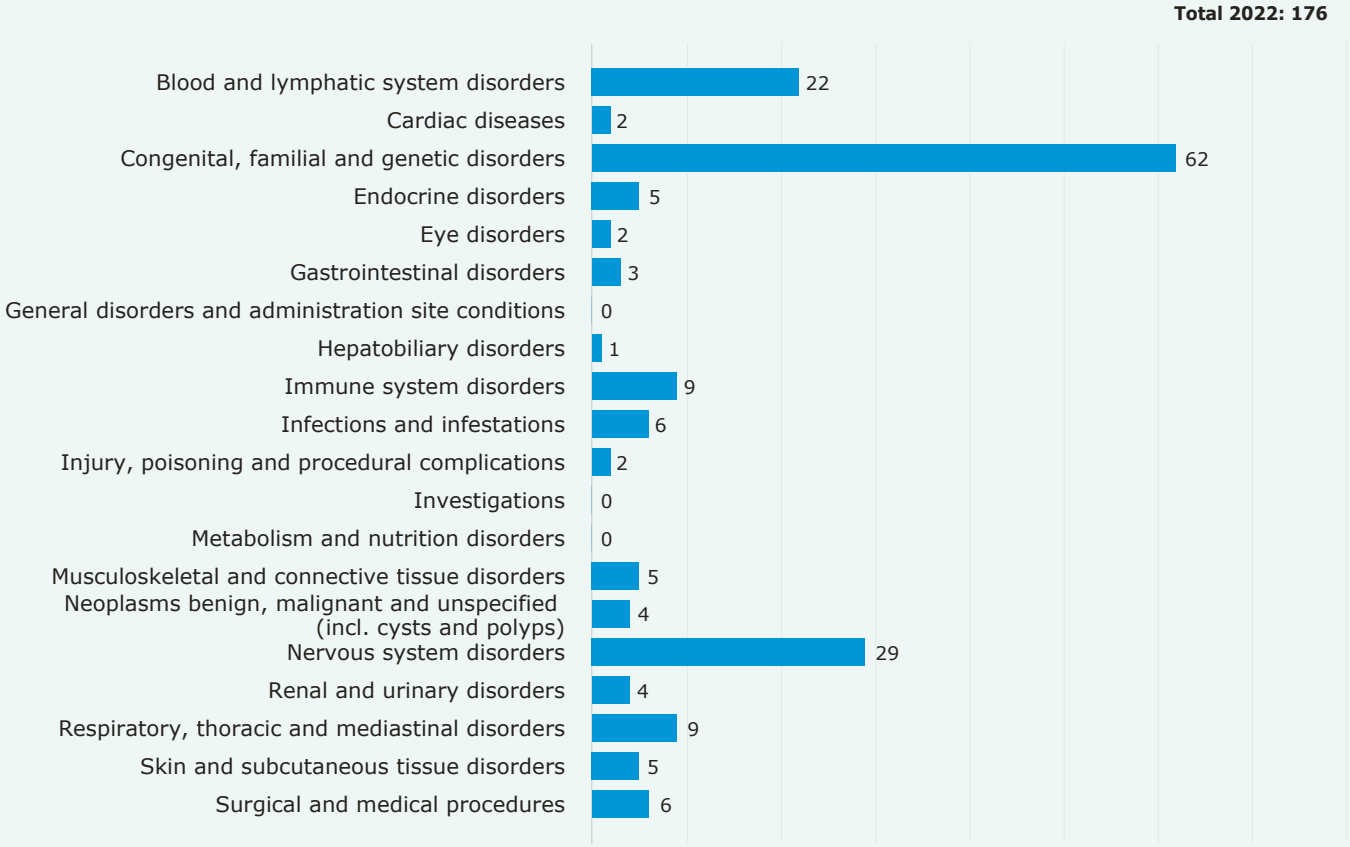
Orphan-medicine designation procedures



The number of applications for orphan designations was 269 in 2022, a slightly higher number than previous years. Of these, 176 were granted a designation, allowing them to benefit from the incentives under the EU Orphan Framework, 77 were withdrawn, and two received a negative opinion from the COMP.

The European Commission supports the development of medicines for rare diseases financially, with €12,895,000 provided in 2022. More than 61% of the Commission's special contribution was used to provide protocol assistance to medicine developers and more than 20% for the assessment of applications for marketing authorisation.

Opinions on oprhan designation by therapeutic area (2022)



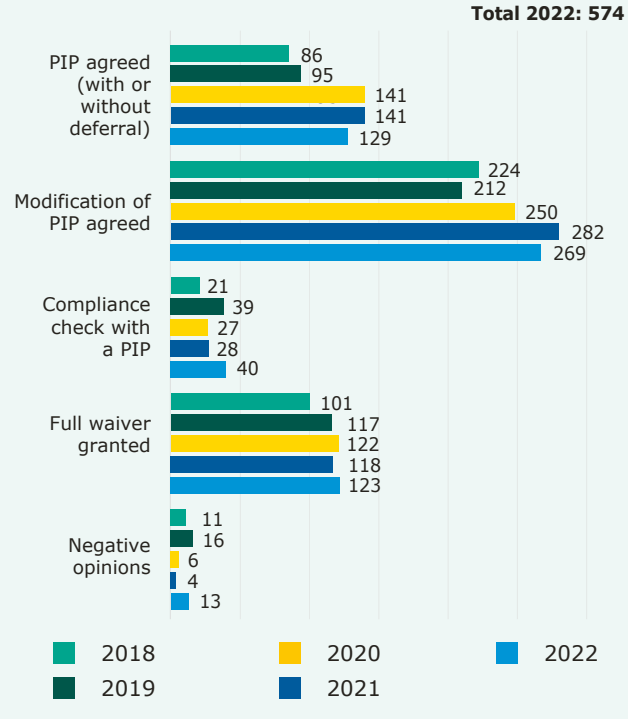
Medicines for children

The Agency also promotes the development of medicines for children. EMA's Paediatric Committee (PDCO) assesses and agrees paediatric investigation plans (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 for children, EMA provides the secretariat for the European Network of Paediatric Research at the European Medicines Agency (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 2022, the PDCO agreed 129 initial PIPs.

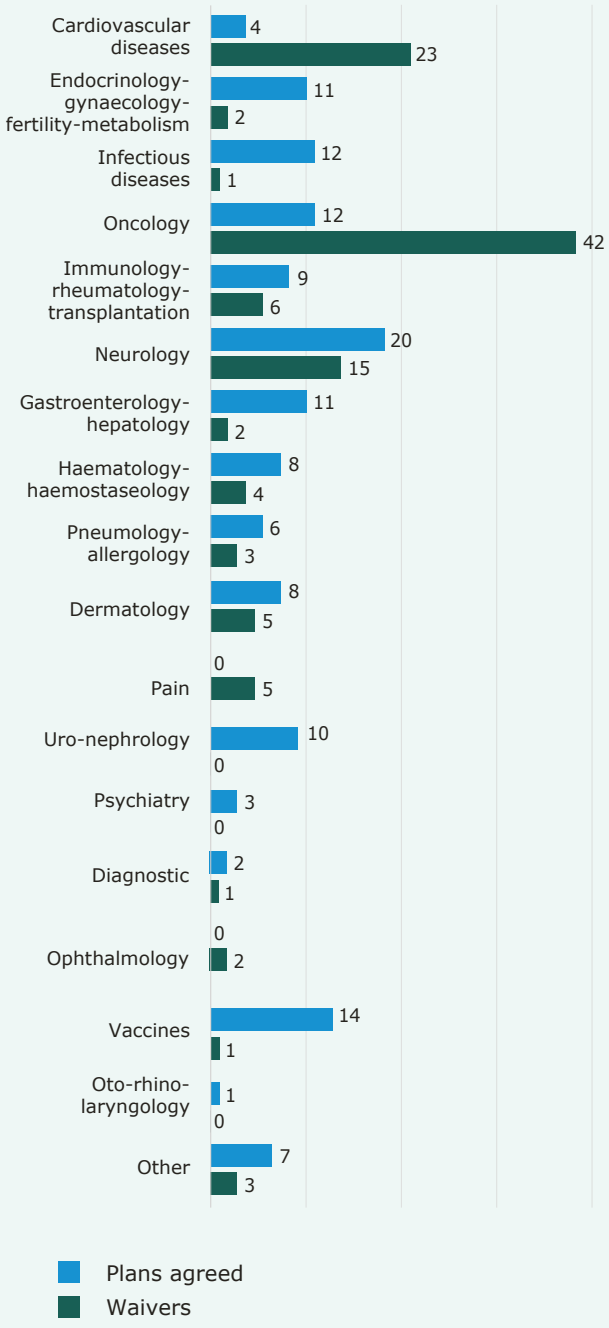
In 2022, the number of requests for scientific advice on paediatric issues dropped 41% compared to 2021.

Opinions on PIPs and waivers



Article 46 of the Paediatric Regulation requires marketing authorisation holders to submit studies on the use of already authorised medicines in children to regulatory authorities. This ensures that all paediatric studies are assessed by the relevant competent authorities. In 2022, EMA assessed 128 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 (2022)

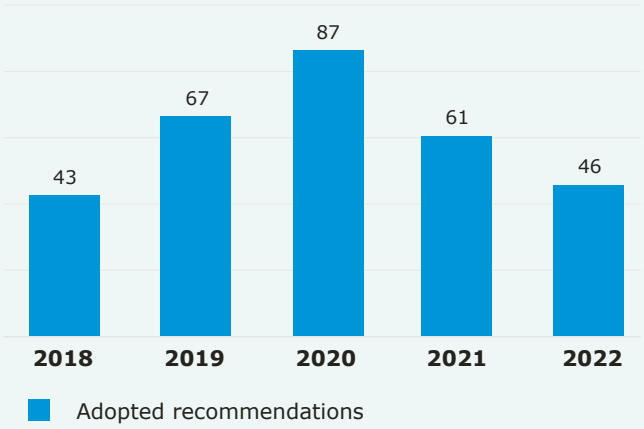


Advanced-therapy medicinal products

Advanced-therapy medicinal products (ATMPs) are medicines based on genes or cells that have the potential for ground-breaking 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 2022, the CAT received 51 requests for ATMP classification and adopted 46 recommendations.

Six ATMPs were recommended for marketing authorisation by the CHMP in 2022, compared to two in 2021. This confirms a rising trend in the number of applications and approvals of advanced therapies in the EU.

The six ATMPs approved in 2022 were Breyanzi, Carvykti, Ebvallo, Hemgenix, Roctavian and Upstaza.

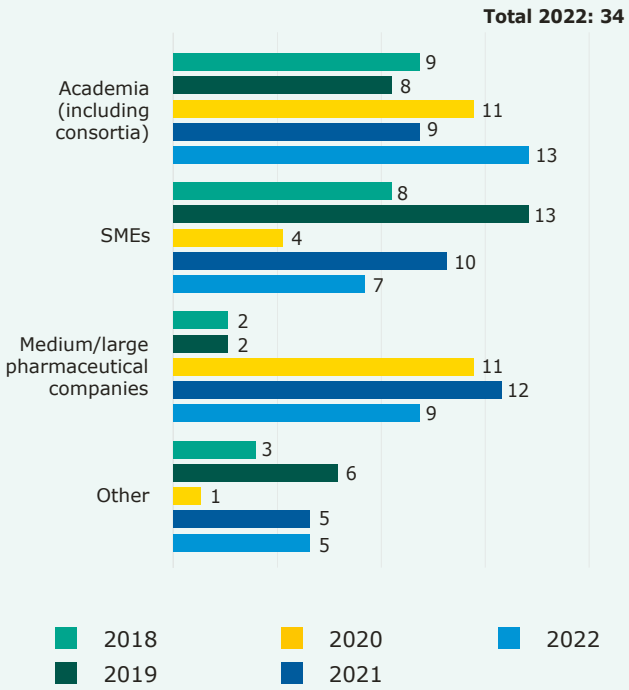
Innovation Task Force

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 held 34 ITF briefing meetings in 2022. Of these 34 meetings, 38% were requested by academia, another 26% by large pharmaceutical companies and 21% by SMEs.

A third of the 68 requests received concerned innovative methods, e.g. statistics, manufacturing, software, biomarkers, and around 15% technologies, e.g. 3D printing, e-health. Innovations linked to COVID-19 discussed in 2021 included novel manufacturing methods and decentralised clinical trials. Further discussions on innovative developments included genome editing and biomaterials.

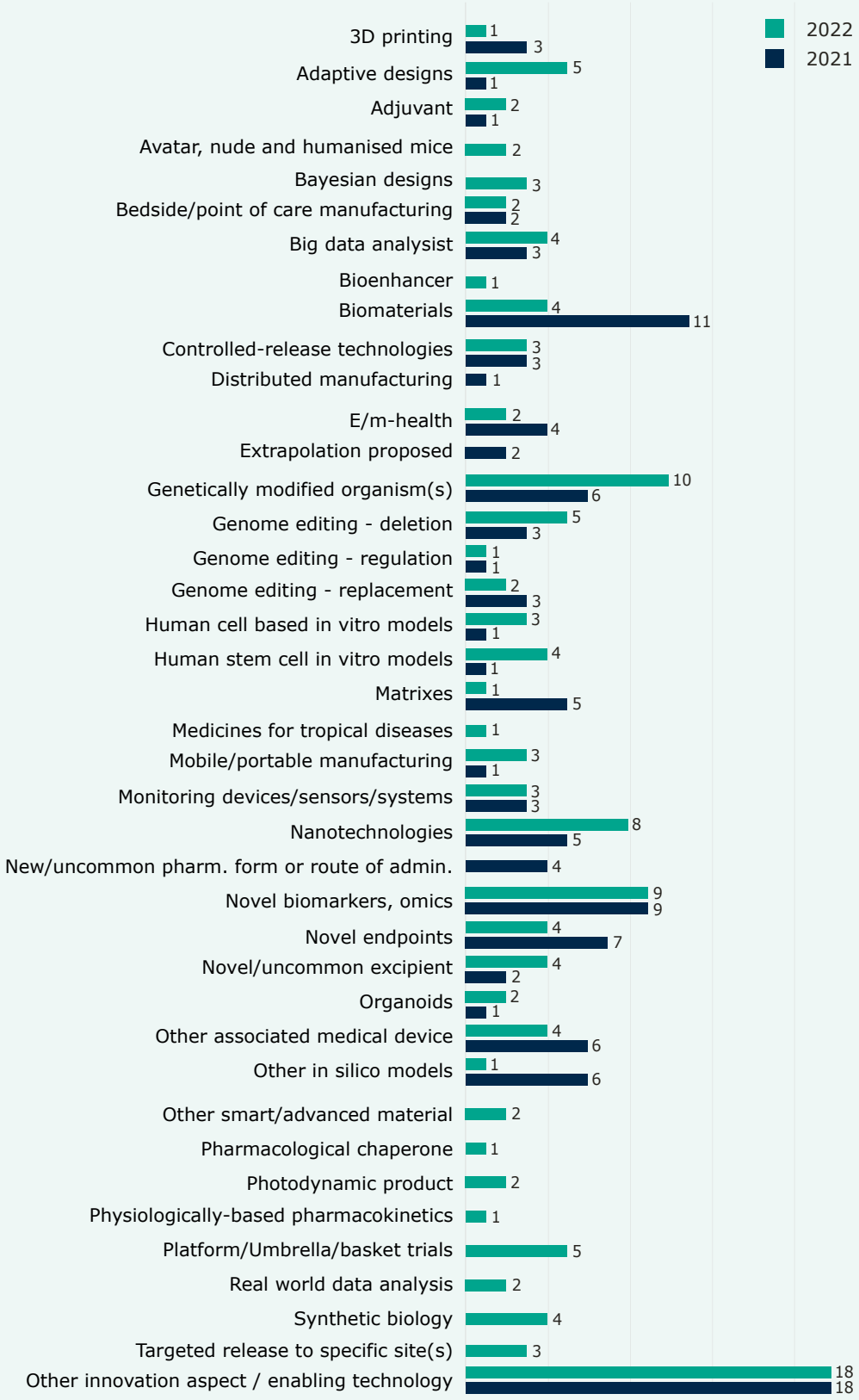
ITF briefing meetings by affiliation



REQUESTS RECEIVED BY ENABLING TECHNOLOGY

Each request could be associated with up to three of the categories in the table:

Enabling technology



Key scientific guidelines

The Agency develops scientific guidelines to provide advice to applicants or marketing authorisation holders, competent authorities and other interested parties on the most appropriate way to test and monitor the safety, efficacy and quality of medicines.

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.

The Agency's work on guideline development and revision continued to be suspended or scaled back due to business continuity planning around COVID-19. A selection of reflection papers and guidance issued or revised in 2022 is listed below:

Topic	Content
Scientific guideline on a selective approach to safety data collection in specific late-stage pre-approval or post-approval clinical trials	This guideline provides internationally harmonised guidance on the use of selective safety data collection that may be applied in specific late-stage interventional clinical trials that may be pre-approval or post-approval. The guideline details factors that can justify, after thorough consideration, a reduced collection of certain data in a clinical trial.
Scientific guideline on testing for carcinogenicity of pharmaceuticals	Guidance is available for marketing authorisation holders on approaches for evaluating the carcinogenic potential of pharmaceuticals. It embraces all pharmaceutical agents that need carcinogenicity testing as indicated in the ICH S1A.
Scientific guideline on continuous manufacturing of drug substances and drug products	This guideline describes scientific and regulatory considerations for the development, implementation, operation, and lifecycle management of continuous manufacturing (CM). Building on existing ICH Quality guidelines, this guideline provides clarification on CM concepts, describes scientific approaches, and presents regulatory considerations specific to CM of drug substances and drug products.
Toolbox guidance on scientific elements and regulatory tools to support quality data packages for PRIME and certain marketing authorisation applications targeting an unmet medical need	This guidance summarises scientific and regulatory approaches that developers of medicines, supported by EMA's PRIME scheme, can use to generate robust quality data packages for an EU marketing authorisation application, to enable patients to benefit from these therapies as early as possible.

Recommendations for marketing authorisation

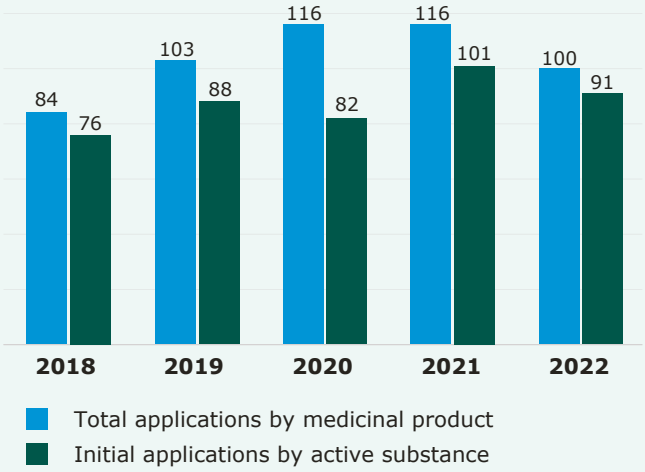
Applications for initial evaluation

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

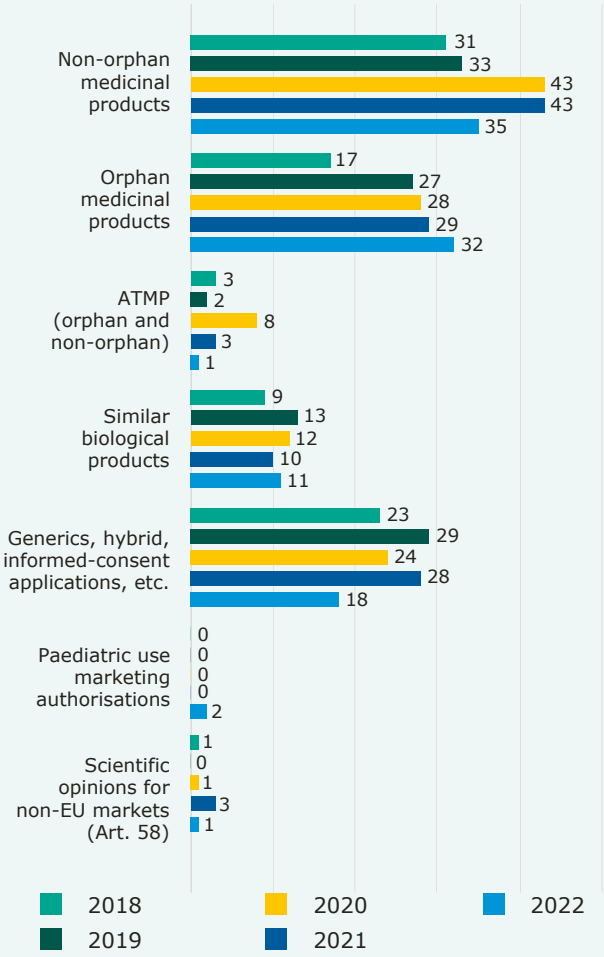
The initial evaluation covers all activities relating to the processing of marketing authorisation applications for new medicines which have never been assessed before, from the pre-submission discussion with future applicants, through to the evaluation by the CHMP and the granting of the marketing authorisation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

A total of 100 applications were received in 2022. Among these was one application for scientific opinions for non-EU markets (art 58).

Initial-evaluation applications

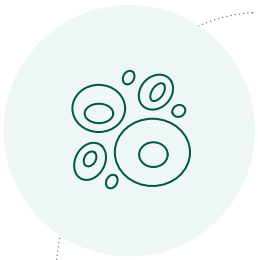


Initial-evaluation applications by type of application



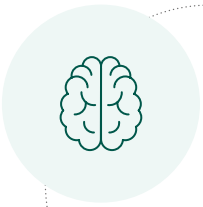
Outcome of initial evaluation

Cancer



Breyanzi
Camcevi
Carvykti
Celdoxome pegylated liposomal
Ebvallo
Imjudo
Kimmtrak
Lunsumio
Opdualag
Orgovyx
Pemetrexed Baxter
Pepaxti
Plerixafor Accord
Pluvicto
Scemblix
Sorafenib Accord
Tabrecta
Tecvayli
Thalidomide Lipomed
Tremelimumab AstraZeneca
Vegzelma
Zolsketil pegylated liposomal
Zynlonta

Neurology



Amifampridine SERB
Amvuttra
Dimethyl fumarate Mylan
Dimethyl fumarate Neuraxpharm
Dimethyl fumarate Polpharma
Dimethyl fumarate Teva
Melatonin Neurim
Quviviq
Rayvow
Sugammadex Amomed
Sugammadex Fresenius Kabi
Upstaza
Vydura
Vyvgart

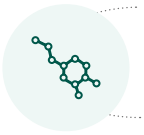
Endocrinology

Eladynos
Inpremzia
Kauliv
Mounjaro
Mycapssa
Pombiliti
Sitagliptin Accord
Sitagliptin / Metformin hydrochloride Accord
Sondelbay
Teriparatide SUN
Truvelog Mix 30
Vildagliptin / Metformin hydrochloride Accord

Haematology/ Haemostaseology

Cevenfacta
Dasatinib Accord
Dasatinib Accordpharma
Hemgenix
Roctavian
Stimufend

Metabolism



Amversio
Nulibry
Pyrukynd
Xenpozyme
Zokinvy

Covid-19

Evusheld
Paxlovid
COVID-19 Vaccine Valneva
VidPrevtyn Beta

Infections

Beyfortus
Ertapenem SUN
Livtencity
Sunlenca

Immunology/ Rheumatology/ Transplantation

Dimethyl fumarate Accord
Enjaymo
Teriflunomide Accord
Teriflunomide Mylan

Nephrology

Kapruvia
Lupkynis
Kinpeygo

Ophthalmology

Ranivisio
Vabysmo
Ximluci

Pneumology/ Allergology

Pirfenidone axunio
Pirfenidone Viatris
Tezspire

Dermatology

Filsuvez
Spevigo

Diagnostic agents

Illuzyce
Locametz

Vaccines

PreHevbri
Qdenga

Gastroenterology/ Hepatology

Livmarli

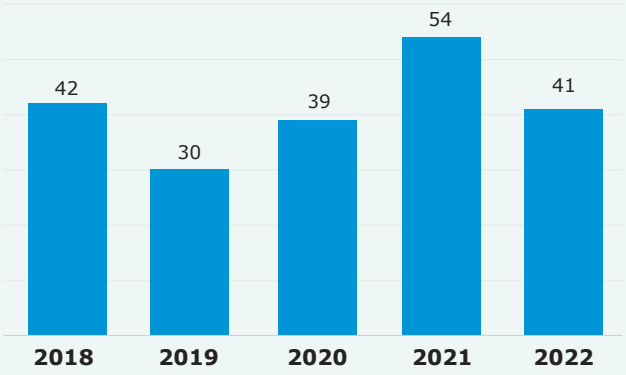
Reproductive

Ganirelix Gedeon Richter

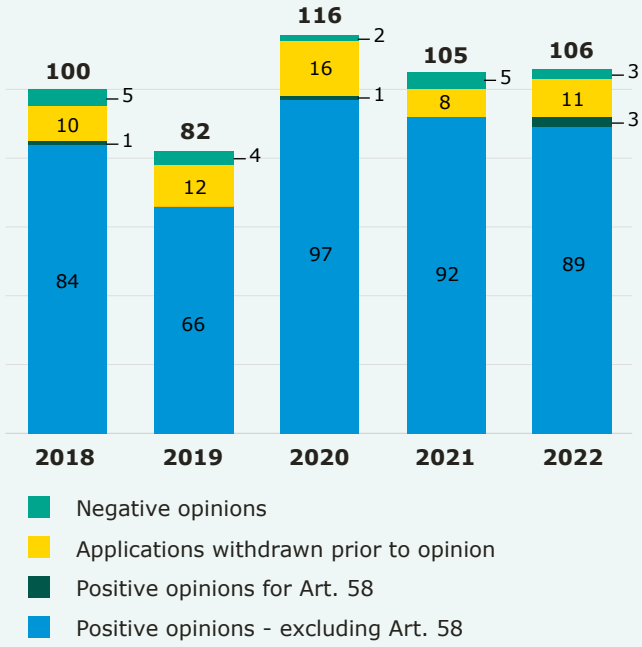
● PRIME ● ATMP ● Orphan medicine ● Accelerated assessment ● Conditional marketing authorisation ● Approval under exceptional circumstances ● Biosimilar

Medicines that contain a new active substance are highlighted in bold

Positive opinions - new active substances



Outcome of initial-evaluation applications



In 2022, EMA recommended 89 medicines for marketing authorisation. Of these, 41 had a new active substance which had never previously been authorised in the EU, a decrease of 24% compared to 2021.

The CHMP adopted negative opinions for three medicines in 2022: **Hervelous**, **Omblastys** and **Tuznue**.

The applications for 11 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.

Applicants for 62% of the medicines granted a positive opinion by the CHMP in 2022 had received scientific advice during the development phase of their medicine.

Conditional marketing authorisations

In 2022, nine medicines received a recommendation for a conditional marketing authorisation (CMA), one of the possibilities in the EU to give patients early access to new medicines: **Carvykti**, **Hemgenix**, **Kinpeygo**, **Lunsumio**, **Paxlovid**, **Roctavian**, **Spevigo**, **Tecvayli** and **Zynlonta**.

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 2022, 14 medicines (**Adcetris**, **Bosulif**, **Caprelsa**, **Comirnaty**, **Crysvita**, **Jcovden**, **Libtayo**, **Nexpovio**, **Polivy**, **Rubraca**, **Spikevax**, **Vaxzevria**, **Veklury** and **Zolgensma**) that had previously received a CMA were granted a recommendation for a full marketing authorisation by the CHMP after fulfilling their post-authorisation obligations.

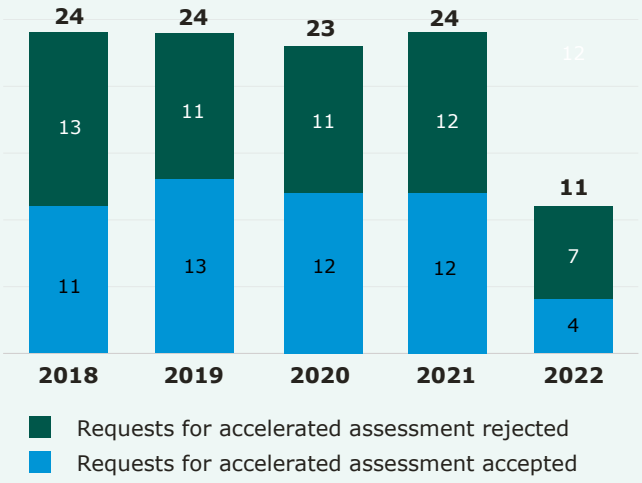
CMA and switch to standard marketing authorisation (excluding withdrawals)

	2018	2019	2020	2021	2022
Positive opinions for CMAs	1	8	13	13	9
Opinions recommending switch of CMA to standard marketing authorisation	2	1	2	1	14

Accelerated assessment

Five medicines (**Beyfortus**, **Kimmtrak**, **Lunsumio**, **Tecvayli** and **Xenpozyme**) received a recommendation for marketing authorisation following an accelerated assessment in 2022. 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 2022, four requests from applicants for accelerated assessment of their medicine were accepted and seven requests were rejected. The main reasons for rejection were either that the unmet medical need the medicine is expected to address was not adequately justified, or that the data provided did not justify a major public health interest.

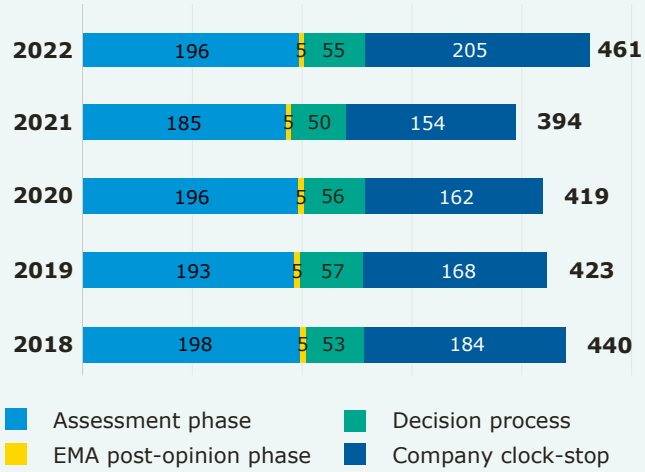


Average assessment time

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 is received, the counting of the days continues.

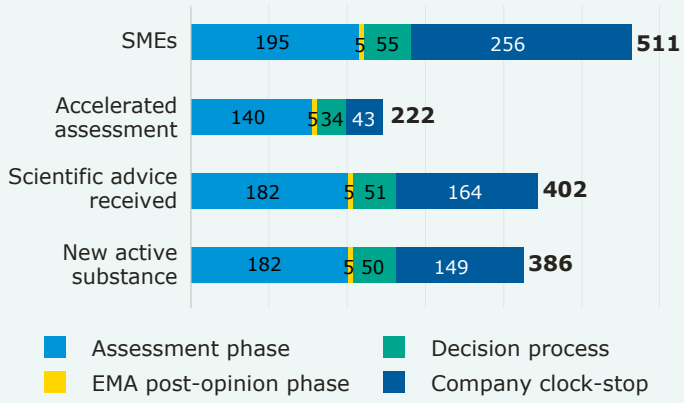
Once issued, the CHMP opinion is transmitted to the European Commission, which has the ultimate authority to grant a marketing authorisation and will take a decision within 67 days of receipt of the CHMP opinion.

Average number of days for centralised procedures - positive opinions



The overall total time required for the centralised procedure, from start of the evaluation process to the adoption of a decision by the European Commission, was an average of 461 days in 2022, 67 days more than in 2021.

Average number of days for centralised procedures - subset (2022)



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 accelerated assessment, the total time from start of assessment until granting of authorisation was reduced by around 8 months (from 461 to 222 days), potentially facilitating the subsequent decision-making steps at a national level and ultimately patient access.

Post-authorisation activities

In 2022, the CHMP gave 90 positive recommendations for extension of the therapeutic indication of already authorised medicines. Over one third of these extensions of indication related to medicines to treat tumours (or neoplasms), either malignant or benign.

Important extensions of indication included:

- **Adcirca**, for the treatment of pulmonary arterial hypertension (PAH) in paediatric patients aged 2 years and above;
- **Dupixent**, for the treatment of eosinophilic esophagitis (a rare, chronic, inflammatory disease of the oesophagus) in adults and adolescents 12 years and older who cannot follow conventional medicinal therapy;
- **Jakavi**, for the treatment of paediatric patients with acute and chronic Graft vs Host Disease (when white blood T cells in donated stem cells or bone marrow attack the host's body cells) from 12 years of age, who have inadequate response to corticosteroids or other systemic therapies;
- **Jardiance**, for the treatment of all types of heart failure, including those with preserved ejection fraction;
- **Xydalba**, for the treatment of acute bacterial skin and skin structure infections in adults and paediatric patients aged 3 months and older.

In 2022, EMA started the evaluation of:

- 3,586 type-IA variations;
- 3,354 type IB variations;
- 1,388 type-II variations;
- 31 extensions of marketing authorisations.

The product information for 467 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 it was authorised. 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 (CAPs), managing assessment procedures, e.g. for periodic safety update reports (PSURs), and the operation and maintenance of the EudraVigilance system.

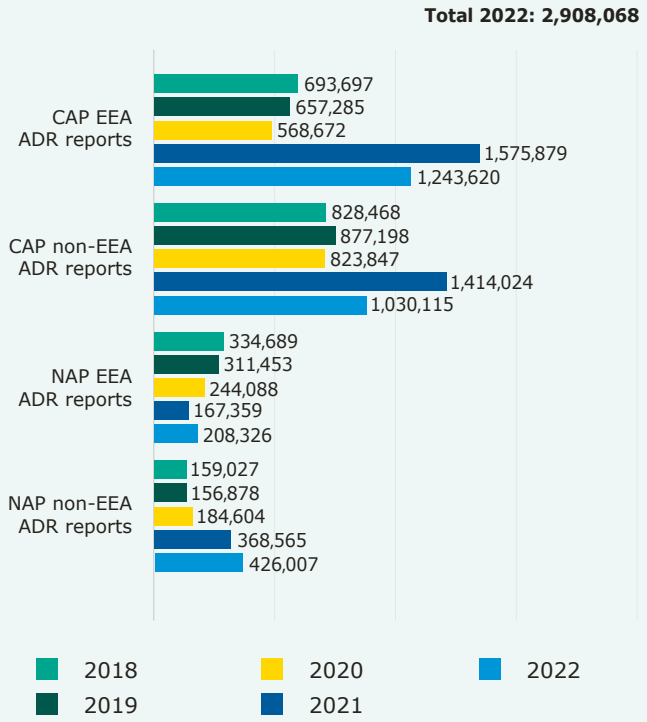
EudraVigilance

Both EMA and national competent authorities (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.

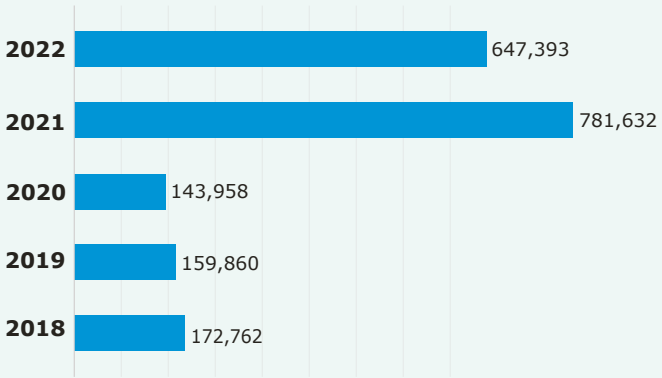
Over 2.9 million ADR reports were submitted to EudraVigilance in 2022, representing a slight decrease (17%) compared with 2021. However, the number of reports remains significantly higher than before 2021.

Over 50% of all reports in EudraVigilance originated in the EEA. As already noted last year, the share of reports submitted by European patients and consumers has increased compared to the period before 2021. This increase is due to the unprecedented roll-out of COVID-19 vaccines to hundreds of millions of EU citizens who have been encouraged to report all suspected side effects to the authorities. Out of the 647,393 ADR reports submitted by European patients and consumers through the NCAs and MAHs in 2022, 551,716 (85%) were related to COVID-19 vaccines.

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 in 2018, 2019, 2020, 2021 and 2022 include reports of non-serious, in addition to serious suspected adverse drug reactions.

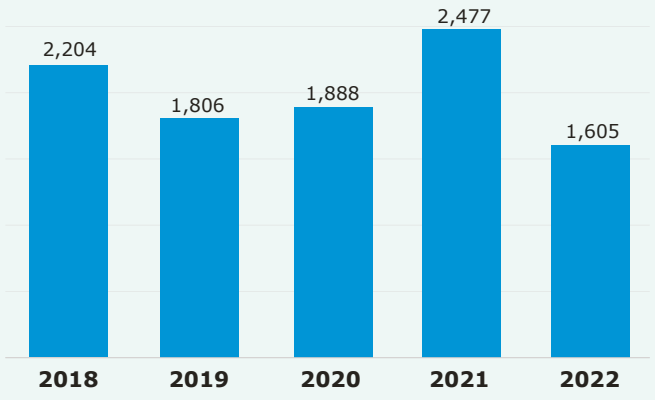
Signal detection

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 medicine and a reported adverse event.

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 2022, 1,605 potential signals were reviewed by EMA, a decrease of 35% compared to 2021. Approximately 83% of these signals originated from monitoring the EudraVigilance database, highlighting its central role for safety monitoring. The PRAC assessed 64 signals and of these, EMA validated 39. The number of signals validated by Member States and assessed by the PRAC decreased (25 vs 31). 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 peer-reviewed by EMA



OUTCOME OF SIGNAL ASSESSMENT

1,605 potential signals reviewed by EMA

↓

64 confirmed signals were prioritised and assessed by the PRAC

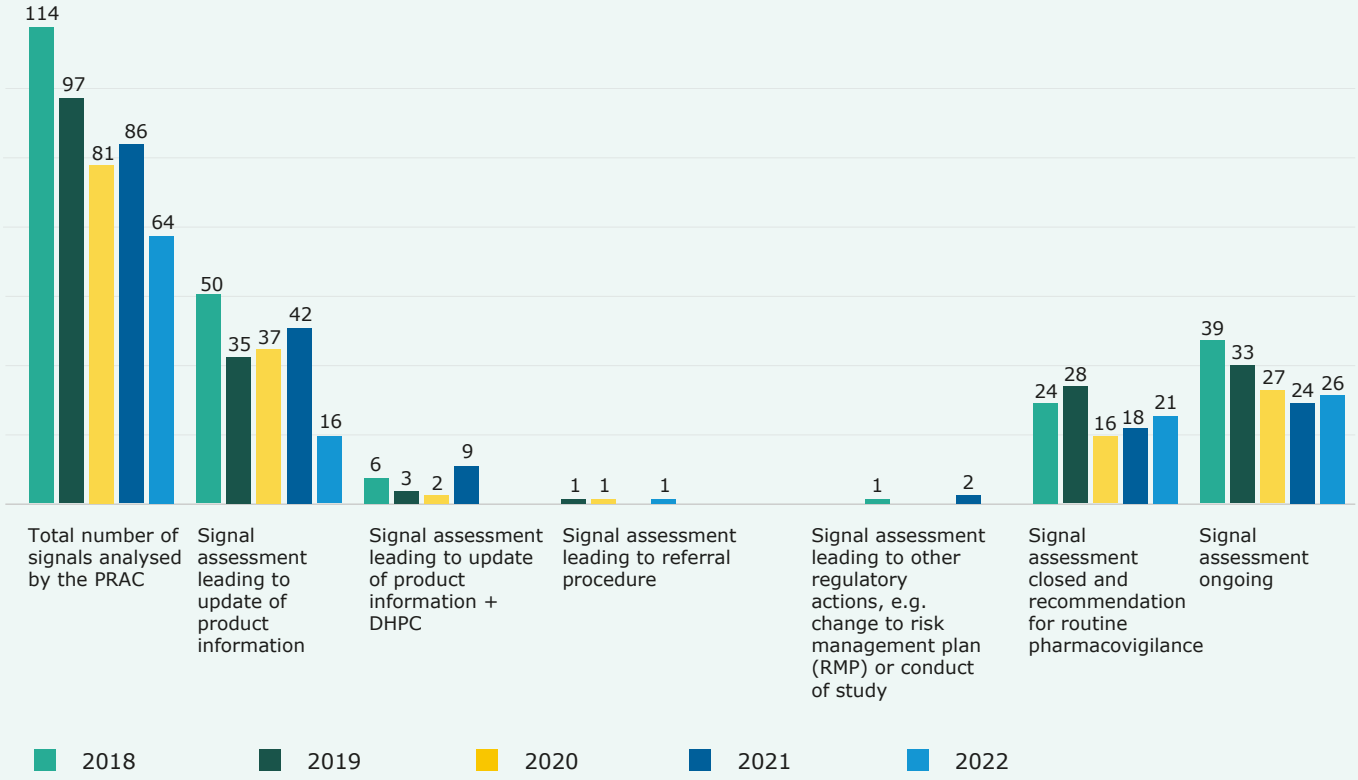
Of these, 39 signals were detected and validated by EMA	25 signals were detected and validated by EU Member States

↓

Out of 64 confirmed signals

16 signals led to a product information update	1 signal led to referral procedure	21 signals led to a recom-mendation for routine pharma-covigilance	26 signals were still under review by the PRAC at the end of 2022 as further data were required

Signal assessment



Periodic safety update reports (PSURs)

Marketing authorisation holders 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 studies carried out with it, both in authorised and unauthorised indications.

The Agency is responsible for procedures supporting the analysis of these reports for both CAPs and for nationally authorised medicines (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 procedures are referred to as periodic safety update single assessments or PSUSAs.

In 2022, the PRAC started the assessment of 873 PSURs and PSUSAs, of which 31% represent single assessments of active substances only contained in NAPs. 860 recommendations were issued by the PRAC based on the assessment of PSURs and PSUSAs, of which 32% consisted of single assessments of active substances only contained in NAPs.

Close to the half of 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	2018	2019	2020	2021	2022
PSURs – standalone (CAPs only) finalised	537	558	516	575	542
PSURs – single assessment finalised	364	270	258	336	318
PSURs – single assessment (CAPs with NAPs) finalised	43	48	49	49	46
PSURs – single assessment (NAPs only) finalised	321	222	209	287	272
Total outcomes	**901**	**828**	**774**	**911**	**860**

PRAC outcomes of PSURs and PSUSAs	2018	2019	2020	2021	2022
Maintenance	**735**	**655**	**630**	**748**	**720**
NAPs only	245	166	161	226	216
CAPs/NAPs and CAPs only	490	489	469	522	504
CHMP variation	**166**	**173**	**144**	**163**	**140**
NAPs only	76	56	48	61	56
CAPs/NAPs and CAPs only	90	117	96	102	84
Total outcomes	**901**	**828**	**774**	**911**	**860**

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 RMP assessments.

In 2022, the PRAC assessed 11 imposed PASS protocols that were requested to obtain further information on a medicine's safety, which was in line with 2021. The Committee assessed 233 non-imposed PASS protocols.

In addition, the PRAC started to assess the results of two imposed PASS, a number five times lower than that of 2021.

Post-authorisation safety studies					
	2018	**2019**	**2020**	**2021**	**2022**
Imposed PASS protocol procedures started	17	12	17	22	17
Imposed PASS protocol procedures finalised	9	13	13	23	16
Non-imposed PASS protocol procedures started	195	144	158	143	217
Non-imposed PASS protocol procedures finalised	196	180	167	226	233
PASS amendment	11 (started), 11 (finalised)	11 (started), 9 (finalised)	19 (started), 14 (finalised) + 9 follow up amendments (started) and 7 (finalised)	17 (started), 18 (finalised) + 15 follow up amendments (started) and 11 (finalised)	20 (started), 18 (finalised) + 12 follow up amendments (started) and 14 (finalised)
Imposed PASS result procedures started	8	3	4	11	2
Imposed PASS result procedures finalised	8	3	2	6	5
PASS scientific advice through SAWP	3	3	1	1	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.

The CHMP imposed ten PAES on companies in order to collect further data on the benefits of medicines while they are used by patients in real life.

Post-authorisation efficacy studies					
	2018	**2019**	**2020**	**2021**	**2022**
PAES (imposed)	4	9	8	8	10
PAES (non-imposed)	2	0	0	0	0

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 CAPs, 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 also published on the EMA website.

The number of notifications of withdrawn products has almost halved between 2021 and 2022 (597 vs 285).

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 2022, 365 medicines were subject to additional monitoring, in line with previous years. 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 European Commission and regulatory authorities in the Member States. In 2022, two 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 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 2022, 30 non-urgent information or rapid alert notifications were submitted via EPITT, an increase of one third compared to 2021.

Scientific and medical literature is an important source of information to identify 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 2022, 8,278 Individual Case Safety Reports (ICSRs) resulted from EMA's medical literature monitoring (MLM) service, a 10% decrease compared to 2021.

Other pharmacovigilance activities	2018	2019	2020	2021	2022
Cumulative number of products on the list of products to be subject to additional monitoring	351	342	343	372	365
Number of incident management plans triggered	11	3	6	4	2
Number of non-urgent information or rapid alert notifications submitted through EPITT	44	43	15	20	30
Number of external requests for EudraVigilance analyses	17	13	15	30	16
Number of MLM ICSRs created	13,275	9,676	9,550	9,193	8,278

Referral procedures

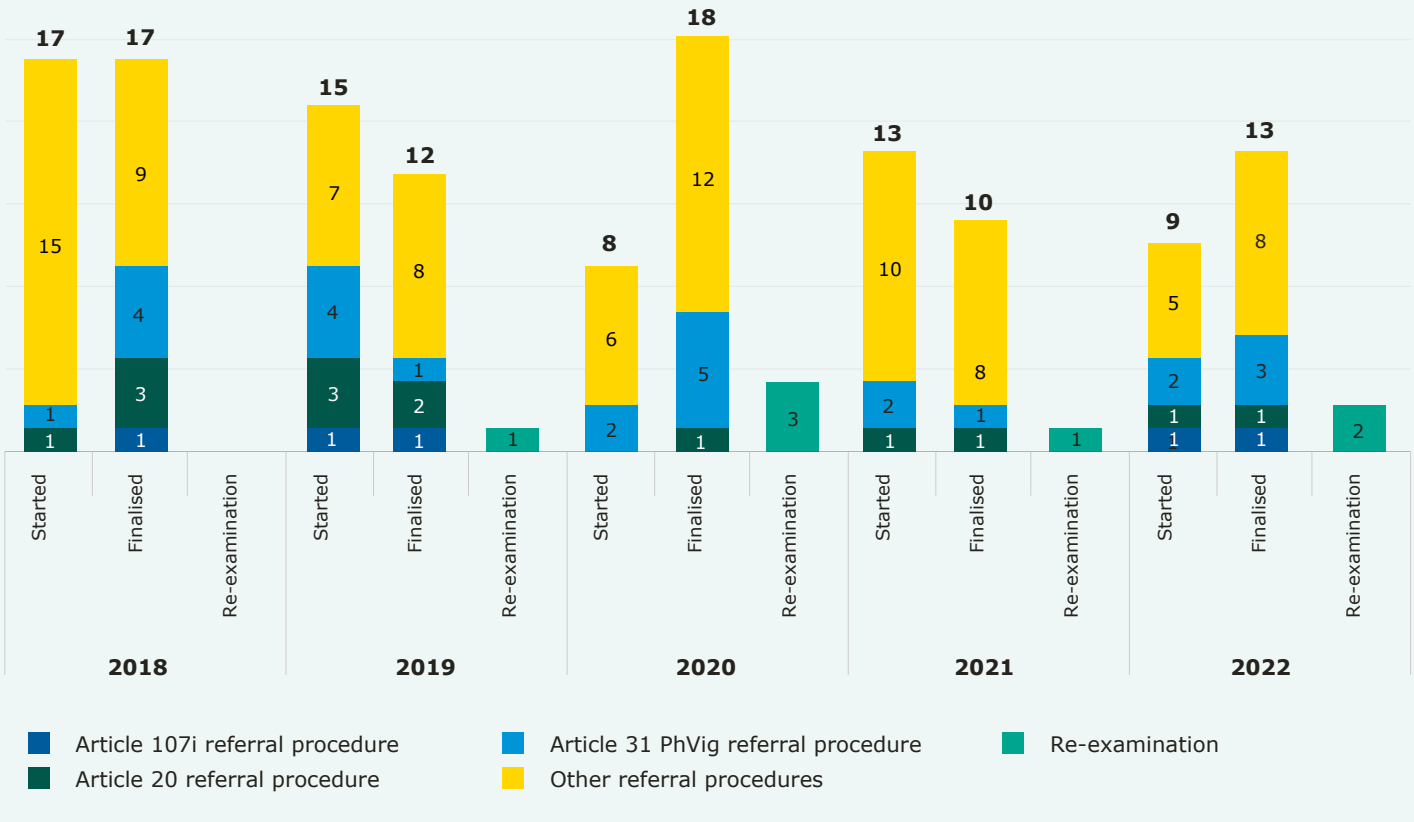
Referral procedures are initiated to address concerns over the safety or benefit-risk balance of a medicine, as well as to deal with disagreement among Member States on the use of a medicine. In a referral, EMA is requested, on behalf of the EU, to conduct a scientific assessment of a particular medicine or class of medicines and issue a recommendation. Following the recommendation, the European Commission will issue a legally binding decision for the EU. Less often, in cases where only NAPs 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 majority, rather than by consensus of all CMDh members, the European Commission will issue a final decision applicable throughout the EU.

In 2022, 13 referral procedures were finalised, of which five were related to the safety of medicines, initiated under articles 31, 20 or 107i of the pharmacovigilance legislation. Three led to changes in the product information.

The remaining eight 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.

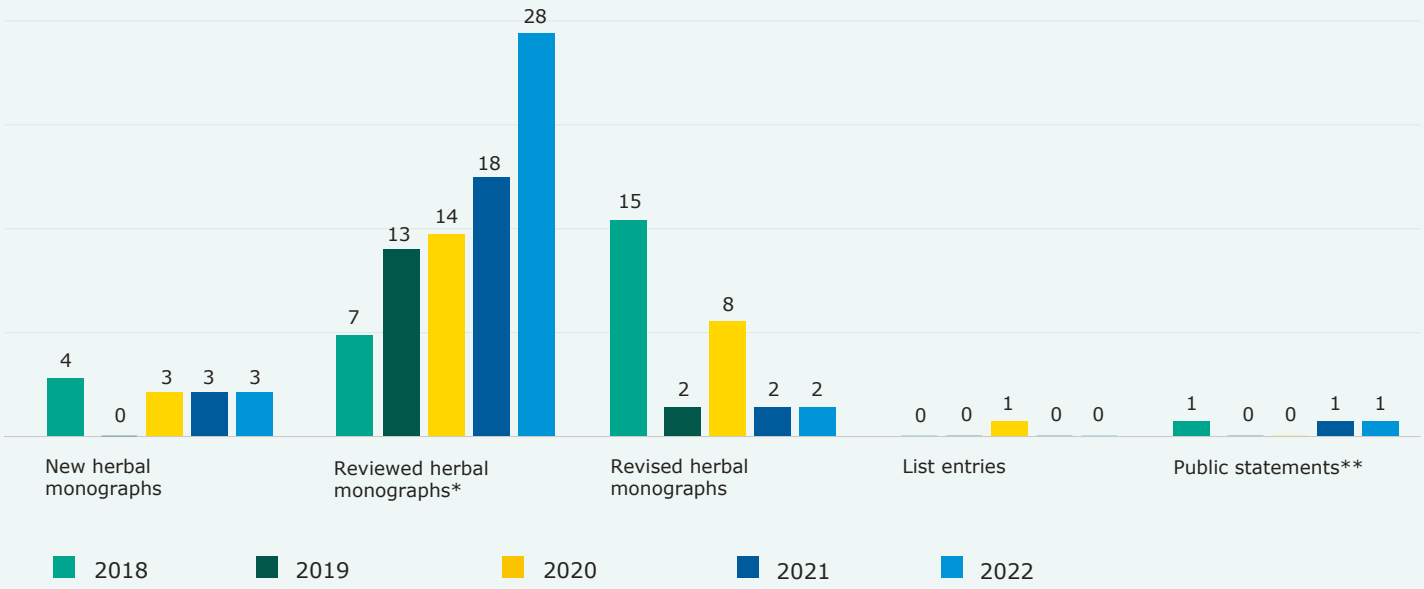
Referrals for human medicines finalised or re-examinations



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 European Commission's list of herbal substances, preparations and combinations thereof for use in traditional medicines. In 2022, 28 monographs were updated following a systematic review of newly available data. This represents a 56% increase compared to 2021.

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.

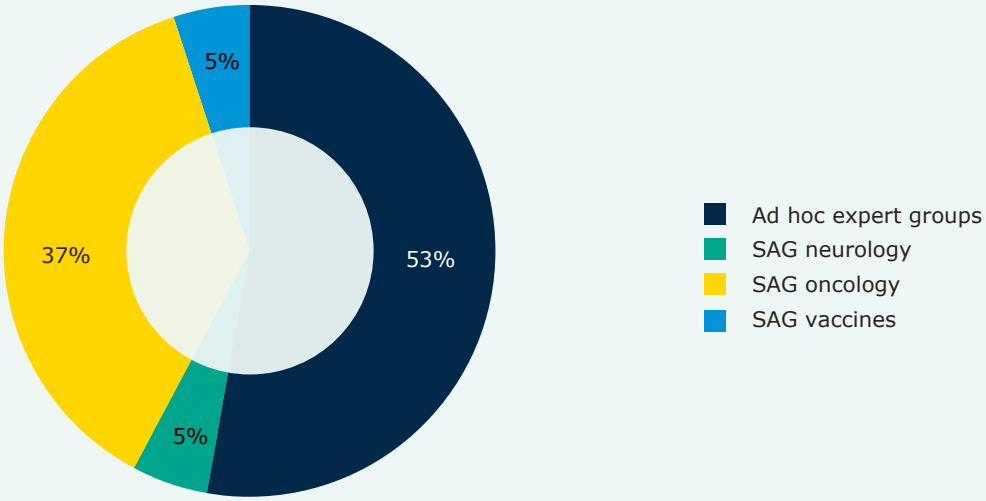
Note: A complete list of recommendations on herbal medicines can be found in the annexes.

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 19 consultations took place in 2022 in the form of SAG meetings, 27% more than in 2021.

Areas of discussions - SAGs and ad hoc expert group meetings (2022)



Procedures with Scientific Advisory Group or ad hoc expert group involvement (number of consultations)	2018	2019	2020	2021	2022
Marketing authorisation (new MAA, new MAA re-examination, Art 58)	19	15	18	11	10
Extension of indication (including line extensions)	10	3	7	2	7
Referral (including re-examination)	3	6	0	1	2
Guideline	0	1	0	0	0
Other topics (renewal, PSUR, signal, class review)	0	2	3	1	0
Total	**32**	**27**	**28**	**15**	**19**

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	2018	2019	2020	2021	2022
Scientific advice/protocol assistance	107	143	97	90	n/a
SAGs/ad hoc expert meetings	37	46	42	25	n/a
Scientific committee/working party consultations	112	355	227	122	n/a
Patient membership in Management Board, committees, working parties	59	57	57	56	57
EMA Management Board	2	2	2	2	2
Scientific committees	15	11	14	13	12
Patients' and Consumers' Working Party	42	44	41	41	43
Active patient experts nominated by EMA					80
Number of eligible PCO organisations					42
Document reviews conducted by patients and consumers	178	169	203	192	n/a
EPAR summaries	43	40	50	55	n/a
Package leaflets	75	101	123	112	n/a
Safety communications	35	11	16	25	n/a
Herbal summaries	25	17	14	n/a	n/a
Total cases of patient/stakeholder engagement in EMA activities	**493**	**770**	**594**	**485**	**n/a**

Healthcare-professional involvement in EMA activities	2018	2019	2020	2021	2022
Scientific advice/protocol assistance	0	2	1	4	n/a
SAGs/ad hoc expert meetings	31	36	39	21	n/a
Scientific committee/working party consultations	47	68	28	94	n/a
Healthcare-professional membership in Management Board, committees, working parties	54	58	62	57	56
EMA Management Board	2	2	2	2	2
Scientific committees	12	12	12	12	12
Healthcare Professionals' Working Party	40	44	48	43	42
Active HCP experts nominated by EMA					140
Number of eligible HCP organisations					39
Document reviews conducted by healthcare professionals	80	48	46	26	n/a
Safety communications	40	35	42	20	n/a
DHPCs	40	13	4	6	n/a
Total cases of healthcare-professional engagement in EMA activities	**212**	**212**	**176**	**202**	**n/a**

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 2022 in relation to pharmacovigilance and referrals can be found on the HMA website.

VETERINARY MEDICINES

Activities supporting research and development

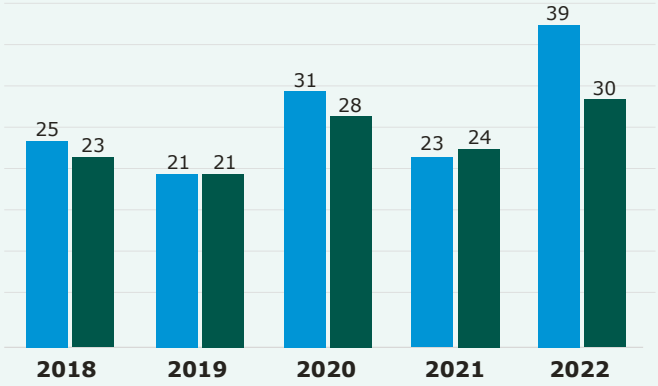
The Agency provides pre-authorisation support to medicine developers to boost innovation and research and enhance the availability of safe and effective veterinary medicines. This is achieved through activities and incentives offered to companies prior to submitting an application for marketing authorisation.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

Scientific advice

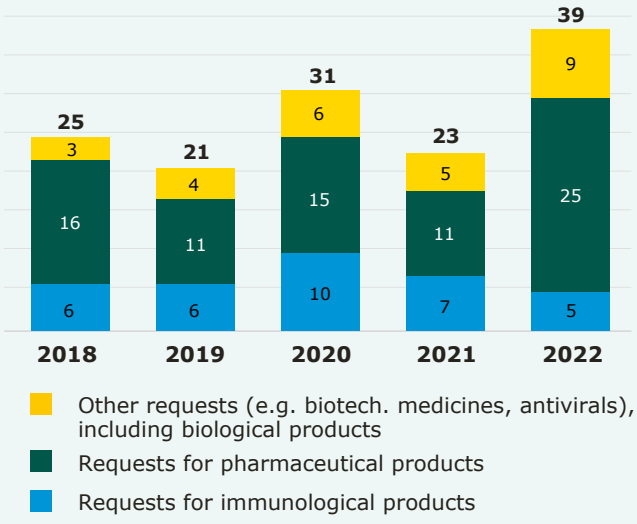
Scientific advice is provided on any aspect of research and development relating to the quality, safety or efficacy of medicines for veterinary use, and to the establishment of maximum residue limits. Scientific advice is a means of facilitating and improving the availability of new veterinary medicines. In 2022, EMA received 39 requests for scientific advice and finalised 30, including some pending from 2021. The number of requests has grown significantly after a decline last year, indicating an increased interest from medicine developers in engaging early with the Agency.

Five 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. In addition, veterinary vaccines can be an efficient tool in reducing the need to use antibiotics in animals, thereby contributing to the fight against AMR.

Scientific-advice requests received and finalised



Scientific-advice requests received by area



Veterinary limited markets

The Agency's minor use minor species (MUMS)/ limited market policy was introduced in September 2009 to stimulate 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. The policy expired in January 2022 when the limited market provisions of the new Veterinary Medicinal Products Regulation came into force.

Of the medicines classified previously as MUMS/ limited market, one product was recommended by the CVMP for marketing authorisation in 2022:

- **RenuTend** – a new product to improve healing of injuries of tendons and suspensory ligaments in horses.

The Veterinary Medicinal Products Regulation introduced a specific authorisation route for medicines intended for veterinary limited markets in the EU when it became applicable on 28 January 2022. It enables the CVMP to recommend granting a marketing authorisation for such medicines based on less comprehensive data than normally required, where the benefit for animal or public health of placing the medicine on the market is greater than the risk of having a reduced data package on the medicine. The Regulation aims to further stimulate the development of veterinary medicines for small markets, in order to increase the availability of treatments for serious or life-threatening animal diseases and unmet veterinary medical needs.

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 1,922 SMEs developing and marketing medicinal products registered with EMA at the end of 2022, 66 were developing veterinary products and 89 both human and veterinary products. In 2022, the Agency received a total of 12 new requests for scientific advice relating to the quality, safety or efficacy of medicines for veterinary use submitted by SMEs. The number of requests has grown after a decline in 2021, indicating more interest from medicine developers in engaging early with the Agency.

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. One ITF meeting was held in 2022 concerning the development of a veterinary medicine.

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. 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 2022 is listed below:

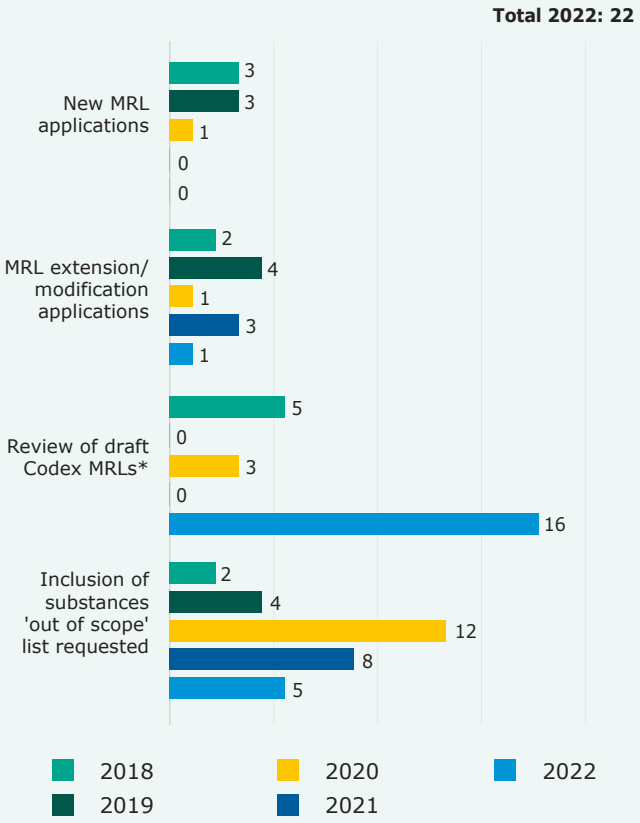
Topics	Content
Antimicrobial resistance	Reflection paper on prophylactic use of antimicrobials in animals in the context of Article 107(3) of Regulation 7 (EU) 2019/6
Biological substances other than immunologicals	Guideline on determination of the need for an MRL evaluation for biological substances
Efficacy of veterinary medicines	Questions and answers on requirements for pre-clinical studies submitted in support of a marketing authorisation application for a veterinary medicinal product
Environmental risk assessment	Reflection paper on criteria for determining that an active substance is essential when considered in the context of Article 37(2)(j) of Regulation (EU) 2019/6
Quality of veterinary medicines	Concept paper on the establishment of a guideline on the development and manufacture of synthetic oligonucleotides

Note: A full list of reflection papers and guidelines issued in 2022 can be found in the annexes.

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 European Commission on the basis of a recommendation from the CVMP. In 2022, the CVMP received an application for the extension or modification of the existing MRL classifications for one substance.

Evaluation of maximum residue limits



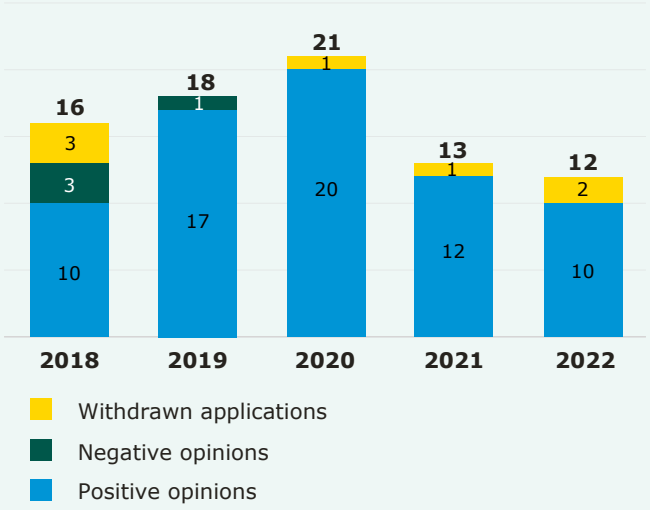
*From 2022, it also includes extrapolations

Recommendations for marketing authorisations

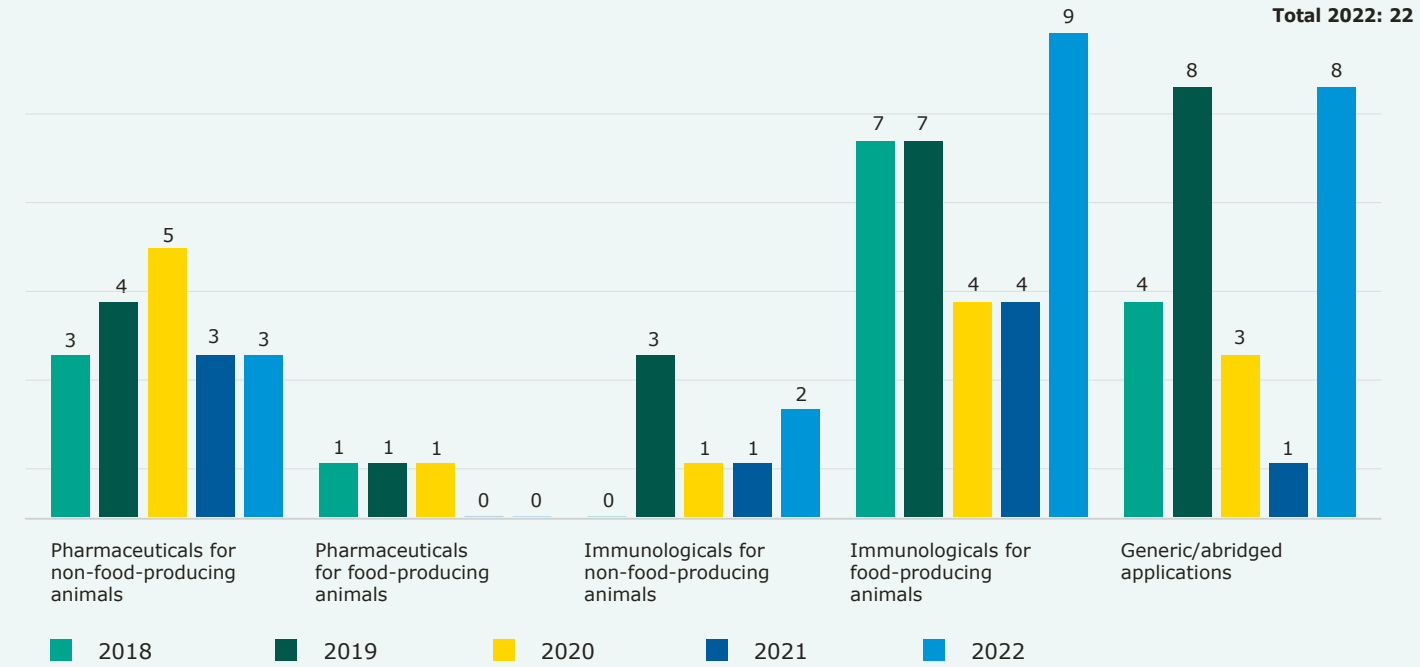
Applications for initial evaluation

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 European Commission. A total of 22 applications were received in 2022, marking a significant increase compared to 2021 when nine applications were submitted because developers of veterinary medicines were waiting for the implementation of the new Veterinary Medicinal Products Regulation. Half of these applications were submitted for vaccines, nine of which were for use in food-producing animals.

Outcome of initial-evaluation applications



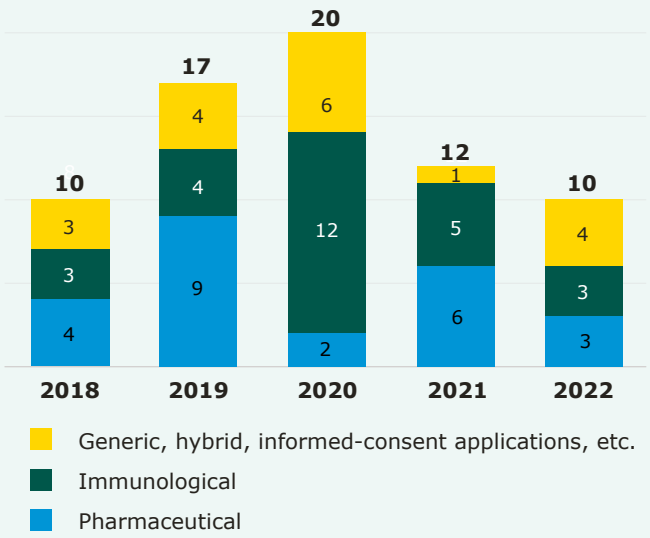
Applications for initial evaluations received



RECOMMENDATIONS FOR AUTHORISATION

In 2022, ten new veterinary medicines were granted a positive opinion. Of these, three had a new active substance. Two were vaccines, including one new biotechnological vaccine. This demonstrates the animal health industry's continued strong interest in developing vaccines.

Positive opinions for veterinary medicines



Medicines recommended for approval in 2022

Dogs

DogStem
Cortaderm
Coxatab
Lotilaner Elanco
Mometamax Ultra
Neoleish

Cattle

Chanaxin

Chickens

Evanovo

Pigs

Chanaxin
Brucellin Aquilon

Horses

RenuTend

Cats

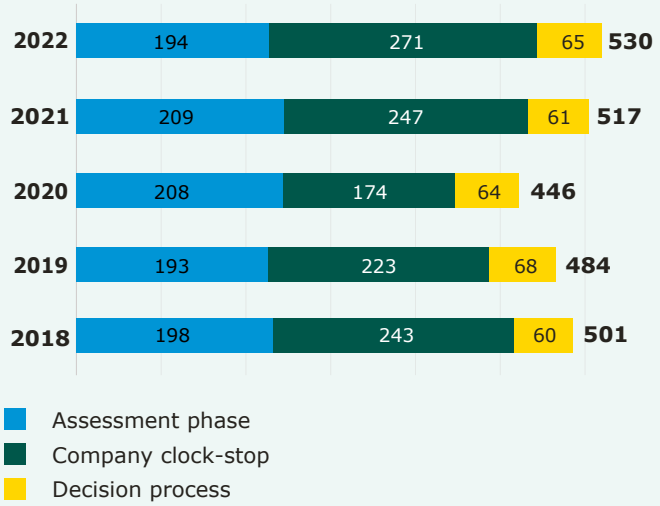
Lotilaner Elanco

Sheep

Chanaxin

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 slightly increased compared to past years, mostly due to longer clock-stops taken by the companies to respond to questions from CVMP.

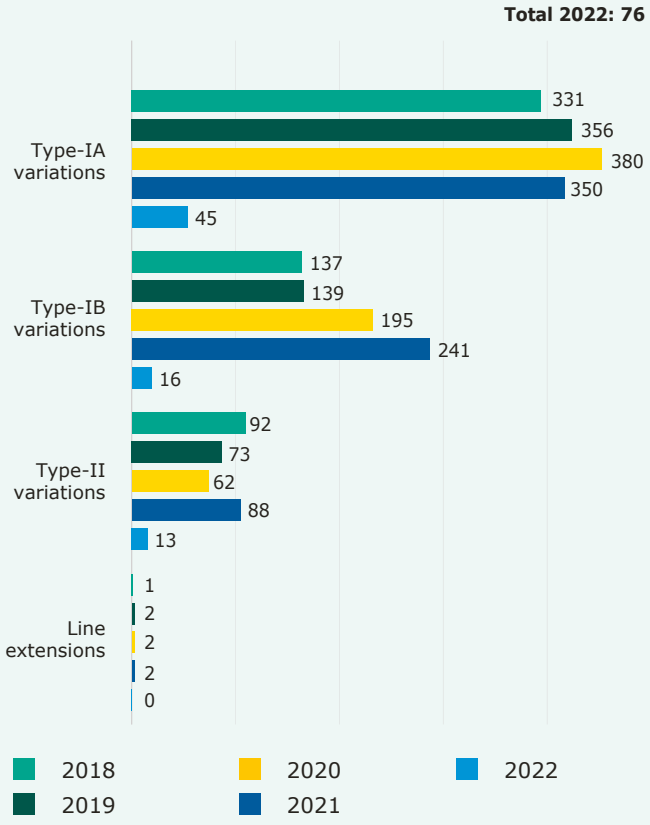
Post-authorisation activities

Post-authorisation activities relate to variations, extensions and transfers of marketing authorisations.

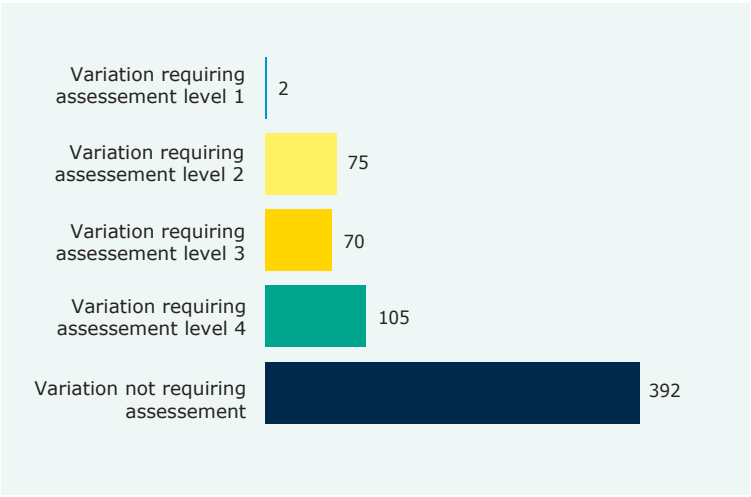
The use of eight already authorised products was expanded in 2022:

- **Advocate** (*Imidacloprid/Moxidectin*) to be also used for the treatment of the lungworm *Troglostrongylus brevior* (adults) in cats.
- **Bravecto** (*fluralaner*) chewable tablets for dogs to be also used for persistent tick killing activity from 7 days to 12 weeks after treatment for *Ixodes hexagonus* and for reduction of the risk of infection with *Dipylidium caninum* via transmission by *Ctenocephalides felis* for up to 12 weeks.
- **Credelio** (*Lotilaner*) to be also used for the treatment of demodicosis (caused by *Demodex canis*) in dogs.
- **Nexgard** (*Afoxolaner*) and **Nexgard Spectra** (*Afoxolaner/Milbemycin oxime*) to be also used for the treatment of tick infestations with *Hyalomma marginatum* and for the treatment of ear mite infestations (caused by *Otodectes cynotis*). The product information was also amended to allow the use of these veterinary medicines in breeding, pregnant and lactating female dogs.
- **Simparica** and **MiPet Easecto** (*Sarolaner*) to be also used for reduction of the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* for 28 days after treatment.
- **Suprelorin** (*Deslorelin*) to be also used in female dogs and in male cats.

Post-authorisation applications received



Under the Veterinary Medicinal Products Regulation there are two types of variations (i.e. changes to the terms of a marketing authorisation): variations not requiring assessment, which have minimal or no impact on the quality, safety or efficacy of the medicine, and variations requiring assessment, including different levels of complexity.
In 2022, the number of post-authorisation requests increased in line with the trends over the past years.



Note: For an explanation of the different variation levels, please refer to the Explanatory note on general fees payable to the European Medicines Agency.

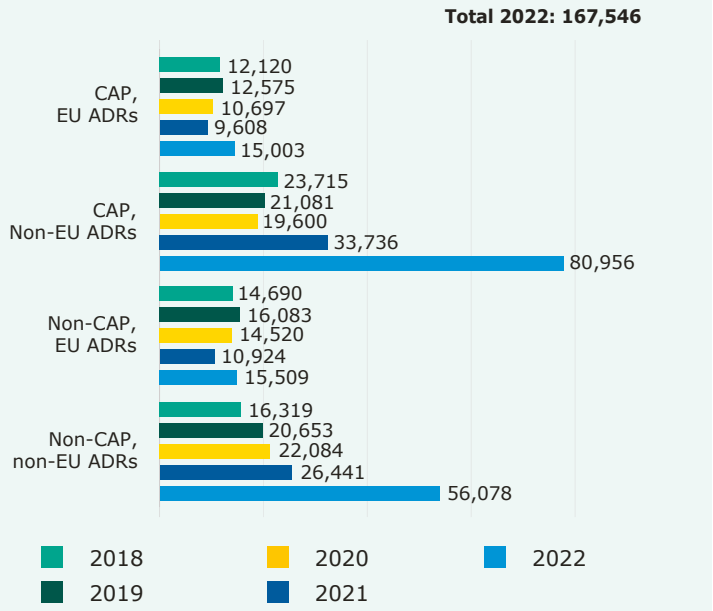
Safety monitoring of medicines

Pharmacovigilance covers activities related 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.

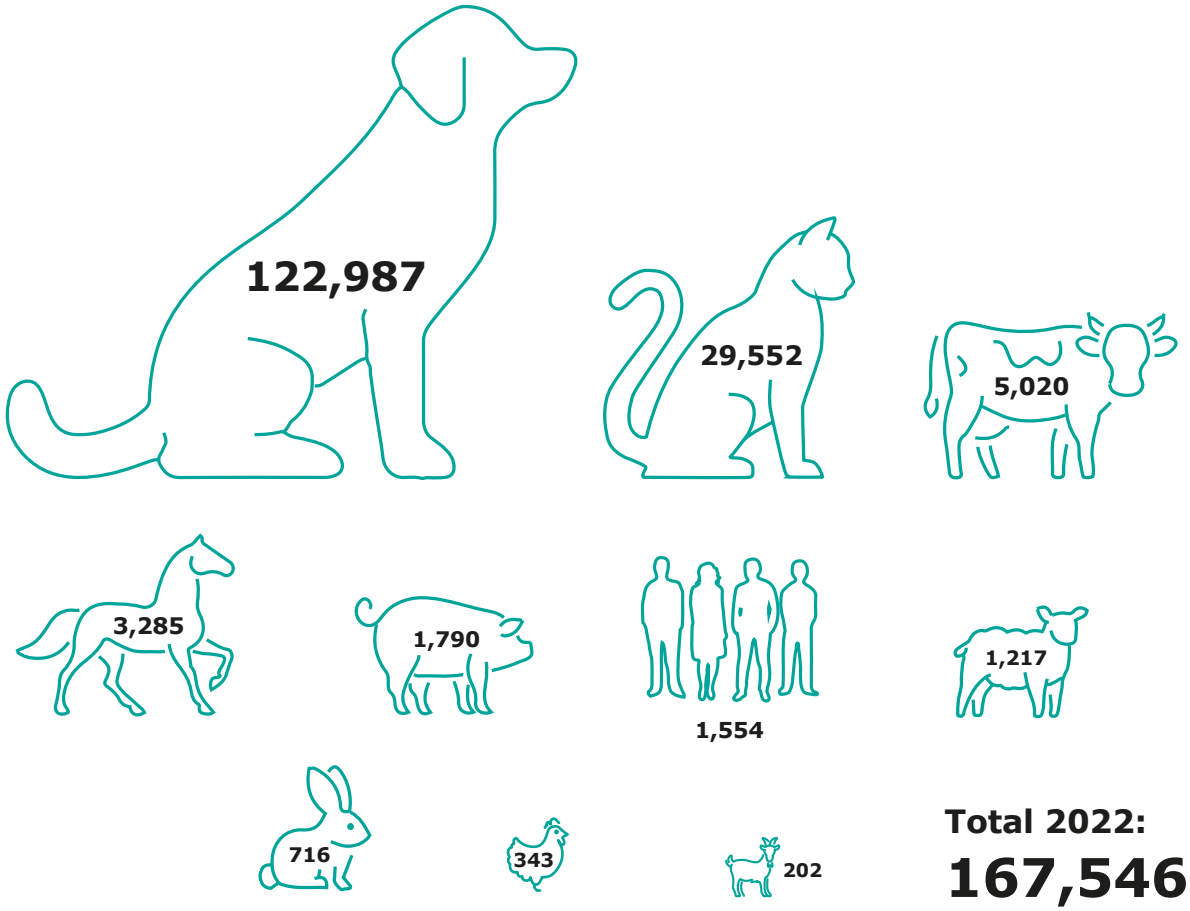
EudraVigilance

The new Veterinary Medicinal Products Regulation requires reporting of both serious and non-serious AE reports. In addition, a backlog of AE reports was submitted in 2022, leading to a large increase in the total number of reports received in the EudraVigilance system compared to 2021.

Adverse-event reports in animals



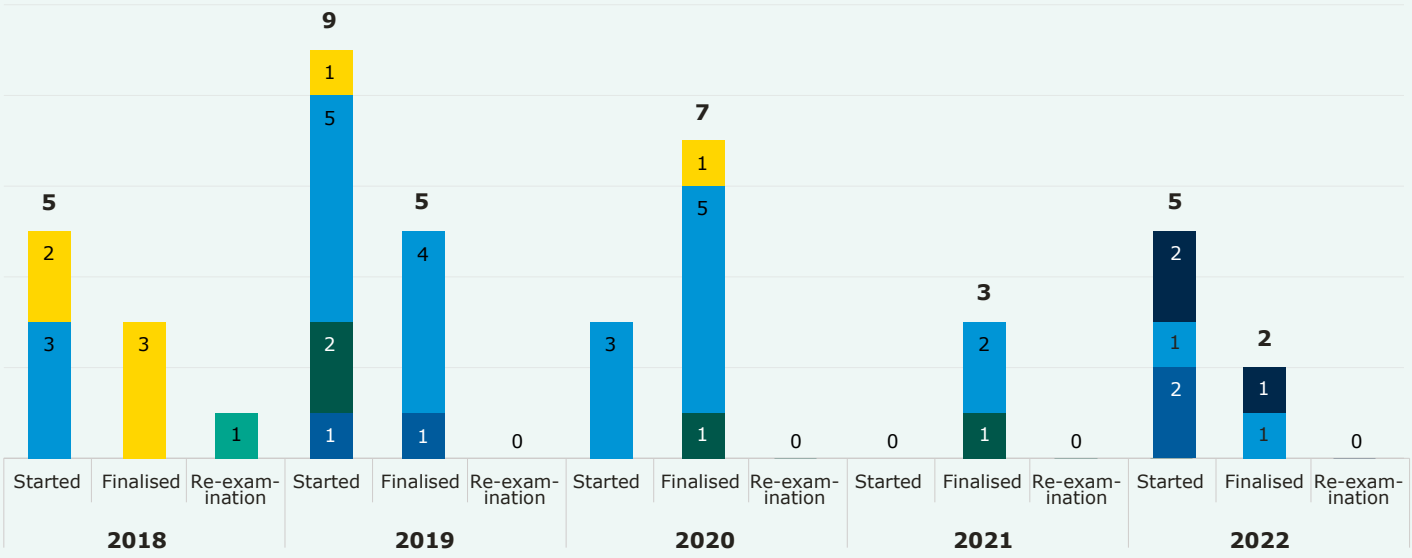
Number of adverse-event reports per species



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 EU issued by the European Commission. Five referral and arbitration procedures related to veterinary medicinal products began in 2022 and two were finalised. Three of them were safety-related (under Article 82 of Regulation (EU) 2019/6 or under Article 35 of Directive 2001/EC/82).

Arbitration and referrals for veterinary medicines



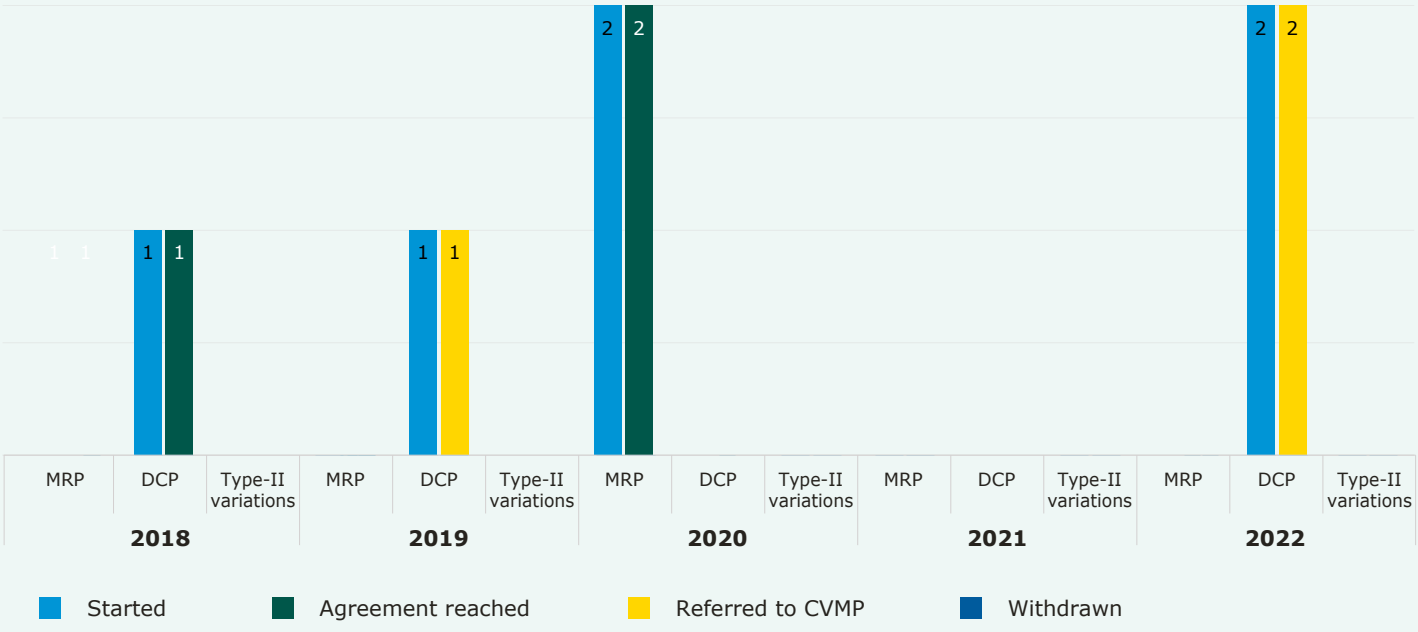
*Including Art.13 of Regulation 1234/2008; Art.78 of Directive 2001/82/EC; Articles 30 or 45 of Regulation 726/2004 and Art.54(8), Art.130(4) and Art .141(1)(c) and (e) of Regulation (EU) 2019/6

Note: Complete information on referral procedures can be found in the annexes.

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 EMA's success.

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, Scientific Advisory Groups (SAGs) and a number of ad hoc advisory groups as well as members of the assessment teams carrying out the evaluation of medicines.

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 take the lead in evaluating any new information on the medicine that may become available.

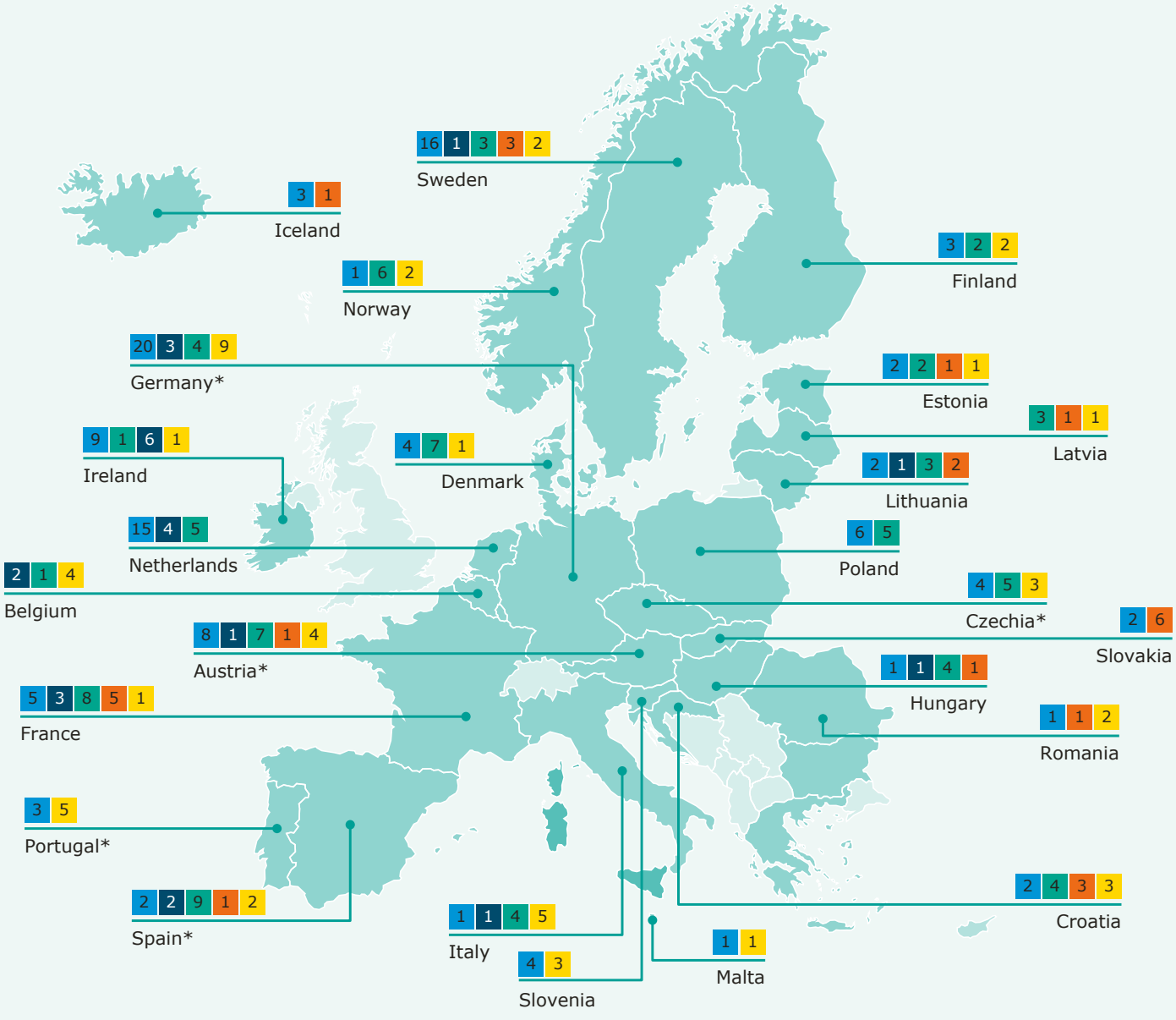
CHMP rapporteurships/co-rapporteurships

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 for which each country in 2022 was appointed 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 2022

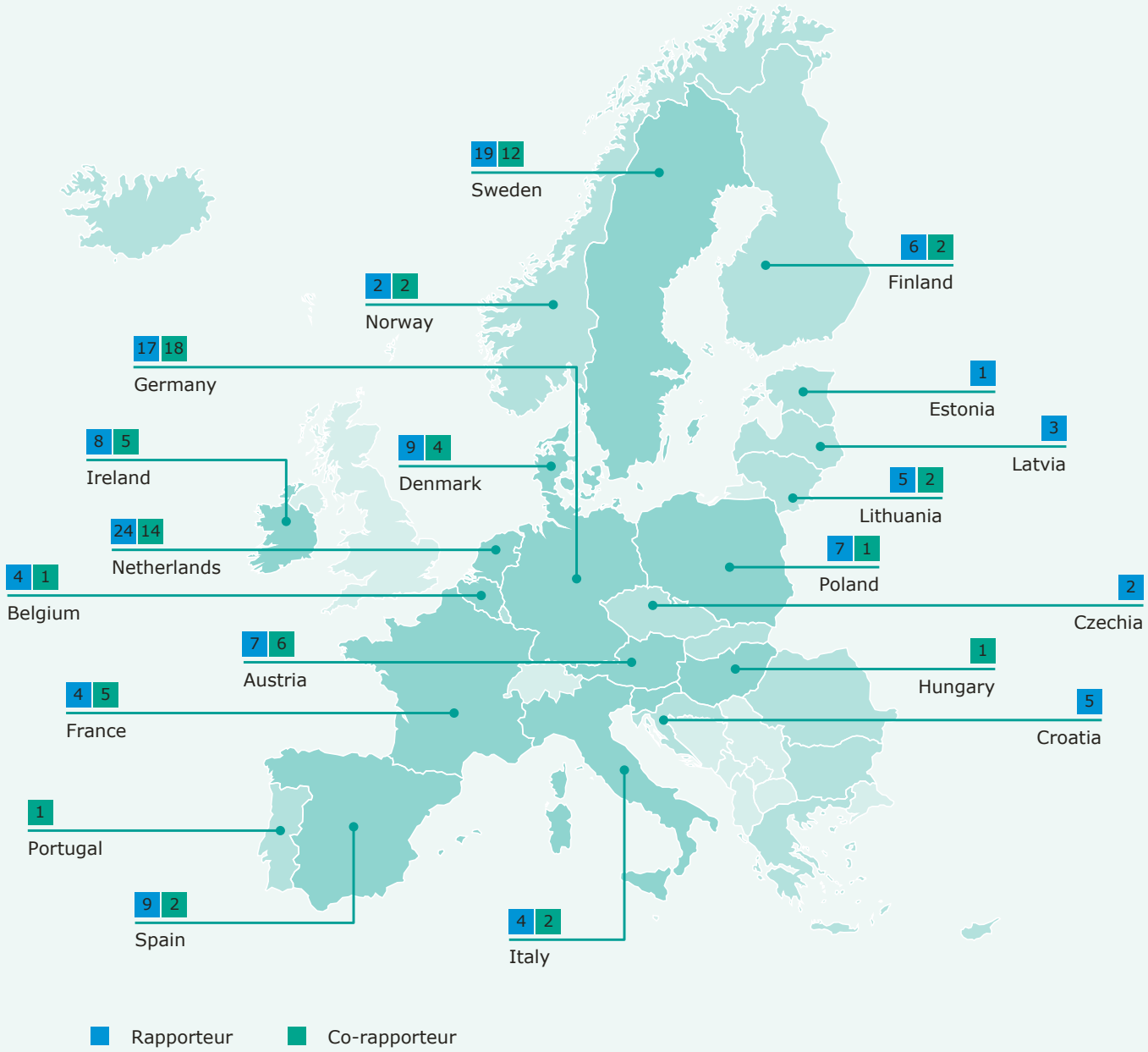
(for initial marketing autorisation applications, including generics)



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

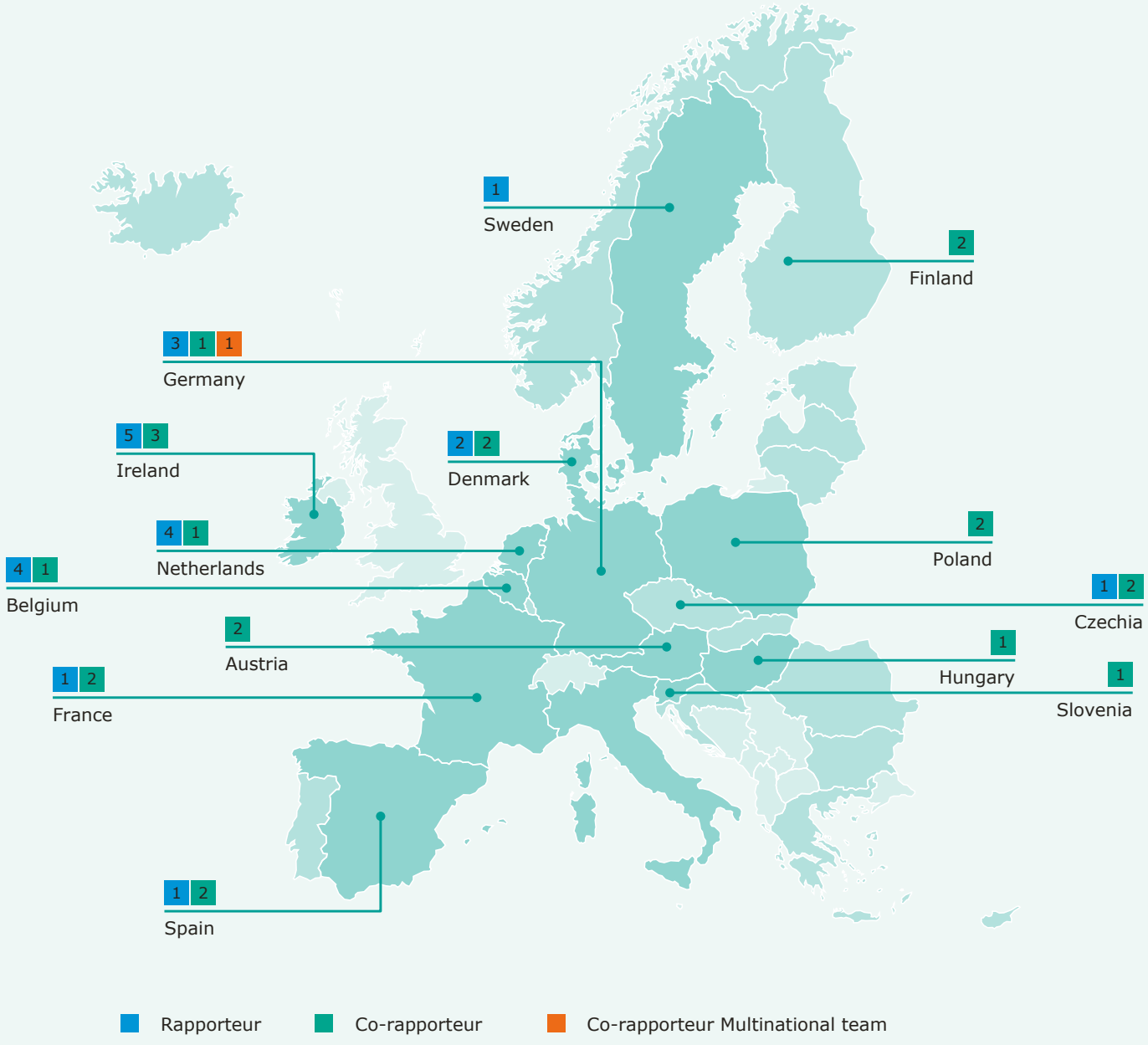
PRAC rapporteurs/co-rapporteurs appointed in 2022

PRAC rapporteurs/co-rapporteurs appointed in 2022
(for initial marketing autorisation applications)



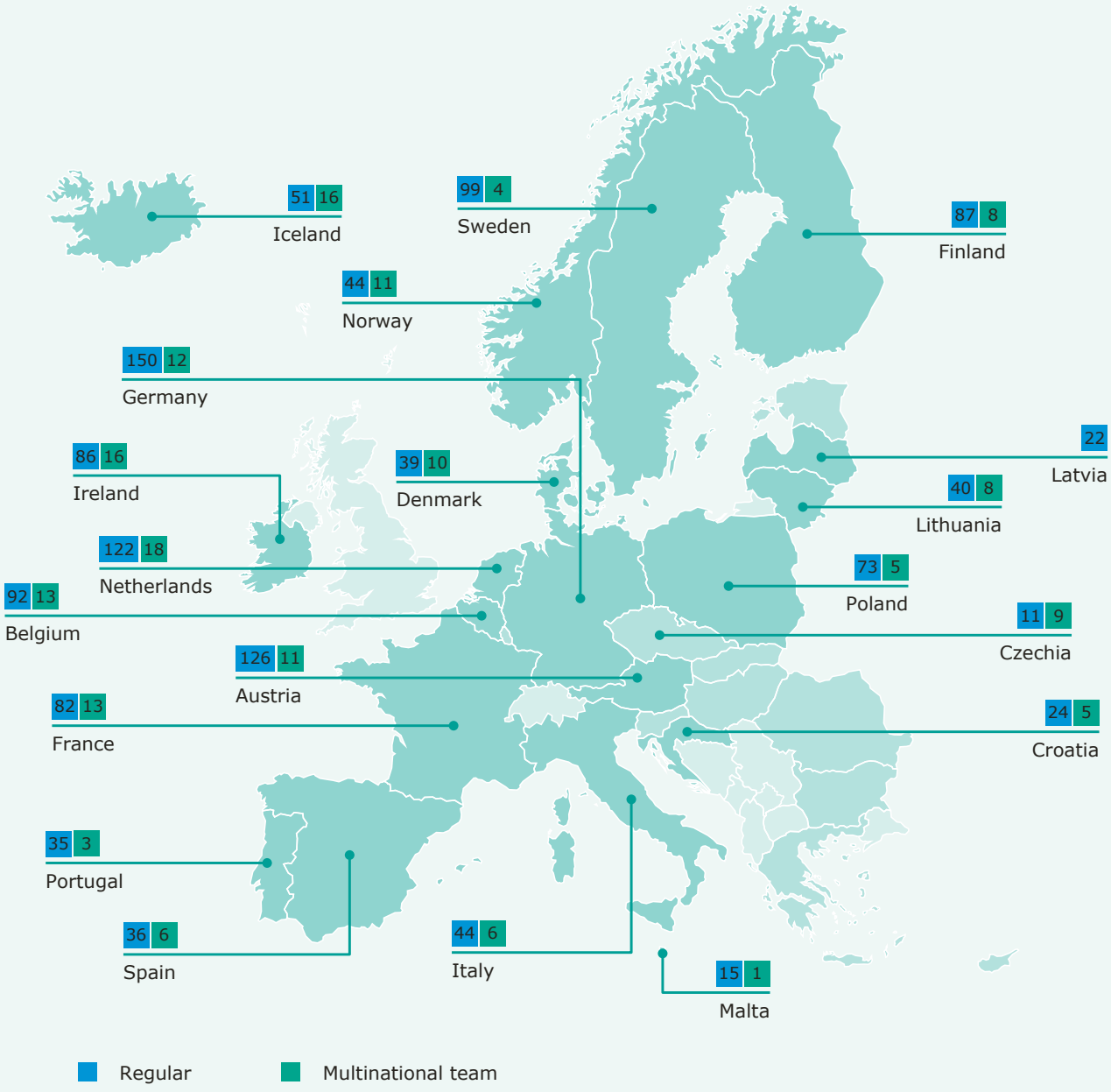
CVMP rapporteurships/co-rapporteurships

CVMP rapporteurs/co-rapporteurs appointed in 2022
(for initial marketing autorisation applications, including generics)



Scientific advice working party (SAWP)

SAWP coordinators appointed in 2022



Working parties: revised role, structure and scope

Following the initial re-organisation of the working parties, the implementation of the new operational model for the EMA Working Parties continued in 2022 with the rationalisation of the structure and operations of the expert groups. The non-clinical, methodology and clinical domains coordinated the activities of the working parties, as well as the drafting of the new three-year workplans, from 2022 to 2024. In addition, in the context of process improvement and best practice, a more streamlined working environment with collaborative tools was deployed to facilitate and optimise interactions between members of the working parties. A pilot was launched to build the first European Specialised Expert Community (ESEC). This new platform will help provide information flow to the network, training development and expertise in a specialised area and will also help gather experience to launch further ESECs in the future.

EU network training centre

The EU Network Training Centre (EU NTC) is a joint initiative of EMA and the national competent authorities. It enables the entire European medicines regulatory network (EMRN) to access and build subject matter expertise through a shared learning ecosystem covering both, human and veterinary medicines. By providing a central resource and platform for scientific and regulatory training, the EU NTC supports the quality and efficiency of operations by addressing the training needs of the EMRN and making best use of available resources. The EU NTC provides tools to drive didactic quality and foster knowledge sharing. The table below highlights its key activities from when it was established in 2015 to 2022.

	2015	2016	2017	2018	2019	2020	2021	2022
New scientific, regulatory and Network Portfolio / IT curricula developed	1	8	0	2	2	2	1	1
Number of training events advertised to the EU Network	105	140	100	60	40	46	77	76
Number of reimbursed training events to the EU Network	7	25	20 (14 by EU NTC)	8 (5 by EU NTC)	12	1	0	4
Number of NCAs that have opened their training for inclusion in EU NTC Learning Management System	6	14	8	7	10	7	15	11
Number of users registered to the EU NTC Learning Management System		2,117	3,583	4,424	5,121	5,290	5,916	6,610
Number of NCA experts registered to the EU NTC Learning Management System		1,225	2,668	3,480	4,143	4,297	4,872	5,485

INSPECTIONS AND COMPLIANCE

EMA coordinates the verification of sponsor/manufacturing compliance with the principles of good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP), good pharmacovigilance practices (GVP) 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 upon a request of 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:

- 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.

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 one focus area for EMA. The Agency is the primary contact point for notification of suspected quality defects for CAPs and coordinates their investigation, evaluation and follow-up. It also operates a sampling-and-testing programme to supervise the quality of CAPs placed on the market and to check compliance of these products with their authorised specifications.

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.

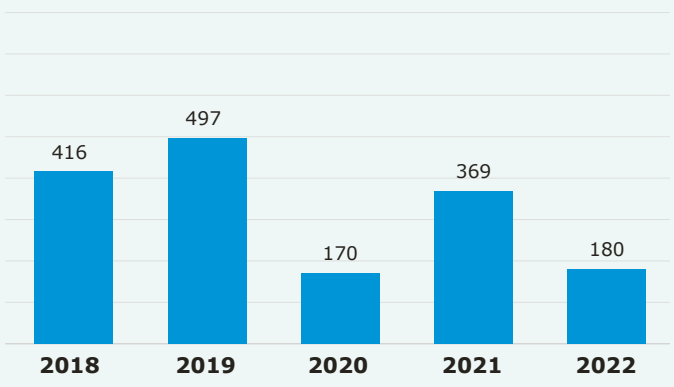
GMP inspections

The number of GMP inspection requests decreased to a similar level as in 2020.

Six GMP inspections conducted by EEA authorities led to the issuing of a non-compliance statement. Medicines manufactured at a site that is not GMP compliant cannot be sold in the EU.

EEA authorities issued one statement of GMP non-compliance relating to CAPs. When inspections lead to findings, companies must implement corrective action plans that were agreed with the inspecting authorities.

GMP inspections



GMP certificates and non-compliance statements issued by EEA authorities

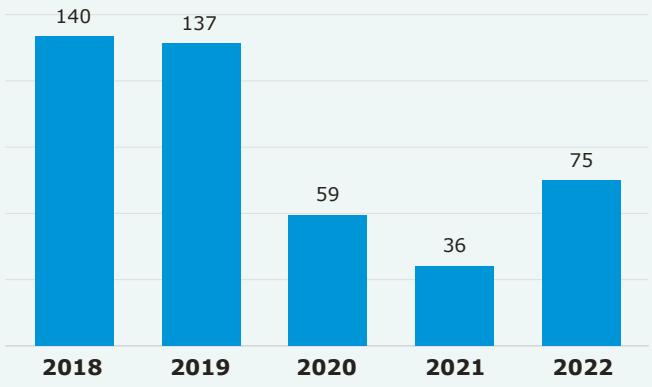
	2018		2019		2020		2021		2022	
	GMP certificate	GMP non-compliance statement	GMP certificate	GMP non-compliance statement	GMP certificate	GMP non-compliance statement	GMP certificate	GMP non-compliance statement	GMP certificate	GMP non-compliance statement
EEA/EU	2,213	6	2,235	11	1,695	1	1,825	5	1,730	2
China	66	4	51	4	11	0	24	0	15	0
India	112	5	105	1	64	0	29	0	81	2
USA	27	0	127	0	35	0	52	0	118	0
Rest of the world	84	1	108	0	38	0	52	0	187	2
Total	**2,502**	**16**	**2,626**	**16**	**1,843**	**1**	**1,982**	**5**	**2,131**	**6**

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 2018 and 2022. It includes GMP inspections requested by the CHMP or the CVMP.

GCP inspections

The number of GCP inspections increased last year, from 36 GCP inspections in 2021 to 75 in 2022 due to the easing of COVID-19 pandemic measures such as travel and safety restrictions.

GCP inspections

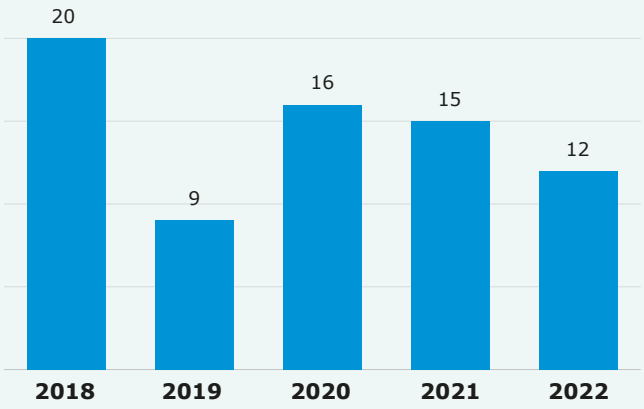


Pharmacovigilance inspections

EMA, in cooperation with competent authorities in the Member States, maintains a risk-based programme for routine pharmacovigilance inspections of marketing authorisation holders 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 2022, 12 pharmacovigilance inspections were requested by the CHMP or CVMP. Most EU/EEA pharmacovigilance inspections (over 90%) are conducted under the national pharmacovigilance inspection programmes, which relate to marketing authorisation holders with product authorisations of all types (including CAPs).

Number of pharmacovigilance inspections



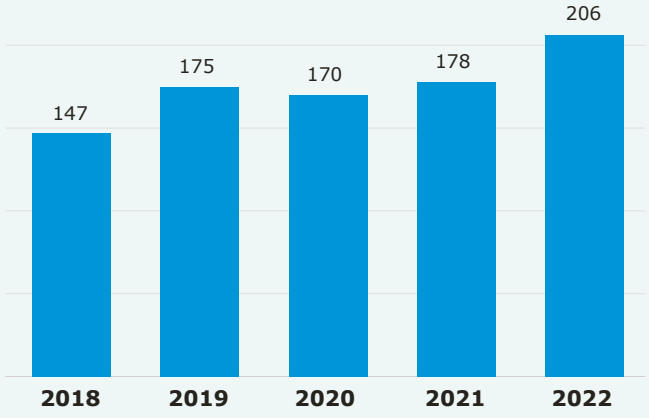
Market surveillance and quality defects

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 the prevention of their release by the manufacturer. Where a defect is considered to be a risk to public or animal health, the marketing authorisation holder is requested to withdraw the affected batches of the CAP from the EU market and the supervisory authority issues a rapid alert. The alert is split into three classes, in line with the expected risk to public or animal health posed by 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 2022, the Agency received 206 suspected quality defect notifications, the highest number in recent years. Of these, 185 cases were confirmed quality defects and led to batch recalls of 11 CAPs.

Number of quality defect notifications received



Recalls due to reported quality defects				
	2019	2020	2021	2022
Quality defects confirmed cases			164	185
Recalls	15	15	10	11
Class 1	3	3	1	2
Class 2	3	3	7	5
Class 3	9	9	2	4

The main reasons for recall of CAPs in 2022 included:

- **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 CAPs from one Member State to another by a company independent of the marketing authorisation holder is compliant with the rules.

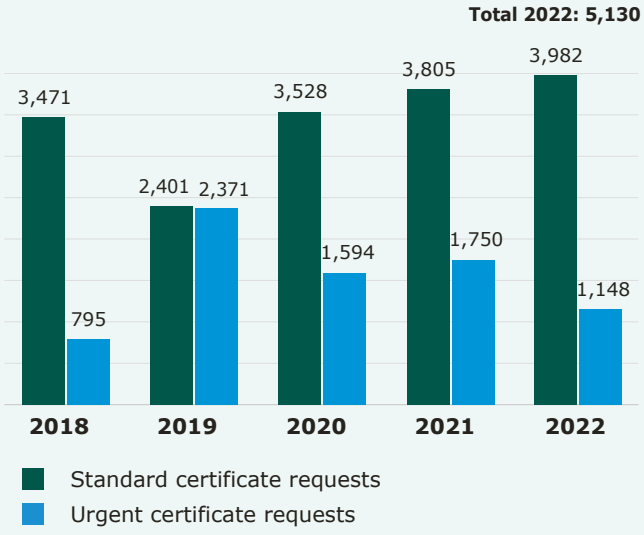
Parallel distribution notifications received

	2018	2019	2020	2021	2022
Initial notifications	2,304	2,468	3,172	2,555	1,816
Notifications of change	2,184	2,103		0	0
Notifications of bulk change	11	12	10	19	32
Annual updates	5,245	4,270	11,624	4,816	5,509
Total	**9,744**	**8,853**	**14,806**	**7,390**	**7,357**

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.

Certificates



MEDICAL DEVICES

For certain high-risk devices, EU legislation requires notified bodies to consult expert panels before issuing a CE certificate.

These high-risk medical devices include:

- Class III implantable devices and class IIb active devices that are intended to administer or remove medicinal products from the body;
- Class D in vitro diagnostic medical devices.

The expert panels can provide:

- opinions on the notified body's assessment of the manufacturer's clinical file of class III and class IIb medical devices, known as the clinical evaluation consultation procedure (CECP);
- views on the manufacturer's performance evaluation report of class D in vitro diagnostic medical devices, known as the performance evaluation consultation procedure (PECP).

CECP dossiers are first reviewed by the screening experts who decide whether or not an opinion should be provided on the clinical evaluation assessment report.

29 applications for CECP were screened in 2022. Among these, screening experts decided that an opinion was needed for seven CECPs.

In 2022, only one application for PECPs received the opinion of the expert panels.

Figures on opinions by expert panels on high-risk medical devices

	2021	2022
Number of screened applications for CECP	9	29
Number of Clinical Evaluation Consultation Procedures CECP	3	7
Number of Performance Evaluation Consultations PECP	15	1

COMMUNICATION AND STAKEHOLDERS

External communication

EMA's response to the COVID-19 pandemic and the new adapted vaccines continued to attract high interest of the media and EU citizens in 2022. Altogether, EMA responded to 1,268 press queries and organised 36 media interviews, of which about half were COVID-19 related.

EMA held 15 virtual COVID-19 press briefings, which were regularly attended by journalists working for media outlets from across the EU and beyond such as Politico, Reuters, Financial Times and Bloomberg. In the autumn, the scope of these regular press briefings was expanded to other public health emergencies, such as the mpox. The regular briefings provided to the media helped to further reduce the high number of queries and interview requests from journalists that the small team had to deal with in the previous year.

In response to a huge number of requests to help with myth-busting and fact-checking, the Agency organised a workshop for fact checkers working for major news organisations. The webinar took place in March 2022 and focused on how EMA monitors the safety of COVID-19 vaccines. Journalists were informed in-depth about EudraVigilance (the European database of suspected adverse drug reaction reports) and they also learned how to collect and interpret data from this database themselves.

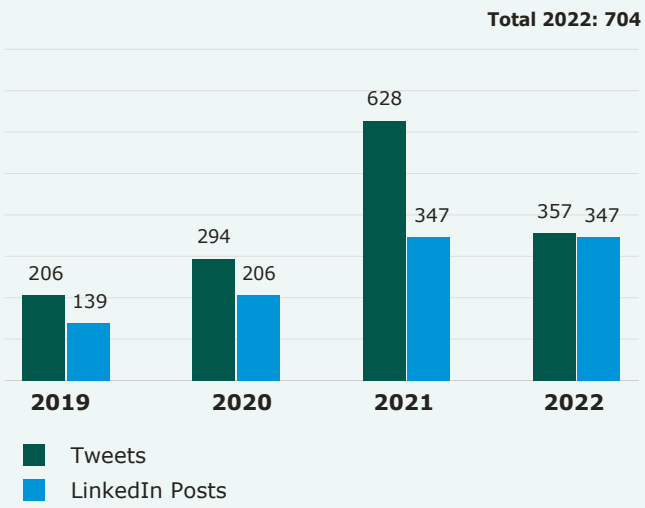
In the course of the year, EMA published 164 news announcements informing EU citizens about milestones in medicine assessment and safety monitoring and about new initiatives. Furthermore, the Agency published and updated 2,851 webpages on its corporate site.

EMA also expanded its activities on social media. By the end of 2022, the Agency had 116,859 Twitter followers, 249,729 LinkedIn followers and approximately 17,200 YouTube subscribers.

The Agency published 704 social media posts and ran several EU-wide awareness campaigns that reached hundreds of thousands of Europeans, for example on the Clinical Trials Information System (CTIS), European Antibiotic Awareness Day and World Antimicrobial Awareness Week.

EMA staff and experts published articles on scientific and regulatory topics in international journals. The list of scientific publications is available in Annex 24.

Social media posts

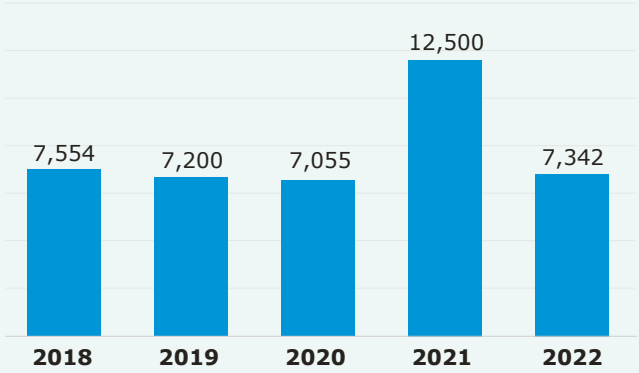


Requests for information and access to documents

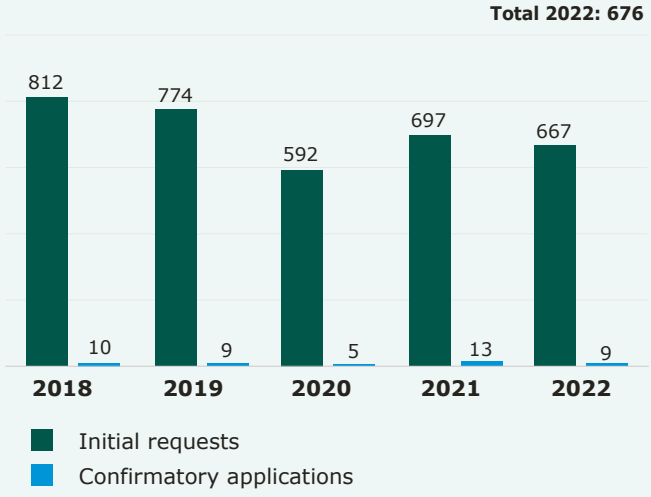
EU citizens have the right to access documents held by EU institutions, bodies, offices and agencies. EMA grants this access according to the principles and conditions defined by Regulation (EC) No 1049/2001 and the Agency's policy on access to documents.

In 2022, EMA received 676 requests for access to documents and 7,342 requests for information. Following the COVID-19-related spike in 2021, the number came down almost to pre-pandemic levels. Most of these requests were sent by the pharmaceutical industry and patients or consumers. The number of documents EMA released did not increase compared to the previous year, whereas the number of pages did.

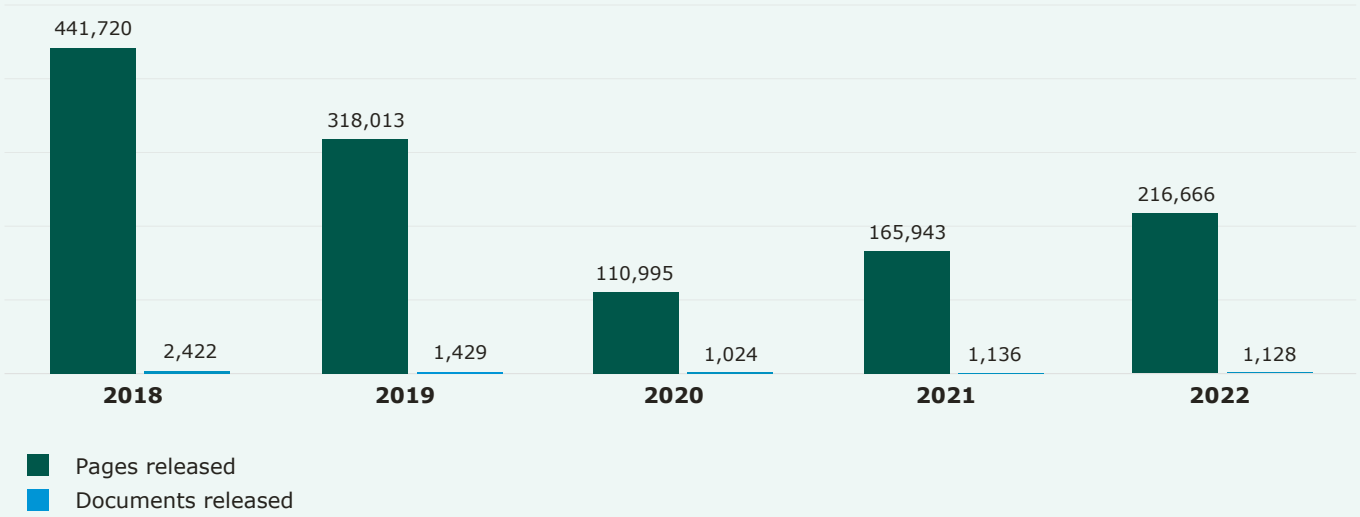
Requests for information received



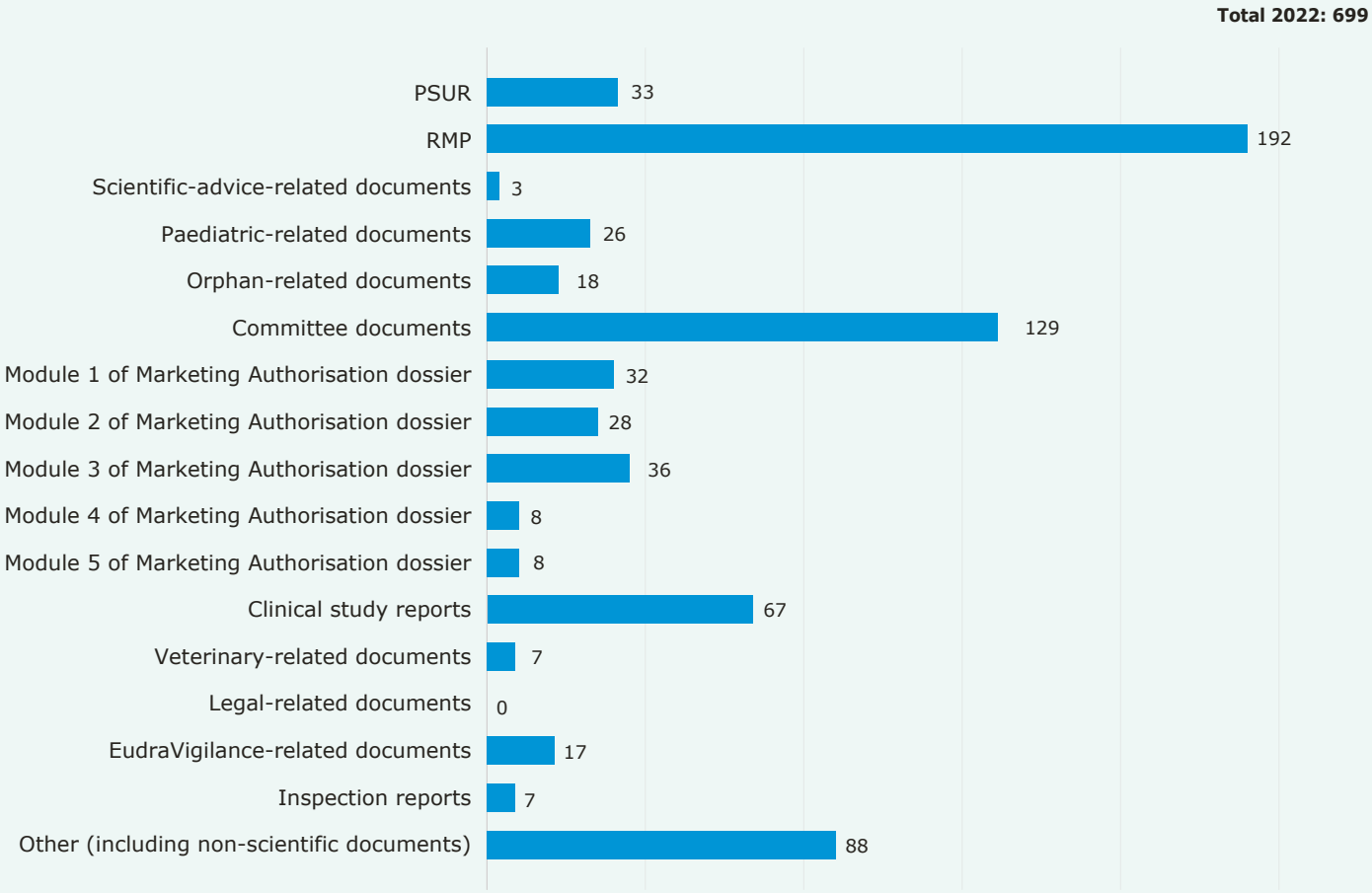
Requests received for access to documents



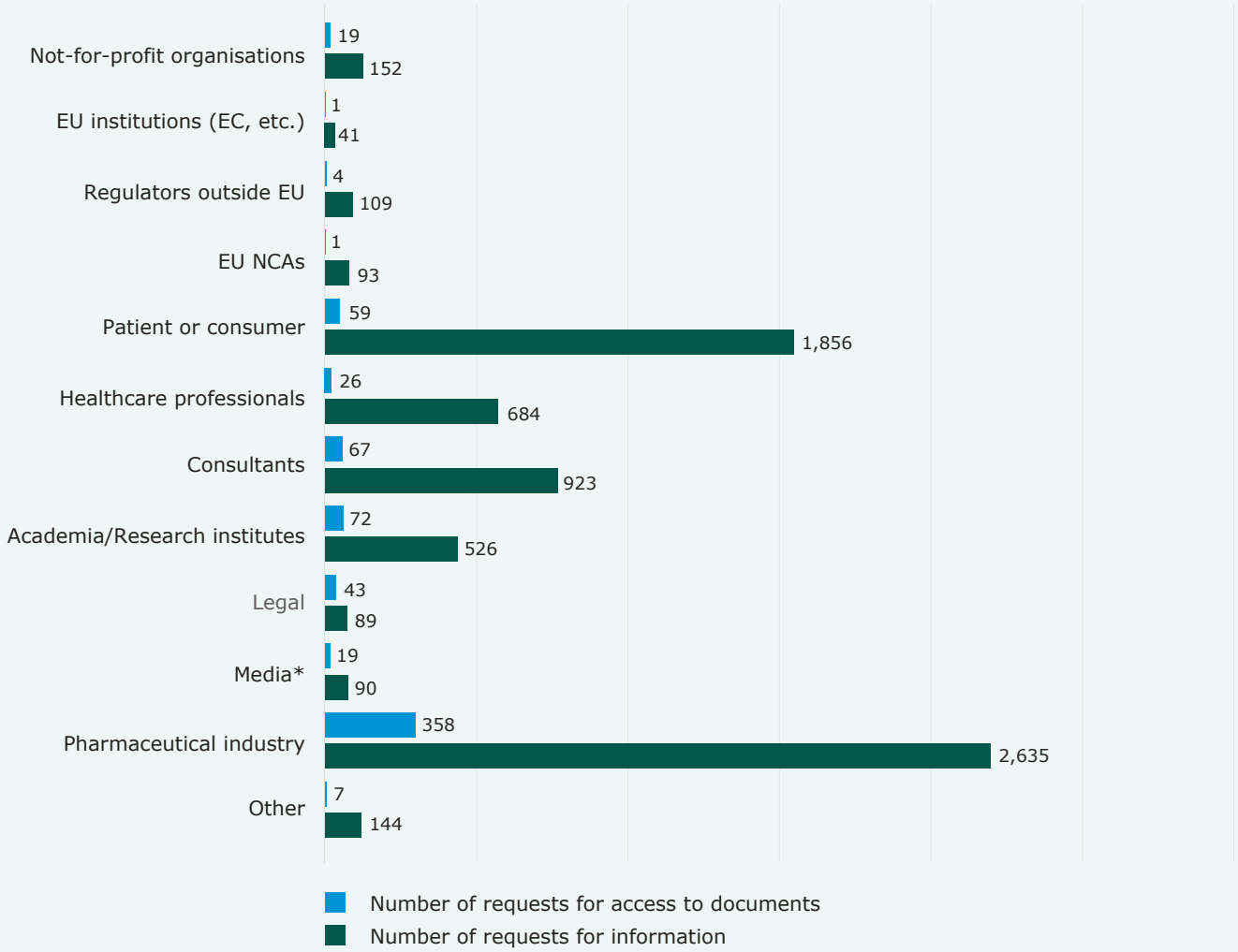
Documents and pages released following access-to-documents requests



Access to documents by type of document (2022)



Affiliation of requestors of access to documents and of information (2022)



* Requests from the media submitted via the online form do not include requests sent directly to the press email inbox.

Publication of clinical data

In 2016, EMA became the first regulatory authority in the world to give open access to clinical data that companies submit to support their marketing authorisation applications for human medicines.

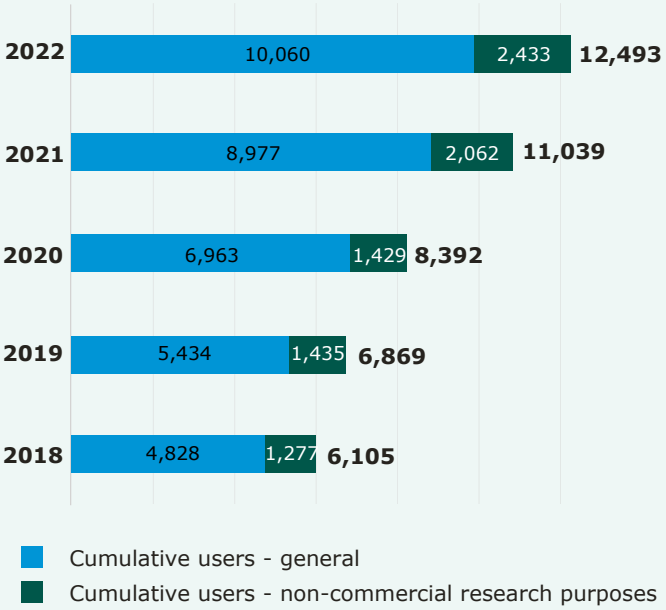
To ensure business continuity in the context of the Agency's relocation, EMA had to temporarily suspend all new activities related to clinical data publication in 2018. This was then maintained to allow EMA to respond appropriately to the COVID-19 pandemic.

However, in line with its exceptional transparency measures for COVID-19, EMA published the clinical data supporting the authorisation of COVID-19 vaccines.

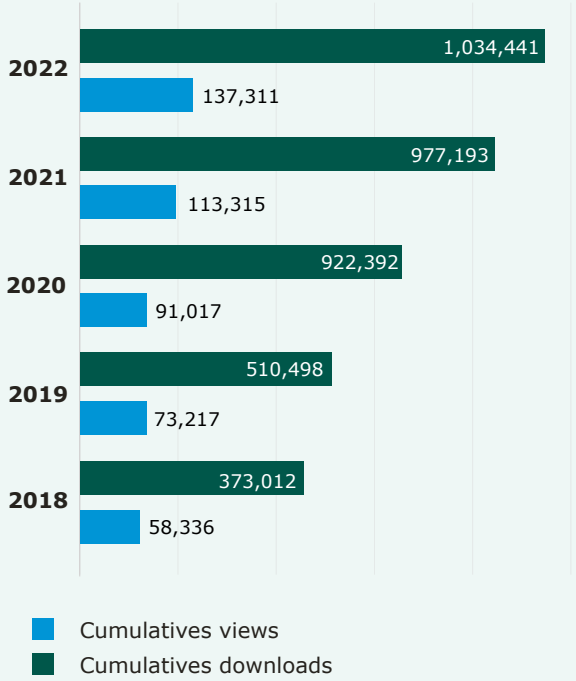
In December, EMA announced its plans for a phased restart of clinical data publication for centrally authorised medicines beyond the scope of COVID-19. EMA's efforts to proactively publish extensive (non-confidential) information on the quality, safety and efficacy of COVID-19 vaccines has been commended by the European Ombudsman.[1]

On 3 May 2022, the applicant in Case T-713/21, *Agentur für Globale Gesundheitsverantwortung v EMA* requested the discontinuance of court proceedings, which had initially been brought against EMA's decision to grant partial access to an interim clinical study report concerning a COVID-19 vaccine. The case was removed from the Register of the General Court on 8 July 2022.[2]

Clinical data website - users



Clinical data website - usage



1 In this respect, see decision of the European Ombudsman of 10 November 2021 in case 1458/2021/MIG; available at: https://www.ombudsman.europa.eu/en/decision/en/149025.

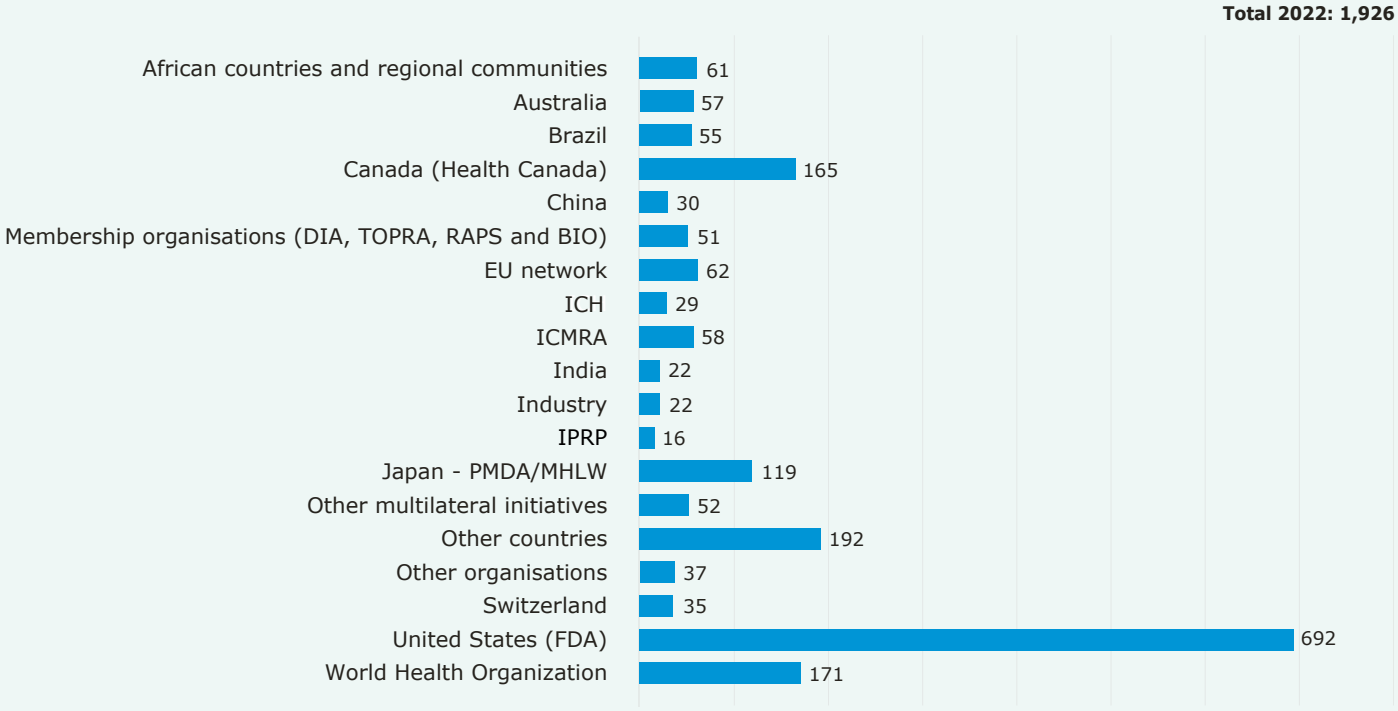
2 In this respect, see order of the General Court of 8 July 2022 in *Agentur für Globale Gesundheitsverantwortung v EMA*, T-713/21.

Interaction with international stakeholders

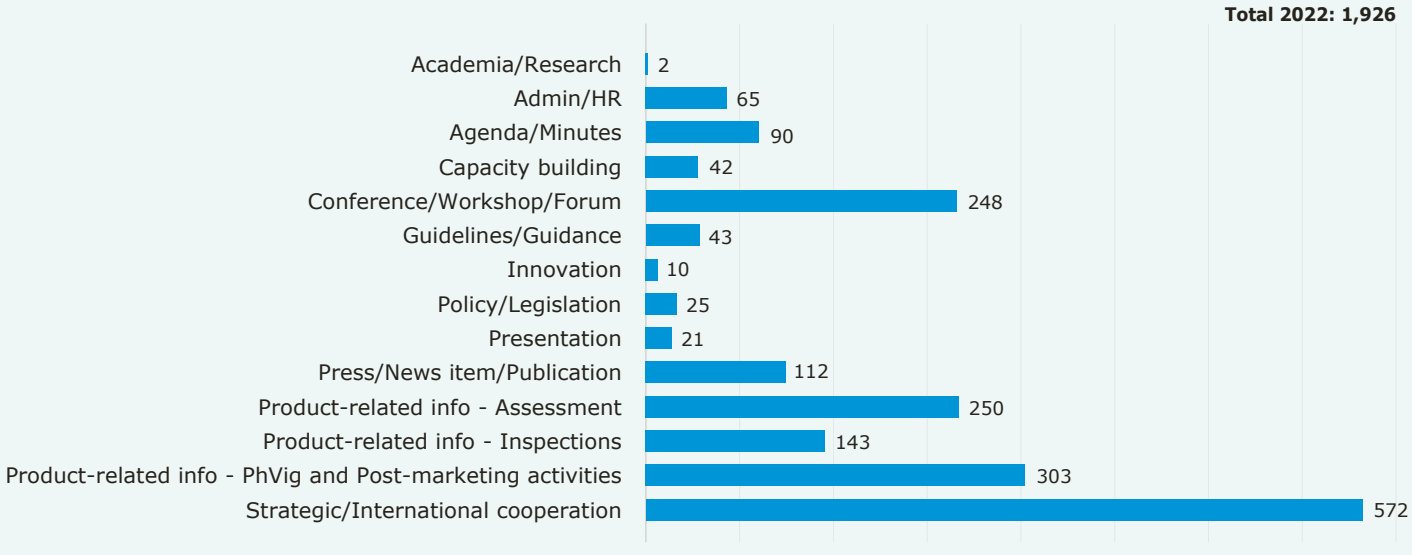
EMA has continued to strengthen its collaboration at international level to promote harmonisation of regulatory requirements, sharing of information and addressing common challenges. EMA's founding regulation gives the Agency a specific responsibility to provide technical and scientific support for the evaluation of medicines also to countries outside the EU.

In 2022, EMA engaged in 1,926 interactions with international stakeholders through its International Affairs department. The highest number of interactions took place with the Food and Drug Administration (FDA) in the United States.

Number of interactions per stakeholder (2022)



Topics of interactions with international stakeholders (2022)



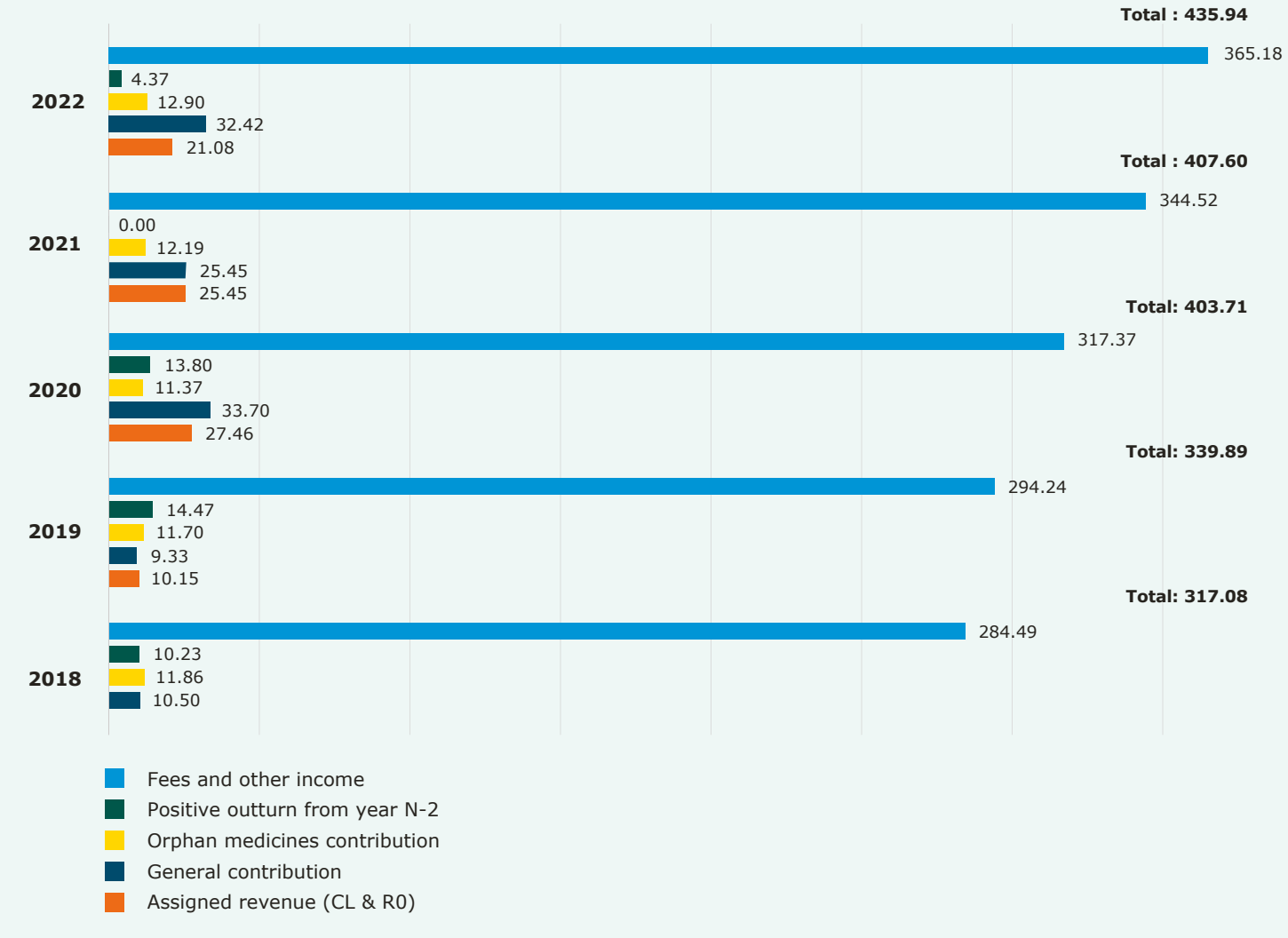
ADMINISTRATIVE ASPECTS

Budget – total revenue

The Agency's total revenue in 2022 was €435.94 million compared to €407.60 million in 2021.

In addition, the Agency operates with fund sources for assigned revenue, mainly CL for internal assigned revenue (rent and building charges received from the Agency's subtenant in London) but also for R0 for external assigned revenue. In 2022, assigned revenue (funding sources R0 and CL) amounted to €21.08 million.

Revenue (in million €)



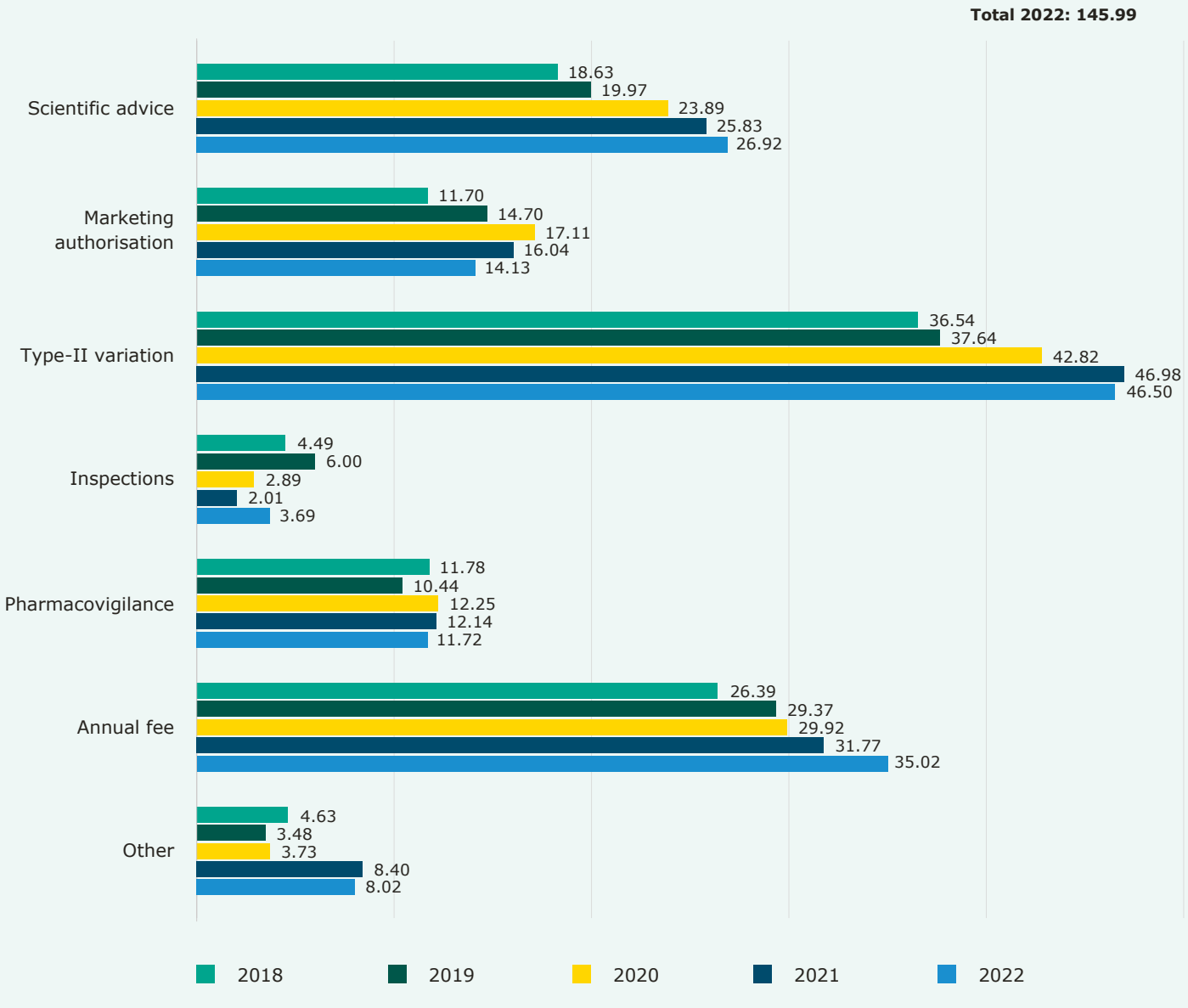
Remuneration to national competent authorities

NCAs 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 2022, EMA paid a total of €145.99 million to the NCAs, compared to €143.18 million in 2021.

This figure includes payments for pharmacovigilance procedures, including the assessment of PSURs, PASS protocols and study results, and of pharmacovigilance-related referrals.

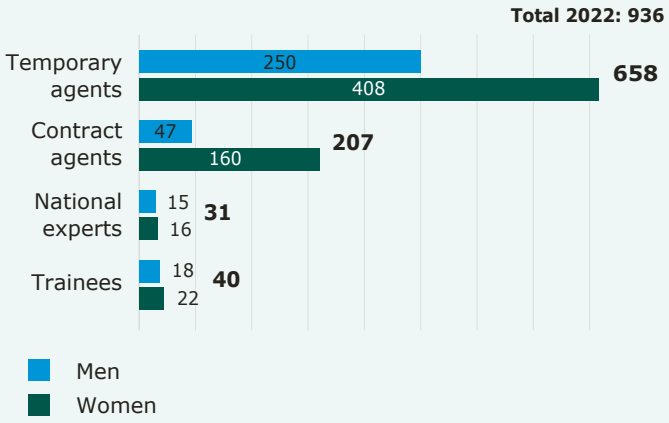
Remuneration to NCAs per fiscal year (in € millions)



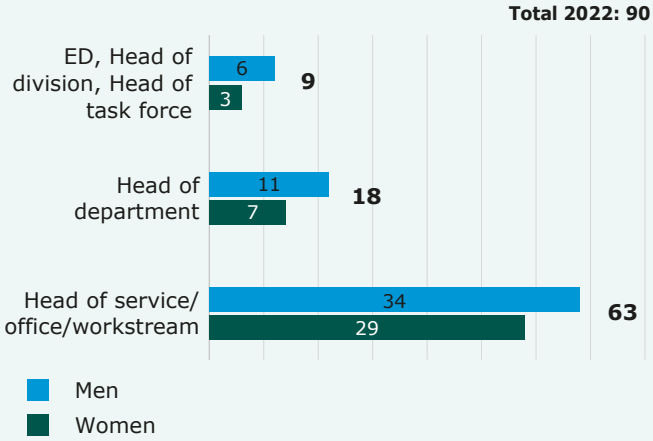
Agency staff

As of December 2022, the Agency had 936 staff members: 606 women and 330 men.

Agency staff
(as of 31 December 2022)



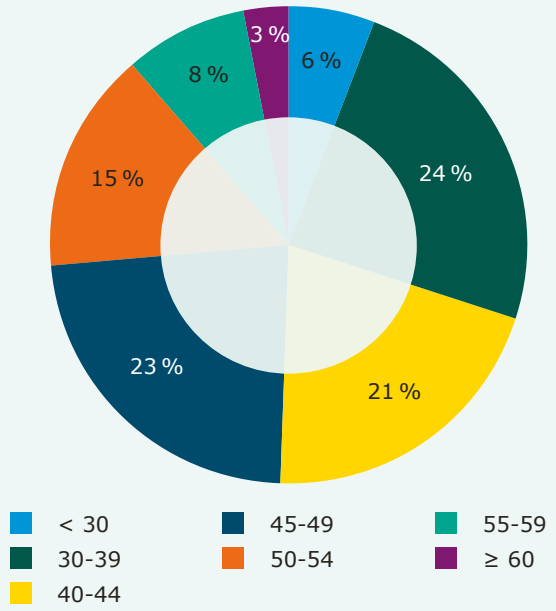
Gender balance of Agency management
(as of 31 December 2022)



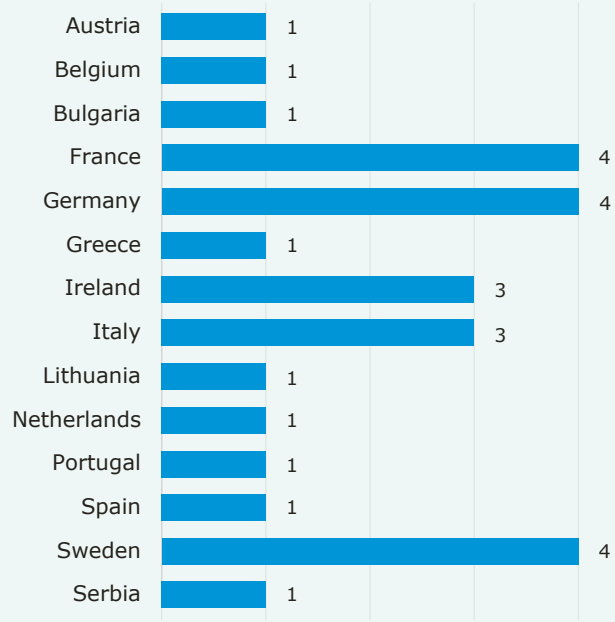
Gender balance of Agency staff in 2022

Status	Category AD (administrators)		Category AST (assistants)		TA/CA - all grades	
Temporary agents	215	211	35	197	250	408
Contract agents	28	80	19	80	47	160
Total	**243**	**291**	**54**	**277**	**297**	**568**
Total in %	**46%**	**54%**	**16%**	**84%**	**34%**	**66%**

Age-range statistics (31 December 2022)

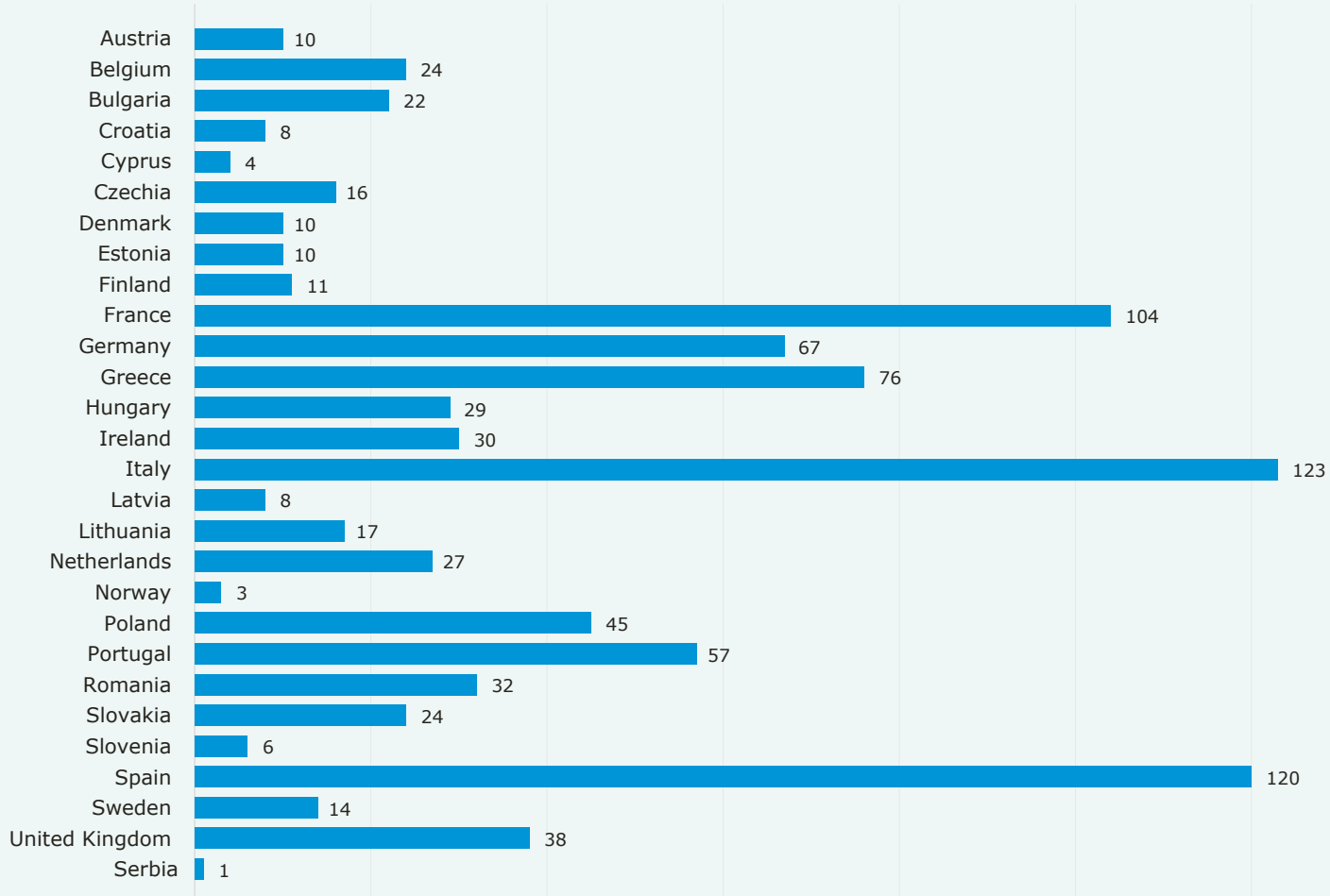


National origins of Agency management (as of 31 December 2022)



Note: Management with non-EU national origins have a second EU nationality.

National origins of Agency staff (as of 31 December 2022)



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 2022

Annex 11 – Guidelines and concept papers adopted by CHMP

Annex 12 – CVMP opinions on medicinal products for veterinary use in 2022

Annex 13 – Guidelines and concept papers adopted by CVMP in 2022

Annex 14 – COMP opinions on designation of orphan medicinal products in 2022

Annex 15 – HMPC European Union herbal monographs in 2022

Annex 16 – PDCO opinions and EMEA decisions on paediatric investigation plans and waivers in 2022

Annex 17 – Referral procedures overview 2022 – human medicines

Annex 18 – Arbitrations and referrals in 2022 – veterinary medicines

Annex 19 – Budget summaries 2021-2022

Annex 20 – European Medicines Agency establishment plan

Annex 21 – Litigation activities of EMA in 2022

Annex 22 – Access to documents requests

Annex 23 – Clinical Data Publication

Annex 24 – Publications by Agency staff members and experts in 2022

The annexes are available on EMA's website.

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