EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

01 June 2022
EMA/75685/2022
Executive Director

Annual activity report 2021

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Introduction

The consolidated annual activity report provides an overview of the activities and achievements of the European Medicines Agency (EMA) in 2021. The EMA annual activity report 2021 is a report of the EMA Executive Director. It is a key component of the strategic planning and programming cycle and the basis upon which the EMA Executive Director takes their responsibility for the management of resources, and the achievement of objectives. It also allows the EMA Executive Director to decide on the necessary measures in addressing any potential management and control weaknesses identified.

The annual activity report 2021 comprises five main parts and annexes, as follows:

Part I: Key achievements in 2021. This section provides information on achievements of objectives and performance indicators set in the EMA annual work programme. This section mirrors the structure of the annual work programme of EMA for the year 2021 and provides information on achievements of objectives set in the annual work programme. This section also includes references to key performance indicators (KPIs) and targets.

Part II: Management. This section provides an overview of the Agency's major achievements and includes information on EMA governance; information on budgetary, financial and human resources management; assessment of audit results during 2021; as well as the follow-up on recommendations and action plans resulting from audits. It also includes components of the follow-up on observations from the Discharge Authority.

Part III: Assessment of the effectiveness of the internal control systems. This section includes the assessment of the effectiveness of the internal control systems and their components.

Part IV: Management assurance. This section describes the building blocks of assurance and the materiality criteria on the basis of which the Authorising Officer by Delegation determines whether significant weaknesses should be subject to a formal reservation. Any reservations are also detailed in this section.

Part V: Declaration of assurance. The report concludes with a declaration of assurance, in which the EMA Executive Director, in her role as the authorising officer, takes responsibility for the legality and regularity of all financial transactions.

In the *annexes*, the report provides information on the EMA establishment plan, human and financial resources used by activity, the organisational chart, project implementation, and further specific annexes related to Part II and Part III of the report.

The EMA annual activity report is a public document and is available on the EMA corporate website.

Management Board’s assessment report

The Management Board,

having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004,

having regard to the Financial Regulation applicable to the budget of the European Medicines Agency ('the Agency') and in particular Article 48 thereof,

having regard to the 2021 work programme of the Agency, adopted by the Management Board at its meeting in December 2020,

having regard to the annual report 2021 of the Agency adopted by the Management Board on 16 March 2022,

having regard to the annual activity report 2021 of the Agency presented to the Management Board at its meeting of 15 June 2022,

1. Recognises that 2021 has been another extremely challenging year marked by the COVID-19 and the emergence of different virus variants. The Agency, yet, demonstrated great resilience and determination to ensure a high level of activities while successfully supporting global efforts to combat the pandemic.
2. Praises the Agency and the EMRN for the outstanding service provided to the European citizens during an unprecedented public health crisis; appreciates their remarkable efforts for the protection of animal health.
3. Acknowledges the results presented in the annual activity report 2021 and recognises that the Agency, after successfully adjusting to the new working environment (e.g., remote meetings and teleworking patterns), continued to fulfil its mission to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health.
4. Is pleased of the alignment of the Agency's work with the European policy agenda, and the European Pharmaceutical strategy.
5. Welcomes the final adoption by the EU institutions of the legislative proposal to extend the Agency’s mandate to facilitate a coordinated EU-level response to future crises.

COVID-19 PANDEMIC

6. Is pleased with the cooperation between the Agency and the national competent authorities (NCAs) to tackle the pandemic and protect the health of EU citizens. Particularly, praises the information transfer made through the celebration of periodic meetings of the EMRN.
7. Commends the achievements by the Agency, its staff, scientific committees’ members and experts in dealing with the COVID-19 pandemic with minimal impact on output and productivity. Praises that health and safety of staff was constantly addressed as a priority throughout the year.
8. Acknowledges EMA and the European medicines regulatory network (EMRN) introduction of a variety of measures and regulatory flexibilities as part of its response to the COVID-19 crisis. Is pleased with the lessons-learned exercise initiated in 2021, from which several elements for further improvement are expected to emerge.

9. Acknowledges the intensification of EMA communication, media monitoring and social listening activities to scrutinise public queries and closely collaborated with other EU entities and international public health bodies to identify harmful health advice and address concerns in a timely manner. Is pleased with the frequent updates on EMA's website for the general public, regular press briefings and media interviews, as well as frequent social media posts provided the public with factual, and up-to-date information about COVID-19 related activities.

10. Praises the Agency's resilience and responsiveness in managing the activities addressing the COVID-19 pandemic and mitigating its impact on the supply of medicines, also through supporting the increase of the manufacturing capacity for COVID-19 vaccines.

11. Acknowledges the efforts made by CHMP which led, during 2021, to granting a conditional marketing authorisation for 4 vaccines and 5 therapeutics (including 2 extensions of indication) to prevent and treat the SARS-CoV-2 infection.

12. Congratulates the EU Executive Steering Group on shortages of medicines caused by major events for the work done to prevent and mitigate supply disruptions within the EU during the pandemic; looks forward to the formalisation of its structure into the Medicines Shortages Steering Group as part of the EU Regulation 2022/123.

13. Praises the effort of the EMA Emergency Task Force (ETF) for its contribution to the accelerated evaluation of vaccines and therapeutics for the prevention and treatment of SARS-CoV-2 infection.

14. Recognises the exceptional measures implemented by the Agency to maximise the transparency of its regulatory activities regarding vaccines and medicines for COVID-19 during evaluation and after approval.

ACTIVITIES

15. Notes the work on marketing authorisations via the centralised procedure, both in human and veterinary medicines, which resulted, in 2021, in EMA recommending for marketing authorisation 92 new human medicines, including 54 new active substances, and 12 new veterinary medicines, including 7 new active substances.

16. Acknowledges the work done by the EU network and, in particular, by the EU Executive Steering Group on Shortages of Medicines Caused by Major Events, in monitoring ongoing or anticipated shortages for COVID-19 related and non-COVID-19 related human and veterinary medicines.

17. Appreciates the extended cooperation with the institutions of the European Union. Praises the work done with the European Commission and ECDC on vaccines and, in particular, through the Joint Advisory Board for the coordination of independent post-authorisation studies on COVID-19 vaccines.

18. Is pleased with the Agency's contribution to the Pharmaceutical Strategy for Europe and to the initiatives of the EU Beating Cancer Plan. Acknowledges EMA contribution to foster wider patient access to innovative medicines via its collaboration with the European Network for Health Technology Assessment.

19. Commends the Agency for continuing to ensure EU standards in medicine development and manufacturing, in particular, by establishing the Nitrosamine Implementation Oversight Group (NIOG) to oversee the implementation of the CHMP's Article 5(3) opinion on nitrosamines in human medicines.

20. Recognises the work undertaken by the Agency to unlock the potential of big data for medicines regulation in the EU, and is pleased with the update of the HMA-EMA joint Big Data Steering Group multiannual workplan, which includes eleven priority recommendations of the HMA-EMA Joint Big Data Task Force.

21. Applauds the significant steps forward made in 2021 for the establishment of the Data Analysis and Real World Interrogation Network (DARWIN EU), which will be a pivotal tool for EMA and NCAs to exploit real-world evidence from across Europe on diseases, populations and the uses and performance of medicines.

22. Acknowledges the Agency's work and initiatives carried out with its EU and international partners to address the global public health problem of antimicrobial resistance; congratulates CVMP for the adoption of a strategy on antimicrobials for 2021-2025; acknowledges the publication of the third JIACRA report, as well as the report of the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC).

23. Recognises the activities carried out to implement the EU-UK Trade and Cooperation Agreement and its IE/NI Protocol.

INFORMATION MANAGEMENT

24. Appreciates the Agency's communication and response relative to the cyber-attack against EMA of 1 December 2020 and the initiative to strengthen its cybersecurity capabilities to protect its IT systems from future attacks.

25. Is pleased with the review of the EMA's Information Management governance model and appreciates the adoption of the agile way of working and the implementation of the Scaled Agile Framework (SAFe).

26. Applauds the achievement of the milestones enabling the go-live of the Veterinary Union Product and Pharmacovigilance Database, as well as the Union Manufacturers and Wholesale Distributors Database, planned for January 2022.

27. Commends the notable progresses made towards a fully functional Clinical Trial Information System (CTIS) and is pleased that the system will finally go live in January 2022. Welcomes the Accelerating Clinical Trials in the EU (ACT EU) initiative, which aims to further develop the EU as a focal point for clinical research and to better integrate clinical research in the European health system.

LEGISLATION

28. Congratulates the Agency for the completed preparations for the implementation of the Veterinary Medicinal Products Regulation (Regulation (EU) 2019/6), the Clinical Trial Regulation, EU-DPR, and the Medical Devices Regulation.

29. Praises EMA for the preparations for the implementation of the EC legal proposal for a reinforced role for the Agency in crisis preparedness and management for medicinal products and medical devices.

FINANCES AND HUMAN RESOURCES

30. Is pleased that the European Parliament has granted, on 4 May 2022, the discharge regarding the implementation of the budget of the Agency for the financial year 2020.

31. Notes that the Agency's final budget for 2021 amounted to EUR 379,288,000; 89.40% derived from the evaluation of medicines and other business-related activities, 9.85% from the European Union budget to fund various public health and harmonisation activities, and 0.75% from various sources.

32. Notes the draft financial outturn, a surplus of approx. EUR 24.98 million, representing 6.13% of total revenue, was caused partly by higher-than-budgeted fee-related income being collected at the end of the year, exchange rate gains, and unused and cancelled expenditure appropriations mainly driven by the volatile pandemic context.

33. Notes the 2021 provisional accounts and looks forward to giving an opinion on the EMA 2021 final accounts, following the receipt of the European Court of Auditors' observations on the provisional accounts.

34. Acknowledges the efforts to address the situation of EMA's previous premises in London, while safeguarding the Agency's financial interests. Is still deeply concerned with the Agency being forced to act as a landlord for a property in a third country, and the ensuing financial, operational, and reputational risks and implications.

35. Acknowledges that the Agency managed to reach 98% occupancy rate for temporary agents, and notes that during 2021 the total number of staff joining EMA amounted to 284, while the total number of staff leaving the Agency during the same year amounted to 116.

AUDITS AND INTERNAL CONTROLS

36. Notes the results of the audit of the European Court of Auditors, confirming the reliability of the 2020 accounts and the legality and regularity of the transaction underlying the accounts of the Agency.

37. Notes that the report of the ECA draws attention to the uncertainty with the lease agreement for the Agency´s previous premises in London and includes two observations on the legality and regularity of transactions.

38. Notes that the report of the ECA includes a follow-up of eight previous years´ observations, of which two have been completed, two are ongoing, and four are outstanding, one of which is not under the Agency´s control.

39. Is satisfied that no recommendations stemming from audits carried out by the Internal Audit Service of the Commission were open as of 31 December 2021.

40. Notes the result of the activities carried out by the Agency's internal audit capability, where no critical recommendations where open, and 22 very important recommendations remained under implementation as of 31 December 2021 (one from 2019 audits, 10 from 2020 audits and 11 from 2021 audits).

41. Is pleased that the Internal Control system functions reasonably well, even though some of its principles could be adjusted or improved to enhance its overall efficiency and effectiveness.

42. Notes with satisfaction that the ex-post controls carried out highlighted no significant weaknesses of the processes analysed; that only two areas with potential for improvement were identified (Staff members' declaration of interests and publication of documents prior and post committee meetings) and that these are being addressed by specific improvement action plans.

DECLARATION OF ASSURANCE

43. Takes note of the declaration of assurance of the Executive Director and acknowledges that no reservations were made.

44. Reiterates the concerns regarding the adequacy of the EU network's staffing levels in light of the continuously increasing workload, the significant responsibilities assigned to the EMRN over the last years, including those deriving from the new EMA mandate, the Clinical Trial Regulation, the implementation of the Veterinary Medicinal Products regulation, the General Data Protection Regulation, the medical device regulation, the ACT EU initiative, and the expected digital transformation.

45. Calls for an EU action at a political level to resolve the current unsustainable situation with the EMA premises in London, which forces the Agency to act as a landlord, diverting resources to perform an activity outside of its legal mandate.

46. Thanks again the scientific committees' members, experts, and patient representatives, as well as all EMRN staff for their exceptional commitment and dedication during the COVID-19 pandemic and appreciates the good collaboration in the network.

Amsterdam, 16 June 2022

Lorraine Nolan
Management Board Chair
[signature on file]

Executive summary

European Medicines Agency in brief

The European Medicines Agency is a decentralised agency of the European Union (EU), created in 1995. The mission of EMA is to protect human and animal health in the EU, and to ensure access to medicines that are safe, effective and of good quality. It is the sole EU body responsible for the scientific assessment of medicines for human use, with respect to the authorisation, maintenance, and supervision, for treatment of cancer, diabetes, neuro-degenerative dysfunctions, viral diseases, acquired immune deficiency syndrome, and auto-immune diseases and other immune dysfunctions and rare human diseases ('orphan' medicines). Medicines derived from biotechnology processes (such as genetic engineering), as well as advanced-therapy medicines (such as gene-therapy, somatic cell-therapy, or tissue-engineered medicines) must also be submitted for assessment to EMA on behalf of the EU. For veterinary medicines, innovative and technologically advanced products, in particular those derived from biotechnology, must also be assessed by the Agency. To achieve this, EMA provides a single route for the evaluation of innovative medicines in the EU, thus avoiding the duplication of the evaluation in each of the Member States. This allows making highly needed medicines available to all EU citizens and within the shortest possible timeframe, whilst guaranteeing a robust scientific assessment process.

In addition, EMA monitors the safety of all medicines authorised in the EU throughout their lifecycle and provides for regulatory action (such as restricting a medicine's use or withdrawing a medicine from the EU market) within the shortest possible timeframe, where public or animal health is endangered. Information to patients and healthcare professionals is simultaneously made available in all EU languages, ensuring that consistent information on medicines is provided to all EU citizens. To achieve its tasks, EMA brings together the best scientific expertise on medicines from across the EU. This translates into 7 scientific committees which evaluate medicines along their lifecycle, from early stages of development, through marketing authorisation, to safety monitoring once they are on the market. These scientific committees are supported by working parties and scientific advisory groups and can draw from a network of over 4000 scientific experts, made available by the Member States to the Agency.

EMA is also involved in other public health activities, such as in stimulating research and innovation in the pharmaceutical sector. It facilitates medicines development by giving scientific advice and guidance to developers of medicines, including on the development of medicines for children or medicines to treat rare diseases. On behalf of the EU, EMA coordinates inspections to verify compliance with the principles of good manufacturing, clinical, pharmacovigilance and laboratory practices.

EMA is responsible for the provision of data and information technology (IT) services to implement European pharmaceutical policy and legislation. These services are provided to the EU regulatory network, comprising national competent authorities (medicines regulatory authorities in Member States), the European Commission, and EMA. In this context, EMA delivers, maintains, and provides data services, IT systems and infrastructure to Member States.

On behalf of the EU, EMA hosts several databases important for public health, such as EudraVigilance — one of the largest databases in the world of adverse reactions reported for all medicines authorised in the EU. In addition, EMA plays a key role in tackling public health threats, such as antimicrobial resistance, and public health emergencies. Over the past years, EMA has also become a recognised pioneer in terms of transparency and openness of operation, and in terms of interaction with patients.

Since its creation in 1995, the environment in which EMA operates has undergone major changes. As a result of the Agency's achievements over the years, EMA's responsibilities have continuously increased,

resulting not only in a well-established and mature agency, but also an agency that covers a wide range of activities in the regulation of human and veterinary medicines.

The success of EMA is based on the EU regulatory system for medicines. At the heart of it is a network of around 50 medicines regulatory authorities from the European Economic Area (EEA) Member States, the European Commission, and EMA. National competent authorities (NCA) work closely with EMA, providing scientific expertise to EMA committees, working parties and expert groups for: assessing centralised products; supporting innovation, including centralised scientific advice; working on orphan and paediatric medicines; and EU-wide safety procedures. This network is what makes the EU regulatory system unique. The diversity of the experts from across Europe, involved in the regulation of medicines in the EU, encourages the exchange of knowledge, ideas, and best practices between scientists striving for the highest standards for medicines regulation.

Based on the 'lessons learned' package (Building a European Health Union: Reinforcing the EU's resilience for cross-border health threats), the European Commission proposed for 2021 a revision of EMA's legal mandate, with the aim of extending the remit of the Agency's activities by formalising and strengthening the Agency's crisis-coordination role. The legislative process concluded in January 2022, with the adoption of the final legal text by the European Parliament and the European Council.

2021 in brief

In 2021, the Agency continued to focus on the assessment of vaccines and therapeutics for COVID-19 and on the evaluation of the quality, safety, and efficacy of these products. Moreover, following the EC proposal to extend the EMA mandate in the remit of crisis preparedness activities and medical devices, in 2021 EMA carried out an impact assessment of the proposal. Key achievements are detailed in section 1 below, whereas major developments are reported in section 2.2. The full set of key quantitative data of the reporting year can be found in section 1 and section 2.

Key conclusions

Although 2021 was another challenging year, EMA continued to successfully fulfil its mission to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health. The Agency supported the EU response to the global pandemic, by assessing in a timely manner vaccines and therapeutics for the prevention and treatment of infections from SARS-CoV-2 virus.

The EMA budget for 2021 has been fully implemented, with a surplus of €25M, which will be returned to the European Commission. The Agency's strong financial position and a satisfactory cashflow is denoted by its net assets (€209 millions).

Based on all the facts presented in the report, including the management of the control system and the positive opinion expressed by the Court of Auditors on the accounts, the Agency can conclude that the systems in place provide reasonable assurance that the resources under the responsibility of the Executive Director were used for their intended purposes and in accordance with the principles of sound financial management. It has to be noted, however, that under-resourcing at the Agency continues to pose a challenge in delivery of its legal mandate. Moreover, the uncertainty linked to the management of the lease agreement for EMA's previous premises in London, an activity outside of the remit of the organisation, places additional pressure on the Agency.

1. Achievements of the year

2021 at a glance

HUMAN MEDICINES

In 2021, EMA recommended 92 medicines for **marketing authorisation**[1]. Of these, 54 had a new active substance which had never been authorised in the European Union before. The Agency also recommended 89 **extensions of indication** of medicines already authorised for marketing in the EU, offering new treatment opportunities for patients.

During 2021, three medicines received a recommendation for marketing authorisation following an **accelerated assessment** (this mechanism is reserved for medicines that are able to address unmet medical needs, allowing for faster assessment of eligible medicines by EMA's scientific committees); 13 medicines received a recommendation for a **conditional marketing authorisation**, one of the possibilities in the EU to give patients early access to new medicines - and this was particularly important in the response to a public health emergency, such as that currently being experienced with COVID-19; four medicines 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.

In the context of the **PRIME scheme**, which aims to help patients benefit as early as possible from promising medicines that target an unmet medical need, six PRIME-designated medicines were recommended for approval. In addition, the Agency confirmed 19 **orphan-status designations** under the EU framework for orphan medicines, the purpose of which is to encourage the development and marketing of medicines for patients with rare diseases.

COVID-19

The COVID-19 pandemic continued to be the number one priority for EMA and the European medicines regulatory network in 2021. EMA recommended **four more vaccines** for approval in 2021 that formed the basis of the largest mass vaccination campaign ever seen in the EU. EMA also recommended **five new COVID-19 treatments** that brought much needed therapy options for people who had contracted the virus.

The network's operation under these circumstances relied on the existing health threats preparedness plan, the mobilisation of experts from the COVID-19 EMA pandemic Task Force (COVID-ETF), and the close collaboration with international regulators and ECDC. The **quick mechanism for scientific advice** on the development and evaluation of COVID-19 medicines for marketing authorisation and accelerated agreement of **paediatric development plans**, both activated in 2020, continued to be deployed successfully throughout 2021.

This also required intensive safety monitoring to enable quick action where needed, in line with EMA's practices for **EU safety monitoring and risk management system,** to ensure detection of any potential new risks. EMA continues to conduct rigorous scientific assessments of all safety data. Despite the unparalleled extent of the vaccination campaigns and the related large volume of safety information on vaccines, EMA analysed and built safety recommendations, strengthening the EU pharmacovigilance system. An **increased level of transparency** was maintained with monthly updates issued for every authorised COVID-19 vaccine. Safety updates allowed regulators to swiftly assess data emerging from a range of different sources, and take appropriate regulatory action to protect public health.

[1] The full overview of the 2021 human medicines highlights is available here https://www.ema.europa.eu/en/news/human-medicines-highlights-2021

The Agency also worked to help **increase manufacturing capacity** for COVID-19 vaccines. The number of approved manufacturing sites increased from 19 to 52 by the end of 2021, leading to a significant increase in vaccine supply, both in the EU and globally.

EMA and the European medicines regulatory network introduced a variety of measures and regulatory flexibilities as part of its response to the COVID-19 crisis. A **lessons-learned exercise** was initiated in 2021, and although this is still ongoing, several learnings have already emerged as important elements, some of which will be implemented as part of EMA's extended mandate.

ENSURING MEDICINES AVAILABILITY DURING THE PANDEMIC

The EU network continued to **monitor ongoing or anticipated shortages** for COVID-19 related and not related to -COVID-19 human and veterinary medicines. In June 2021, the EU Executive Steering Group on Shortages of Medicines Caused by Major Events adopted a reflection paper, recommending the forecast of demand for human medicines across the EU during public health emergencies.

As a follow-up, the EU network also launched a **pilot phase to forecast demand data** for five medicines used in ICU setting, on the basis of the methodology described in the reflection paper. The pilot phase proved to be successful in demonstrating the practical implementation of the approach. In addition, the aggregated results from the pilot were deemed robust and representative of the actual demand in the EU/EEA.

CTIS

Development of the **Clinical Trials Information System (CTIS)** continued in 2021. Following a successful audit and a decision of EMA's Management Board, the European Commission confirmed that the entry into application of the Clinical Trials Regulation (CTR) and the go-live date for CTIS would take place on 31 January 2022.

CTIS supports the harmonisation of the assessment and supervision processes for clinical trials, and will be the single point of entry for all clinical trial applications in the EU/EEA. Throughout 2021, EMA ran a programme of activities to make sure sponsors and Member States were prepared for the CTIS go-live.

Finally, EMA, in collaboration with Member States and the European Commission, delivered safety monitoring and coordination tools for the clinical trial Safety Implementing Regulation, which also entered into application on 31 January 2022. The Safety Implementing Regulation lays down the rules for Member States cooperation on safety assessment, on the basis of the Clinical Trials Regulation.

Accelerating Clinical Trials in the EU (ACT EU)

In late 2021, the European Commission, the Heads of Medicines Agencies (HMA) and EMA agreed to launch 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.

ACT EU will reinforce the European environment for clinical trials, whilst maintaining the high-level of protection of trial participants, data robustness and transparency that EU citizens expect.

ACT EU will help achieve the ambitious goals for innovation in clinical trials as set out in the European medicines agencies network strategy to 2025 and the European Commission's Pharmaceutical Strategy.

ENSURING EU STANDARDS IN CLINICAL TRIALS AND MEDICINES MANUFACTURING

In March 2021, the European medicines regulatory network established the **Nitrosamine Implementation Oversight Group (NIOG)** to oversee the implementation of the CHMP's Article 5(3) opinion on nitrosamines in human medicines. The group includes representatives from the Committee for Medicinal Products for Human Use (CHMP), the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh), EMA working parties, the European Directorate for the Quality of Medicines and HealthCare (EDQM), and EMA staff. It also acts as the main interface for pharmaceutical industry stakeholders to discuss regulatory and scientific developments on nitrosamines with EMA and the European medicines regulatory network.

Throughout 2021, EMA continued to contribute to the **Nitrosamines International Steering Group (NISG)** and the **Nitrosamine International Technical Working Group (NITWG)**. The Agency shared information on substances at risk of containing nitrosamine impurities and discussed the approach for ensuring the safety and quality of such medicines. This also includes agreement on acceptable intake limits or testing approaches.

VETERINARY MEDICINES

In 2021, EMA continued to authorise new medicines[1] to benefit **animal health in Europe**. Specifically, the Agency recommended **12 veterinary medicines for marketing authorisation**; seven of these contain a new active substance (i.e. one that had not previously been authorised in the EU). Among the 12 medicines recommended for marketing authorisation, five were vaccines. Of these, four were biotechnological vaccines.

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

EMA also recommended the establishment of **maximum residue limits (MRLs)** for two active substances, and continued to monitor the quality and benefit-risk balance of the authorised medicines.

ANTIMICROBIAL RESISTANCE

EMA supports a **'One Health' approach**, promoting close and integrated cooperation between the human and veterinary fields, in this context EMA and the European Medicine Regulatory Network continued important work to tackle **Antimicrobial resistance** (AMR) - a serious global public health threat, affecting both human and veterinary medicines.

Tackling AMR continued to be a high priority for EMA and the European medicines regulatory network in 2021.

In January 2021, EMA's committee for veterinary medicines (CVMP) adopted a strategy on antimicrobials for 2021-2025. The strategy aims to secure the availability of effective antimicrobial medicines for the treatment of serious infectious diseases in animals, while minimising the risks to animals or people emerging from their use. It provides a status report on ongoing activities on antimicrobials and sets out proposed actions for the CVMP during the next 5 years.

In June 2021, EMA, the European Food Safety Authority (EFSA), and the European Centre for Disease Prevention and Control (ECDC) published the third **JIACRA report** that presented data on antibiotic consumption and development of AMR in Europe for 2016-2018. The report highlighted that the use of antibiotics has decreased and is now lower in food-producing animals than in humans.

[1] The full overview of the 2020 veterinary medicines highlights is available here https://www.ema.europa.eu/en/news/veterinary-medicines-highlights-2020

In November 2021, EMA published the annual **European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) report,** which shows that overall sales of veterinary antimicrobials in European countries were 43% lower in 2020 than in 2011. The significant fall in antibiotic use in food-producing animals suggested that the measures taken at country level to reduce use are proving to be effective, although the situation varies significantly by country and by antibiotic class.

Additionally, EMA continued to work with its EU and international partners on a number of initiatives aiming to address the global public health problem of AMR, such as the ICMRA campaign during World Antimicrobial Awareness Week in November, and other global initiatives to combat antibiotic resistance, such as the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR).

Finally, to mark **European Antibiotic Awareness Day** in 2021, EMA launched a social media campaign to highlight the importance of using antibiotics prudently.

VETERINARY REGULATION

2021 was a year in which the Agency reached many milestones for the implementation of the Veterinary Medicinal Products Regulation (Regulation (EU) 2019/6), which became applicable on 28 January 2022.

- **Union Product Database (UPD):** The main priority for 2021 was the delivery of the UPD components to enable submission of legacy data. By December 2021, 26,458 products had already been entered into the UPD. In parallel, the Agency developed the Veterinary Medicines information website, the public face of the UPD, which is the go-to source of information on all veterinary medicines in the EU/EEA.
- **Union Pharmacovigilance Database (EVVet3):** In January 2021, the Product Owners Group was expanded to include representatives from the veterinary pharmaceutical industry. An access policy was presented during the June 2021 meeting of the EMA Management Board, and subsequently published on the EMA website. In September 2021, the Project Group approved the final requirements for the recording of pharmacovigilance inspection outcomes and for signal management.
- **Manufacturers and Wholesale Distributors database (MWD):** Work started in July 2021, after the approval of the project vision and the finalisation of the detailed requirements. Most of the legislative requirements outlined by the new Regulation were covered by the existing EudraGMDP system, whose functionalities were extended to ensure full compliance. In September 2021, EMA organised a first demonstration of the system under development to NCAs. Webinars were held in October 2021 to support preparedness of NCAs and industry.
- **Antimicrobial Sales and Use data (ASU)** project: The ASU Project Group approved the final business case, project vision, and implementation timeline throughout the year, and started working on gathering detailed requirements. In December 2021, EMA and the Collection of ASU Project Group introduced the project to the members of the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) network. The Agency also published guidance and Q&As for marketing authorisation holders on how to submit data on the volume of sales.

INFORMATION MANAGEMENT

Between Q4 2020 and Q1 2021, EMA carried out a major review of the EMA's Information Management governance model (including the governance structure formerly known as EU Telematics). In June 2021, EMA MB endorsed the adoption of an **agile way of working** and the implementation of **agile governance principles** across all layers of technology delivery: the **Scaled Agile Framework (SAFe)**.

Thanks to the adoption of SAFe, EMA is expected to deliver:

- holistic portfolio management with a strong business value focus, and quick and incremental delivery of IT systems that focus on improving end-user satisfaction and unlocking data;
- a reduction in steering committees and project boards, and thus reduced administrative burden and clearer accountability;
- increased transparency on how and why decisions are made, and on the progress of implementation and their outcomes.

In July 2021, the former EU Telematics governance bodies were dissolved, and a **pilot to test the new way of working** was launched in September 2021. EMA established two new governance bodies in autumn 2021: the Network Portfolio Advisory Group (NPAG), comprised of HMA and Management Board members, and the Network ICT Advisory Committee, which includes four IT Directors and Experts from the NCAs, and a representative from the European Commission. EMA is currently operating a hybrid system, in which the new agile governance model and way of working is rolled out progressively across the full portfolio of IT projects.

ENHANCING THE SECURITY OF EMA IT SYSTEMS

During 2021, EMA successfully strengthened its IT security systems after it had become the subject of a cyberattack in December 2020.

The Agency swiftly launched a full investigation, in close cooperation with the Dutch police authorities, the Computer Emergency Response Team for EU Institutions, bodies and agencies (CERT-EU) and Europol, the EU's law enforcement agency. To support the full investigation, EMA also engaged a specialised IT security company to advise and assess the additional security measures that were immediately put in place in response to the data breach. The Management Board, the European medicines regulatory network and the European Commission were informed promptly and received regular updates.

The criminal intrusion into EMA's IT systems was successfully contained. The Agency and the European medicines regulatory network remained fully functional, and timelines related to the evaluation and approval of COVID-19 vaccines and treatments were not affected.

The investigation showed that data was unlawfully accessed, including a limited number of documents belonging to third parties. Further evaluation revealed that the data breach was limited to one IT application and that the perpetrators primarily targeted data related to COVID-19 medicines and vaccines. This included internal/confidential email correspondence dating from November 2020, relating to evaluation processes for COVID-19 vaccines.

Some of the breached documents, including email correspondence, were leaked on the internet and picked up by some media outlets. Not all documents were published in their integral, original form, and may have been taken out of context. Whilst individual emails were authentic, data from different users were selected and aggregated, screenshots from multiple folders and mailboxes were created, and additional titles were added by the perpetrators.

Some of the unlawfully accessed documents contained personal data. EMA notified the European Data Protection Supervisor and jointly agreed follow-up actions. EMA also informed all concerned third parties of the breach to provide support, assess the nature of the personal data and notify the person concerned in relation to the risk identified. All requests by data subjects to access their data were granted.

The Agency enforced its cybersecurity insurance policy, in place since 2019, and was able to recover 100% of all disbursements borne in connection with the cyberattack.

EMA has, as a result of the cyberattack, **further strengthened its defensive cybersecurity capabilities**. The Agency has been dedicating resources and investing significantly to avoid cybersecurity issues. It has been enhancing its IT systems as a priority, to protect from future attacks. A revision of EMA's information security strategy is also underway, with the aim of putting into place a three-year improvement road map in line with best practices of similar organisations.

BIG DATA

The **HMA-EMA joint Big Data Steering Group** updated its multiannual workplan in August 2021. The workplan aims to increase the utility of big data in regulation, from data quality through study methods, to assessment and decision-making. It is patient-focused and guided by advances in science and technology. The workplan includes eleven priority recommendations based on the HMA-EMA Joint Big Data Task Force final report.

2021 deliverables included the adoption of a Network Data Standardisation Strategy and a suite of stakeholder workshops, including on AI, real world meta-data, standards, and real-world evidence. In December 2021, the European Medicines Regulatory Network organised the second annual **Big Data Multi-Stakeholder Forum**. The Forum informed stakeholders on the delivery of the data pillar of the Network Strategy 2025 via the HMA-EMA joint Big Data Steering Group workplan, provided an opportunity to listen to stakeholders' views and feedback, and discuss the areas for collaboration.

DARWIN EU

The aim of the **Data Analysis and Real World Interrogation Network (DARWIN EU)** is to deliver real-world evidence from across Europe on diseases, populations, and the uses and performance of medicines. This will enable EMA and national competent authorities in the European medicines regulatory network to use these data whenever needed throughout the lifecycle of a medicinal product.

In 2021, DARWIN EU made significant steps forward. EMA launched a tender procedure for the selection of a service provider to establish and run, under the guidance of the Agency, the **Coordination Centre for the DARWIN EU network**. The selection will be concluded in early 2022.

Also, the DARWIN EU Advisory Board was formed in June 2021. The mandate of the board is:

- strategic advice and recommendations to the project team on establishing DARWIN EU and its use of the European Health Data Space (EHDS);
- coordination and alignment with relevant European and EU Member State initiatives and policies;
- supporting two-way communication on DARWIN EU with the EU Regulatory Network, stakeholders and the EHDS.

EMA will be a principal user of DARWIN EU, as it will request studies to support its committees' scientific evaluations and regulatory decision-making. EMA's role in DARWIN EU is crucial, as it is responsible for:

- linking real-world data studies to core benefit risk decision-making;
- providing strategic direction and setting standards;
- overseeing the coordination centre and monitoring its performance;
- ensuring close links to European Commission policy initiatives, particularly the EDHS, and delivering pilots.

DARWIN EU will also contribute to developing the EHDS, and close collaboration took place with the joint action to deliver European principles for the secondary use of health data, **Towards the European Health Data Space (TEHDAS)**.

EMA EXTENDED MANDATE

The COVID-19 pandemic highlighted both strengths and limitations of the current EU health security framework, as well as the need for formalised preparedness and response tools.

The EC addressed these limitations through its proposal to build a '**European Health Union**', which was launched on 11 November 2020.

The Health Union package included a proposal for a Regulation reinforcing EMA's mandate[1] in order to facilitate a coordinated EU-level response to future crises.

In 2021, EMA carried out an **impact assessment** to analyse the consequences of the new legal mandate on the Agency's organisational structure and activities. On this basis, the Agency drafted a **roadmap for the implementation of the new rules,** to be ready for their coming into operation on 1 March 2022.The Agency also put in place a communication plan to inform its stakeholders and provide the necessary guidance about how the new tasks will be implemented.

MEDICAL DEVICES LEGISLATION

In May 2021, the Medical Devices Regulation came into force. This new piece of legislation introduced new responsibilities for EMA, national competent authorities, and notified bodies.

In July 2021, EMA finalised and published the **guideline on quality documentation for medicinal products** when used with a medical device, to help developers prepare for submissions.

The Medical Devices Regulation will be complemented by the Regulation on In-Vitro Diagnostic Devices which will apply from 26 May 2022.

REGULATORY SCIENCE AND INNOVATION

In 2021, EMA continued with its efforts to 'future-proof' the Agency, to ensure it is fit to address the scientific and technological challenges ahead, while operating as efficiently as possible to deliver high-quality outputs for public and animal health. Progress was made to fulfil the recommendations set in the Regulatory Science Strategy to 2025.

Throughout 2021, the Agency completed the **integration of the recommendations of the Regulatory Science Strategy to 2025 into actions** to be taken as part of the 'European medicines agencies network strategy to 2025', which was developed together with the Heads of Medicines Agencies (HMA). The most notable actions include: the establishment of the ACT EU initiative, priority focus on novel manufacturing techniques and advanced therapies and personalised medicines developments, investment in real-world evidence capabilities, various digital innovation initiatives, as well as work on Health Threats as part of the pandemic response.

In February 2021, EMA and the HMA agreed on the establishment of the **Borderline Classification Group**. This initiative, supported by the EU Innovation Network, aims to support a harmonised approach to the classification of innovative borderline products; i.e., products for which doubts arise as to whether they should be considered as medicinal products or fall under another regulatory framework (e.g., devices, food, or cosmetics). This is to avoid situations where the same product could be classified differently depending on the approaches followed by each Member State, with

[1] https://www.ema.europa.eu/en/news/regulation-emas-extended-mandate-becomes-applicable

consequences on the evidence requirements during development. The first meeting of this group took place in March 2021.

In September 2021, EMA opened up its **Innovation Task Force (ITF)** to the discussion of methodologies that minimise animal testing during medicines development. The goal of this initiative is to facilitate the integration of the 3Rs principles into the development and evaluation of medicinal products. The 3Rs are a set of principles supported by the Agency to replace, reduce, and refine animal use for the development, manufacturing and testing of human and veterinary medicines.

In December 2021, EMA published the Regulatory Science Research Needs List, a list of regulatory science topics that need further research to close gaps and improve medicine development and evaluation to enable access to innovative medicines for patients. EMA identified around one hundred specific topics in four categories, relating both to human and veterinary medicines. Based on this list, the Agency stimulates researchers and funding organisations to address these topics in their research agendas and share their findings and results with regulators. The Agency's proactive exchanges with funding organisations and involvement in externally funded research projects also contribute to closing the regulatory science gaps.

INTERNATIONAL REGULATORY COOPERATION TO IMPROVE GLOBAL HEALTH

In 2021, the Agency continued to work, with its partners in Europe and beyond, on contributing to the health of EU citizens and people around the world. In March 2021, EMA and the European Commission's Directorate-General for Health and Food Safety (DG SANTE) signed a **confidentiality arrangement** with the Brazilian Health Regulatory Agency (ANVISA). This brings the number of standing confidentiality agreements to eight. Throughout 2021, EMA, as chair of **ICMRA**, continued to spearhead global efforts to **strengthen regulatory cooperation** on issues that impact people worldwide. While priority was given to activities related to ensuring alignment of regulatory approaches to the COVID-19 response, ICMRA also covered a range of other activities. In its role as chair of the ICMRA working group on supply chain integrity, EMA contributed to the development of a paper with recommendations to facilitate the use of track and trace systems at global level in 2021. The recommendations were developed in consultation with the World Health Organization (WHO), representatives from international medicines regulatory authorities, and experts from the private sector.

EMA led a **horizon-scanning exercise in Artificial Intelligence (AI)**, carried out by the ICMRA Informal Network for Innovation working group. The group developed a report with specific recommendations to help regulators address the challenges that the use of AI poses for global medicines regulation.

CONTRIBUTING TO EU PRIORITIES

COLLABORATION WITH EU INSTITUTIONS

In 2021, EMA continued to promote a functioning single market for human and veterinary medicines, by acting as the hub of the European network of regulatory medicines authorities operating the applicable EU legislative framework for such products. A **functioning single market for medicines** is important both for protecting public and animal health and for allowing the European biomedical industry to innovate and create jobs and growth. By authorising several new cancer medicines (20 cancer medicines were authorised in 2021), EMA continued contributing to the implementation of the ambitions of the EU Beating Cancer Plan.

In 2021, EMA continued to provide support to the **implementation of the EU Strategy for COVID-19 vaccines** (COM/2020/245 final) and the EU COVID-19 Therapeutics Strategy (COM/2021/355 final/2), which aim to coordinate efforts by Member States in the development and access to COVID-19

vaccines and therapeutics. Key performance indicators are included in the 'medicines highlights' section of this Annual Activity Report. In this context, in early 2021, EMA also initiated a structured collaboration (Joint Advisory Board) with the European Centre for Disease Prevention and Control (ECDC) to coordinate independent post-authorisation studies on COVID-19 vaccines.

As one of the EU decentralised agencies at the forefront of the EU's response to COVID-19 pandemic, EMA's activities in 2021 have contributed to the creation of the **European Health Union**. Several of EMA's COVID-19 initiatives were acknowledged and reinforced in the Commission's legal proposal **extending EMA's mandate** under the EU Health Union, which went through the EU legislative process in 2021. Example of such initiatives for EU level coordination, which continued to operate in 2021, include the EU Executive Steering Group on Shortages of Medicines and the EMA COVID-19 Pandemic Task Force. In addition, EMA started contributing to the work of the Health Emergency Preparedness and Response Authority (HERA) by attending as observer the HERA Board together with ECDC.

In 2021, EMA continued the implementation of actions within its remit under the **EU Strategic Approach on pharmaceuticals in the environment**, which aims to address the environmental implications of all phases of the lifecycle of human and veterinary medicinal products, from design and production, through use and disposal. This strategy is a key part of the European Green Deal, which aims to achieve a toxic-free environment and a zero-pollution economy for Europe. In particular, in 2021, EMA supported the European Commission's Pharmaceutical Committee with the preparation of proposals to revise the human pharmaceutical legislation in the areas of environmental risk assessment and of reduction of the impact on AMR and the environment of pharmaceutical manufacturing and consumption. EMA also progressed with the implementation of the new veterinary medicines legislation (Regulation EU 2019/6) which aims to limit the preventive use of veterinary antimicrobials and strengthens the rules and procedures for the environmental risk assessment of veterinary medicinal products.

In 2021, EMA continued to support the implementation of the **European One Health Action Plan against Antimicrobial Resistance**, which was adopted by the European Commission in June 2017 and contains actions running until 2022. The key activity in 2021 in this area was the considerable progress in implementing the new veterinary medicines legislation (see more details in the dedicated section on Regulation 2019/6 in this document).

In 2021, EMA provided scientific support to the European Commission with regards to the preparation of the legislative proposals included in the **Pharmaceutical Strategy for Europe**, notably for the revision of the basic pharmaceutical legislation and the regulations on orphan and paediatric medicines, by participating in technical workshops and expert group meetings, and responding to targeted questionnaires of the Commission.

In 2021, EMA contributed to the EU objective to **foster a wider patient access to innovative medicines**. It did so mainly via its collaboration with the European Network for Health Technology Assessment (EUnetHTA21), which spans across many aspects of scientific collaboration between different decisions makers along the lifecycle of medicines. The EMA-EUnetHTA21 collaboration focuses in particular on parallel scientific advice to medicine developers with HTA bodies and EMA; information exchange between regulators and HTA bodies about the outcome of the EMA's regulatory assessments in support of joint Relative Effectiveness Assessments by HTA bodies, and discussion on post-authorisation data generation, such as optimising patient registries to better serve data needs for various decision-makers.

Work programme implementation

This section includes reference to progress against all key performance and workload indicators set in the Single Programming Document and the Annual Work Programme.

Each of the chapters outlines the achievement of the workload and performance indicators included in each chapter of the work programme, as well as covers a set of objectives, with the relevant activities and results outlined.

The work programme consists of four parts: evaluation activities for human medicines; evaluation activities for veterinary medicines; horizontal activities and other areas, and support and governance activities. Each of these is further broken down into chapters covering the Agency's activities in specific areas or stages in the medicines' lifecycle.

Explanation of symbols used

A traffic light system is used to describe performance against objectives and targets.

	Results more than 10% above the 2021 forecast/target
	Results within +/- 10% of the 2021 forecast/target
	Results 10%~25% below the 2021 forecast/target
	Results more than 25% below 2021 forecast/target
	No activity/result to report

In general, the traffic light system reflects the direction and magnitude of changes, as described above.

However, for some performance indicators, where the optimal results should be lower than the targets, such as average assessment or clock-stop days, the traffic light system is reversed to better reflect the essence of these indicators: results below the target are marked green or blue, while results above the target will appear amber or red.

In cases where absolute numerical change results in disproportionate variation, discretion should be used to reflect more accurately the significance of the change. For example, a number of applications falling from 3 to 2 (or rising from 2 to 3) can be marked green rather than red (blue), if this is in line with regular variations.

For indicators that have been included in the work programme for the first time, data on the previous year's results are not provided.

Human Medicines Division

Pillar 1 - Product related activities

1.1 Pre-authorisation activities

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Parallel scientific advice with international regulators	2	2	6	4	3
Joint scientific advice with HTA bodies	27	20	2	4	2
Scientific advice for PRIME products	36	26	37	40	59
Protocol assistance requests	159	137	143	146	163
Novel technologies qualification advice/opinions	9	16	15	19	25
PRIME eligibility requests	57	60	69	55	52
Orphan medicines applications	236	233	235	250	251
Submitted applications on the amendment of an existing orphan designation	1	1	0	2	0
Paediatric procedure applications (PIPs, waivers, PIP modifications, compliance checks)	669	671	735	670	778
Finalised procedures for compliance check on PIPs	96	94	97	85	98
Requests for classification of ATMPs	55	70	74	70	66

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Scientific advice/protocol assistance procedures completed within regulatory timeframes	100%	100%	100%	100%	100%[1]
PRIME eligibility requests assessed within regulatory timeframe	100%	100%	100%	100%	100%
Orphan designation opinions delivered within the legal timeframe	96%	100%	100%	100%	100%
PDCO opinions sent to applicants within legal timelines	99.9%	99.5%	99.81%	99%	99.8%

[1] The result refers to procedures started in 2021, during which EMA experienced delays at the stage of submission and prior to the start, due to assessment resource constraints.

1.2 Initial evaluation activities

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
New non-orphan medicinal products	31	33	43	68	43
New orphan medicinal products	17	27	28	28	29
Similar biological products	9	13	12	13	10
Generic products, hybrid and abridged applications	23	29	24	23	28
Scientific opinions for non-EU markets (Art. 58)	1	0	0	3	3
Paediatric-use marketing authorisations	0	0	0	1	0
Number of granted requests for accelerated assessment	11	13	12	10	12
Reviews on the maintenance of the orphan designation criteria at MAA stage	45	40	35	30	31
ATMPs applications requests received[1]	-	-	-	9	3
COVID-19 related product applications received[2]	-	-	-	8	14[3]
Companion diagnostics opinions	-	-	-	n/a[4]	n/a[3]

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Applications evaluated within legal timeframes[5]	100%	100%	100%	100%	100%
Average assessment time for new active substances and biosimilars (days)	205.3	192.8	192	205	183
Average clock-stop for new active substances and biosimilars (days)	195.2	178.1	166	180	149
% of MAAs initiated under accelerated assessment that have been completed as accelerated assessment	44%	43%	50%	60%	27%
% of initial marketing authorisation applications (orphan/non-orphan/biosimilar) that had received centralised scientific advice	68%	68%	70%	80%	78%

[1] New indicator introduced in 2021 Work Programme
[2] New indicator introduced in 2021 Work Programme
[3] Two applications were withdrawn during evaluation.
[4] New indicator introduced in 2021 Work Programme, which is linked to the possible extension of the Agency's mandate, following the EC proposal of November 2020. The indicator will not be applicable until 2022.
[5] Includes marketing authorisation and plasma master file applications.

1.3 Post-authorisation activities

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Type IA variations	3,433	3,886	3,989	4,046	3,809
Type IB variations	2,164	2,425	2,675	2,888	3,102
Type II variations	1,119	1,123	1,274	1,243	1,390
Line extensions of marketing authorisations	20	27	35	32	27
PASS scientific advice through SAWP	3	3	1	1	1
Renewal applications	90	107	99	84	123
Annual reassessment applications	22	25	24	29	27
Transfer of marketing authorisation applications	377	63	36	60	95
Article 61(3) applications	258	286	211	300	396
Post-authorisation measure data submissions	812	776	990	900	1,272
Plasma master file annual update and variation applications	19	17	28	25	20

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Post-authorisation applications evaluated within legal timeframes	99%	99%	99%	99%	99%
Average assessment time for variations that include an extension of indication	157	165	167	180	177

1.4 Referrals

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Pharmacovigilance referrals started	2	8	2	5	3
Non-pharmacovigilance referrals started	15	7	6	10	10

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Referral procedures managed within legal timelines	100%	100%	100%	100%	100%

1.5 Pharmacovigilance

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Number of signals peer-reviewed by EMA	2,204	1,806	1,888	1,900	2,447
Number of ICSRs for CAPs (reports received) [1]	-	-	-	1,600,000	2,989,903
Number of signals assessed by PRAC (validated by EMA)	74	50	39	50	55
PSURs (standalone CAPs only) started	554	554	525	573	568
PSUSAs started	327	246	304	327	322
Number of imposed PASS protocol procedures started	17	12	4	4	7
Number of imposed PASS result procedures started	8	3	4	6	11
Number of notifications of withdrawn products received	413	462	510	500	597

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Periodic safety update reports (PSURs standalone CAPs only) assessed within the legal timeframe	100%	100%	100%	100%	100%
Periodic safety assessment reports (PSUSAs result procedures) assessed within the legal timeframe	100%	100%	95%	95%	95%
Protocols and reports for non-interventional post-authorisation safety studies assessed within the legal timeframe	100%	100%	100%	100%	100%
PRAC recommendations on signals and translation of labelling changes in EU languages published	100%	100%	100%	100%	100%

1.6 Inspections and compliance

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
GMP inspections	332	386	130	160	247
GLP inspections	1	0	0	1	0

[1] New indicator introduced in 2021 Work Programme.

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
GCP inspections	140	137	59	40	36
Pharmacovigilance inspections	20	9	16	15	15
PMF inspections	84	111	40	76	122
Notifications of suspected quality defects	147	175	170	250	178
Notifications of GMP non-compliances[1]	25	19	10	20	4
Number of medicinal products included in the sampling and testing programme	53	67	81	94	75
Standard certificate requests	3,703	2,565	3,115	3,585	3,753
Urgent certificate requests	1,069	2,399	1,647	1,654	1,659
Parallel distribution initial notifications received	2,304	2,468	3,172	2,800	2,555
Parallel distribution notifications of bulk change received	11	12	10	20	19
Parallel distribution annual updates received	5,245	4,270	11,624	5,000	4,816

Performance indicators

Performance indicators related to core business	2017 result	2018 result	2019 result	2021 target	2021 result
Inspections conducted within established regulatory timeframes	100%	100%	100%	100%	100%
Standard certificates issued within the established timelines (30 working days)	0%[2]	28%	80%	90%	99.00%
Average days to issue standard certificate	27.3[3]	59.6[4]	23.6	10[5]	12.81
Urgent certificates issued within established timelines (2 working days)	99%	97%	98%	100%	99%
Parallel distribution notifications checked for compliance within the established timeline	97%	37%	90%	90%	99%
Impact of GCP confidentiality arrangements: Additional GCP inspections addressed through information exchange on inspections carried out by international partners	38%	42%	38%	35%	38%

[1] Other GMP inspections-related notifications previously included under suspected quality defects.
[2] Average processing time increased from 10 to over 60 days during the second half of 2018, creating a backlog due to increased shortage of staff through long-term leave and internal mobility to priority areas, together with an increase in requests on Brexit-related variations of the marketing authorisation.
[3] Average processing time increased from 10 to over 60 days during the second half of 2018, creating a backlog due to increased shortage of staff through long-term leave and internal mobility to priority areas, together with an increase in requests on Brexit-related variations of the marketing authorisation.
[4] Average processing time remained significantly higher than the target in 2019, due to continuous staff shortages and backlog issues. Actions were taken during the year to remedy the issues and reduce processing time, which by November 2019 had reduced to 30 days on average.
[5] The target handling time of 10 working days for certificates requested through the standard procedure has been temporarily extended to 30 working days.

1.7 Committees and working parties

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Number of reimbursed meetings	408	321	52	91	311
Committee meetings[1]	76	76	75	38	99
Training	29	29	4	2	6
Workshops	35	4[2]	2	2	7
Others (working groups, working parties, ad hoc expert meetings, SAG etc.)	273	212	112	49	199
Number of virtual meetings (audio-, video- and web-conferences)	4,793	3,443	5,409	6,400	6,854
Number of reimbursed delegates	7,214	6,015	1,003	9,358	6,226
Number of non-reimbursed delegates	1,064	523	60	7,129	13,227
Herbal monographs, new	4	0	3	4	3
Herbal monographs, reviewed	7	13	14	15	18
Herbal monographs, revised	15	2	8	3	2
List entries	0	0	1	1	0

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Evaluation of declarations of interests of committee members and alternates prior to their participation in committee meetings	100%	100%	100%	100%	100%

Pillar 2 – Public health activities

Achievements

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
Support the STAMP scientific advice pilot for repurposing established medicines	1.1	A number of prioritised established medicines are enlisted in the pilot	On track	Pilot launched at the end of October 2021, jointly with NCA (through EU-IN). Presentation given at HMA meeting by Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) and

[1] Indicator updated to include Management Board meetings
[2] Due to the relocation of the Agency and associated logistical challenges, as well as the lack of facilities in the new temporary premises, the 2019 actual number of workshops delivered has been significantly lower than in previous years. These are expected to gradually increase again, as the Agency resumes activities post-relocation

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				presentation given jointly by EMA/ AEMPS at PCWP/HCPWP

Pillar 3 – Programmes and projects

Project title	Long term objective	Achievements/results in 2021
SPM&S - Substances and products management services	Implementation of ISO Identification of Medicinal Products standards to apply interoperability and consistency to the information shared across the regulatory authorities within the EU and internationally	Data migrations from Art. 57 and from SIAMED are being tested and improved, allowing the Variation form to select information from PMS.

Veterinary Medicines Division

Pillar 1 – Product-related activities

2.1 Pre-authorisation activities

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Innovation Task Force briefing requests	5	6	5	5	6
Scientific advice requests received	25	21	31	22	23
Requests for classification as MUMS/limited market, of which	32	34	29	25	14
Reclassification requests	5	9	4	5	5

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Scientific advice procedures completed within set timeframes	96%	95%	100%	100%	100%

2.2 Initial evaluation activities

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Initial evaluation applications	15	23	15	11	9
New MRL applications	3	3	1	2	0
MRL extension and modification applications	2	4	1	2	3
MRL extrapolations	0	0	0	0	0
Art. 10, Biocides	0	0	0	0	0
Review of draft Codex MRLs	5	0	3	0	0

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Procedures completed within legal timeframes	100%	100%	100%	100%	100%

2.3 Post-authorisation activities

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Variations applications, of which:	560	568	637	649	679
Type IA variations	331	356	380	366	350
Type IB variations	137	139	195	205	241
Type II variations	92	73	62	78	88
Line extensions of marketing authorisations	1	2	2	3	2
Transfers of marketing authorisations	17	24	9	8	8

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Post-authorisation applications evaluated within legal timeframes	99.9%	100%	100%	100%	100%

2.4 Arbitrations and referrals

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Arbitrations and Community referral procedures initiated[1]	5	9	3	3	0

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Arbitration and referral procedures managed within legal timelines	100%	100%	100%	100%	100%

2.5 Pharmacovigilance activities

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Periodic safety-update reports (PSURs)	158	159	160	160	188
Total adverse-event reports, of which:	66,844[1]	70,392	66,901	70,000	80,709
Adverse-event reports (AERs) for CAPs	35,835	33,656	30,297	35,000	43,334
Adverse-event reports (AERs) for NAPs	31,009	36,736	36,604	35,000	37,365

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
PSURs evaluated within the established timelines	99%	96%	98%	90%	97%
Adverse event reports for CAPs monitored within the established timelines	98%	95%	97%	95%	96%

Pillar 2 – Public health activities

Achievements

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
Produce further guidance to implement the annex to the new veterinary legislation (Regulation (EU) 2019/6) that defines proportionate and future-proofed technical standards for	3.1	Guidance for novel therapies and biologicals developed	On track	The two operational expert groups (OEGs) on cell therapies and bacteriophages were established in Q3 2021. The OEGs started their work in September 2021. The release for

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
novel veterinary therapies, particularly biologicals.				public consultation of the 'Concept paper on the efficacy of cell therapies: mechanism of action, potency and clinical effects' and the 'Concept paper on quality, safety and efficacy of bacteriophages as veterinary medicines' is planned for Q1 2022.
Engage with EU and international risk-assessment bodies with a view to aligning methodology for estimating consumer exposure to residues, including dual-use substances.	3.1	Analysis of existing models Evaluation of finding and recommendation on harmonised approach	**On track**	The expert group met 7 times in 2021, progressing the work on the recommendation to be sent to the EC by 30 November 2022 (EMA/EFSA joint final report). An intermediate status report, including a summary of the work carried out so far and the current view on the outcome, was presented to CVMP and sent to EC in December 2021.
Together with stakeholders, develop new and improved continuous surveillance and signal detection methodology using the network's pharmacovigilance database.	3.1	Guidance for surveillance and signal detection developed Enhanced communication with the network	**On track**	VGVP guidelines on adverse event reporting and signal management finalised and adopted by CVMP/CMDV and published in November 2021. A central EU pilot signal management expert group has been set up under HMA and EMA as an operational group to manage all EU signal management activities for all EU VMPs.
Using data on the sales of veterinary products, develop methodology to collate, analyse and communicate information about the incidence of	3.1	Methodology established and guidance developed	**On track**	EU Implementation Guide (Vet EU IG) on veterinary medicines product data in the Union Product Database has been published,

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
adverse reactions related to medicines' use.				including specifications for the submission of volume of sales data by MAHs. The P-SMEG will work to define a methodology on how to derive incidence from the sales data.
Establish stakeholder expert groups for different food-producing species to access actual-use data of products in the field, both off and on label.	3.1	Expert groups established with mandate and objectives	**Delayed**	A concept paper was drafted and published for consultation in 2020. Drafting of the guideline has been postponed due to redeployment of resources to more urgent priorities linked to the Veterinary Regulation implementation and the annual ESVAC report publication. The work on the guideline is expected to be resumed in Q1-Q2 2022.
Improve communication of veterinary pharmacovigilance to the general public.	3.1	Establish PhV communication framework	**On track**	System specifications have been developed for the systems set up to ensure transparent and continuous communication. EMA participated to webinars on pharmacovigilance topics organised by the Federation of Veterinarians of Europe (FVE) and the European Association for Porcine Health Management (EAPHM) in Q2 2021. The 'Guideline on veterinary good pharmacovigilance practices (VGVP): Veterinary pharmacovigilance communication' has been adopted by CVMP

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				and published in November 2021.
Contribute to the evaluation of novel approaches to ERA, and the EC considerations on the feasibility of establishing active substance monographs for all substances, including legacy active substances for which there is limited environmental information, providing input as required.	3 (additional RSS recommendation)	Support EC in the monographs feasibility study	**On track**	EMA provided input, in 2020, to the consortium tasked by EC to perform the feasibility study for the monograph system. The study was published by EC in Q4 2021.
Develop further guidance on when the use of persistent, bio accumulative and toxic substances in animals can be justified.	3 (additional RSS recommendation)	PBT guidance developed and published	**Delayed**	Development of a reflection paper on the interpretation of Art.37(2)(j) of regulation 2019/6 was initiated in Q1 2021, the guideline is expected to be released for consultation in Q1 2022.
Increase cooperation in the field of ERA with European agencies, particularly ECHA, EFSA and EEA, and establish cooperation with international institutions, academic organisations, and relevant initiatives.	3 (additional RSS recommendation)	Establish ERA framework with EU and international partners	**On track**	Ad hoc cooperation on identified topics for discussions is ongoing (e.g., AMR in the environment with EFSA). Generally, cooperation with other Agencies and academia is being initiated on a case-by-case basis.
Provide scientific support to the European Commission and the EU network to ensure that a 'One Health' approach is applied to ERA.	3 (additional RSS recommendation)		**On track**	EMA provides input to EC/other Agencies when requested on ERA 'One Health' topics. No specific request was received in the first half of 2021.
Expand current ESVAC system to include other antimicrobials.	4.1	Collection of data expanded to include all antimicrobials	**On track**	In line with the Commission Delegated Regulation (EU) 2021/578, the work on development of the new antimicrobial sale and use data system to

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				receive extended lists of antimicrobials is ongoing. During the second half of 2021, the use cases developed for ASU project include extended lists of antimicrobials; the project is now approved at gate 3.
Establish contributions to JIACRA under CVMP guidance and develop new processes that maintain Member State input and ensure EMA oversight.	4.1	Establish and implement new process for JIACRA report to be led by EMA and CVMP, in cooperation with EU MSs	**On track**	The third JIACRA report was published in June 2021. Preparation for CVMP's oversight, as provided by Regulation (EU) 2019/5, is ongoing. The mandate for the fourth JIACRA report was received in January 2022, and will address data from 2019-2021, with completion anticipated by December 2023.
Adjust the methodology for analysis of antimicrobial data, by considering approaches developed internationally.	4.1	Analyse international approaches and integrate, where possible, in methodology	**Delayed**	A concept paper was drafted and published for consultation in 2020. Drafting of the guideline has been postponed due to redeployment of resources to more urgent priorities linked to the Veterinary Regulation implementation and the annual ESVAC report publication. The work on the guideline is expected to be resumed in Q1-Q2 2022.
Define requirements for harmonised sales and use data collection for antimicrobial medicinal products used in animals.	4.1	Define new requirements Develop guidance on new requirements	**Delayed**	A concept paper was drafted and published for consultation in 2020. Drafting of the guideline has been postponed due to redeployment of resources to more

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				urgent priorities linked to the Veterinary Regulation implementation and the annual ESVAC report publication. The work on the guideline is expected to be resumed in Q1-Q2 2022.
Inform policy decisions via enhanced cooperation with European institutions (EFSA, ECDC) to collate data on antimicrobial use, with information on AMR in animals, humans and food.	4.1	Active participation to policy development	**Delayed**	The activity has been deprioritised due to more urgent work on establishing the antimicrobial sales and use data collection system in line with the requirements of the Regulation (EU) 2019/6.
Participate in international initiatives to reduce the risk of AMR.	4.1	Active participation in international fora	**On track**	Throughout the year, EMA participated to the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) activities, including leading key action activity 1.1 under the new TATFAR work plan to 2026, and contributing to others, in particular the development to alternatives to antimicrobials. EMA participated to the OIE AMR WG in April, and to the PAHO-led EC funded Steering Committee of the project 'Working together to combat antimicrobial resistance (AMR)' in May 2021. EMA participated in the ARDIG workshop on antimicrobial use in March 2021, AACTING 3rd Conference in May

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				2021, and in Codex TFAMR in October 2021. EMA presented a poster regarding AMEG categorisation at the 5th International conference on Responsible Use of Antibiotics in Animals in June 2021. EMA also contributed to enhanced discussions with OIE, on the data collection on antimicrobial use in animals and the option to link EMA and OIE data collection systems.
Update existing guidelines, and initiate new guidance as needed.	4.3	Develop relevant guidance	**On track**	The following guidance was finalised and published in 2021: 'Reflection paper on the use of aminopenicillins and their beta-lactamase inhibitor combinations in animals in the European Union: development of resistance and impact on human and animal health' and 'Guideline on the summary of product characteristics (SPC) for veterinary medicinal products containing antimicrobial substances'.
Finalise the CVMP reflection paper on antimicrobial resistance in the environment, in light of comments received. Invite CHMP to derive conclusions for human medicines based on CVMP reflection paper.	4.3	Reflection paper finalised and published	**On track**	The reflection paper was finalised and published in February 2021. No action has been initiated for the second deliverable yet.
Develop a regulatory approach/framework to promote alternatives to	4.3	Framework developed Communication with stakeholders	**On track**	A reflection paper on promoting the authorisation of alternative to

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
conventional antimicrobials and novel paradigms.				antimicrobials (ATAm) was finalised and published in July 2021. Discussions on implementing the recommendations given in the RP were initiated in the second half of 2021. In addition, discussion on possible regulatory approaches to alternatives are being discussed in the context of TAFTAR work plan (action 3.3). A session on potential claims for alternative products and demonstrations of efficacy was held at the informal CVMP meeting in October 2021. EMA also participated in international fora discussions on ATAm, such as the AVANT workshop in October 2021 and the STAR-IDAZ International Research Consortium (IRC) in November 2021.
Enhance the promotion of responsible use of antimicrobials via updated and/or new regulatory guidance and scientific opinion.	4.3	Guidance development Communication with stakeholders	**Delayed**	The 'Concept paper on update to the CVMP's reflection paper on the use of macrolides, lincosamides and streptogramins (MLS) in food-producing animals in the European Union: development of resistance and impact on human and animal health' was published for public consultation between October 2021 and 31 January 2022.

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				The revised reflection paper will be progressed in 2022. The 'Reflection paper on criteria to determining 'exceptional cases' when antimicrobial administration for prophylaxis would be accepted in regard to Article 107(3) of Regulation (EU) 2019/6' is to be adopted for release for consultation by CVMP at its meeting in January 2022.
Provide scientific and regulatory support to encourage development of veterinary antimicrobials and alternatives to fill therapeutic gaps, without adversely impacting public health.	4.3	Guidance development	**On track**	A reflection paper on promoting the authorisation of ATAm was finalised and published in July 2021. Prioritisation of the relevant guidance to be developed is ongoing. Development of guidance on bacteriophage therapy has already been included in the work plan of NTWP, adopted in July 2021. Development of a guideline on data requirements and potential claims for alternatives to antimicrobial veterinary medicinal products has been included in the CVMP and Efficacy WP work plans.
Work in partnership with EC, other EU Agencies and regulators and international bodies to promote the responsible use of antimicrobials and their alternatives.	4.3	Cooperation at EU and international level for events Common approach agreed	**On track**	EMA has participated at TATFAR meetings under Action 3.3, where the EMA/CVMP 'Reflection paper on promoting authorisation of alternatives to

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				antimicrobial VMPs in the EU' was presented and discussion held on regulatory routes for authorisation of bacteriophages.
Acknowledge that different benefit-risk approaches are required for assessment of specific vaccine types (e.g., vaccines for zoonotic diseases, limited markets, exceptional circumstances).	4 (additional RSS recommendation)	Identify different benefit-risk approaches per type of vaccine Guidance on benefit-risk	**On track**	A guideline on limited market data requirements was finalised and published in July 2021, and a guideline on exceptional circumstances data requirements was released in July 2021 for consultation; both guidelines will be instrumental for establishing benefit-risk of these products. A guideline on exceptional circumstances is expected to be finalised in Q1 2022.
Develop a regulatory framework for authorisation, under exceptional circumstances, of vaccines for emerging health threats and benefit-risk monitoring post-approval.	4 (additional RSS recommendation)	Guidance developed and implemented	**On track**	A concept paper for the development of a guideline on data requirements for authorisation of immunological veterinary medicinal products under exceptional circumstances was published for consultation in January 2021. The draft guideline on data requirements was adopted by CVMP and released for consultation in July 2021. Finalisation of the guideline is expected in January 2022.
Develop appropriate and proportionate guidance to maximise opportunities	4 (additional RSS recommendation)	Guidance developed and implemented	**On track**	Concept papers for all three topics were

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
offered by Regulation (EU) 2019/6 for promoting availability of vaccines (vaccine antigen master files, vaccine platform technology master files and multi-strain dossiers).				published in January 2021 for consultation. Drafts of the 'Guideline on data requirements for multi-strain dossiers for inactivated veterinary vaccines' and 'Guideline on data requirements for vaccine antigen master files (VAMF)' were published for consultation in June 2021; both guidelines took into consideration the comments submitted during the concept papers consultation. Guideline on vaccine platform technology master files (vPTMF) was adopted and released for consultation at the July CVMP meeting. Finalisation of these guidelines is expected in January 2022.
Participate actively in international initiatives that aim to develop strategies to combat antiparasitic resistance and to establish best practices on the use of veterinary antiparasitic medicines.	4 (additional RSS recommendation)	Improve interaction with international organisations Best practices embedded in guidance	**On track**	EMA is part of the OIE Electronic Expert Group (EEG) on Antiparasitic Resistance (APR). The group met virtually throughout the year to progress the work on the 'Prudent use of antiparasitic agents to help control antiparasitic resistance in grazing livestock species' document. EMA provided input into the regulatory requirements in the EU. The final document was published in December 2021 on the OIE website.
Promote responsible use of antiparasitics in the EU.	4 (additional RSS recommendation)	Awareness events and enhanced	**On track**	A 'Concept paper for the revision of the guideline

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
		dissemination of information		on the summary of product characteristics for anthelmintics' was published in April 2021 for consultation. The revised draft 'Guideline on the summary of product characteristics for antiparasitic veterinary medicinal products' was released in July 2021 for public consultation. The revised guideline was finalised and adopted by the CVMP in December 2021 and will come into effect in July 2022.
Veterinary Medicines Regulation: preparation phase – 2021; implementation phase from 2022.	6.1	Prioritised guidance, processes and IT systems in place in time for implementation	**On track**	Work on the prioritised guidance is ongoing and veterinary processes and procedures are being aligned with the new requirements of Regulation (EU) 2019/6. The development of required IT system is on track: - Union product database (UPD) go-live scheduled for 28 January 2022 (95% complete); - Union Pharmacovigilance Database (EVV) go-live scheduled for 28 January 2022 (95% complete); - Antimicrobial Sales and Use (ASU); MVP go-live scheduled for the end of 2022; post-MVP improvements Q2 2023 (30% complete); - Manufacturer and Wholesale Distributors Database (MWD) go-live

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				scheduled for 28 January 2022 (95% complete). Two recommendations are under development and expected to be finalised in Q1-Q2 2022: - List of antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans; - List of antimicrobials, which shall not be used in accordance with Articles 112-114, or which may be used in accordance with these articles subject to certain conditions (Article 107(6)).
Promote systematic application of structured benefit-risk methodology and quality assurance systems in the approach to assessment and consistency of decision-making.	6.2	Analysis of current methodologies, development of harmonised approach and guidance	**On track**	A drafting group of the CVMP is working on a revision of the 'CVMP recommendation on the evaluation of the benefit-risk balance', with the aim to improve the current benefit-risk methodology and align with the Regulation (EU) 2019/6 provisions. A concept paper was published for consultation in November 2021; a draft guideline will be developed and is expected to be finalised by Q1 2023.
Optimise quality and consistency of outputs from EMA and maximise their dissemination to relevant stakeholders, especially for novel technologies.	6.2	Analysis of current methodologies, development of harmonised approach and guidance	**On track**	The newly formed NTWP is developing guidance for new technologies, like bacteriophages and cell therapies products (see activity 5). Two concept papers will be

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
		Enhanced communication with stakeholders		released for consultation in January 2022.

Pillar 3 – Programmes and projects

Project title	Long-term objective	Achievements/results in 2021
EVVet3 - Union Pharmacovigilance Database / EudraVigilance Veterinary v3.0	The EVVet3 project aims to provide a 'Union veterinary pharmacovigilance system', by implementing any remaining requirements from Directive 2001/82/EC (as applicable, in relation to veterinary pharmacovigilance reporting), as well as the VICH guidelines relating to pharmacovigilance reporting.	- All the deliverable to enable the go-live on 28 January 2022 were achieved
UPD - Union Product Database [continues]	Providing a Union Product Database system regarding Veterinary products according to Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018	- All the deliverable to enable the go-live on 28 January 2022 were achieved
ESVAC - Collection of Antimicrobials Sales and Use Data [new]	The European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project collects information on how antimicrobial medicines are used in animals across the European Union (EU). The objective is to obtain reliable data for input into risk profiling and risk assessment regarding antimicrobial resistance and for setting risk management priorities regarding AMR.	- All the deliverable to enable the go-live on 28 January 2022 were achieved
EudraGMDP - Union Manufacturers and Wholesale Distributors Database	The EudraGMDP database is the Community database on manufacturing, import and wholesale-distribution authorisations, and good manufacturing-practice (GMP) and good-distribution-practice (GDP) certificates.	- All the deliverable to enable the go-live on 28 January 2022 were achieved

Task forces

Digital Business Transformation (TDT)

Pillar 2 – Public health activities

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
New scientific, regulatory and telematics curricula developed	2	2	2	2	1
Number of training events advertised to the EU Network	60	40	46	40	77
Number of reimbursed training events to the EU Network	8	12	1	12	0
Number of NCAs that have opened their training for inclusion in EU NTC learning management system	7	10	7	10	15

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Number of users registered to the EU NTC Learning Management System	4,424	5,121	5,290	5,400	5,916
Number of NCA experts registered to the EU NTC learning management system	3,480	3,143	4,297	4,500	4,872

Achievements

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
Establish a digital innovation lab to explore, pilot and develop solutions and processes across the drug regulation spectrum that leverage novel digital technology and artificial intelligence, to support increase in efficiency and regulatory decision-making.	2.2	Review and implement digital business transformation, using analytics, artificial intelligence, and automation methodologies across selected business functions supporting medicines' development, evaluation, supervision and administrative processes Set up an innovation lab	**On track**	The DigiLab was launched in October 2021 with a news item and featured topic intranet page and a governance structure. The Digital Acceleration Leadership Team, composed of senior managers, was set up to help prioritise business opportunities where digital innovation brings most value to the Agency - the focus of the DigiLab. Ongoing DigiLab projects are exploring the application of virtual reality to transform the way we deliver training and upskill staff and the

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				application of QR codes, with the aim to reduce paper waste and improve user experience when searching for information. Other DigiLab projects make use of artificial intelligence to realise efficiency gains in day-to-day operations, or to get easier and faster access to information. The DigiLab pipeline currently consists of 11 projects.
Establish an EU collaboration on AI with other Agencies in the EU Network.	2.2	Develop and promote AI community Share knowledge and increase maturity Collaborate for the implementation of common AI initiatives and projects	**On track**	During 2021, 10 active agencies (EMA, EFSA, EUIPO, CDT, ECDC, FRA, CEDEFOP, ESMA, EUROFOUND, EULISA) in the network, the EC, and more than 10 guest organisations have participated in the community. The community hosted 8 community meetings and 3 EU talks, where more than 15 different AI-related topics were discussed, such as malicious uses and abuses of artificial intelligence; insights on the legal, societal, and ethical considerations of AI; role of AI in fake news and disinformation, and Neural Machine Translation.
Develop capacity and expertise across the regulatory network through curriculum development and knowledge-sharing initiatives on data science, digital technologies, and artificial intelligence-related solutions, products and endpoints, and their applications in the regulatory system.	2.3	Develop a future state learning delivery model and landscape that serves new and existing audiences, in cooperation with the EU-NTC Deliver training on AI	**On track**	EU NTC Learning Ecosystem roadmap and approach was adopted by EXB in July 2021. EU NTC Strategy 2022-2025 prepared for endorsement – the strategy outlines a number of key strategic objectives for the coming years, to allow the EU NTC to evolve to meet future needs and keep up with the changing needs of learners. These included: Extension to new target audiences; strengthening curriculum development; strengthening services and tools for course

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				developers, and strengthening the digital learning ecosystem, both tooling and platform. Work is ongoing on an enhanced learning development toolkit (RfS); on implementation of improvement actions relating to the EU NTC LMS; working with International Affairs and the I-Division on opening up EU NTC training to external audiences, and preparation of survey of learning needs. Collaboration is ongoing with Big Data SG to develop AI training and development of an AI module as part of the Digital Academy in pilot, which will extend to other digital topics.
Develop the integrated evaluation pathways for the assessment of combination products / companion diagnostics.	3.4	Facilitate a regulatory pathway between notified bodies and medicines' regulators	**Delayed**	In view of resource constraints and MDR/IVDR coming into application respectively, in 2021 and 2022, priority is on the implementation of the MDR/IVDR. Also, although not yet a formal integrated pathway in place, EMA has established regular collaborative interactions through notified bodies working groups for the MDR/IVDR implementation (e.g., Art 117 workshop, CDx consultation WG, notified body opinion template).
Identify and enable access to the best expertise across Europe and internationally.	3.4	Map all current working groups (i.e., at EMA, HMA/CAMD, NCA, EC) working on medical devices and in vitro diagnostic, where there is a connection to medicinal products and identify common tasks/topics. Establish a more formal link between the current	**On track**	EMA activities are mapped. Enhanced collaborations and dialogue on MDR and IVDR implementation with EC, MDCG WGs (such as Art 117 TF, and Borderline TF), setting up of CDx Consultation Working Group, EMA-CMDh small group on MDR, and expansion of Art 117 TF to medicines regulators. Updated Q&A providing practical

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
		groups and the experts at the NCA's facilitating systematic interaction.		considerations concerning the application of the MDR. Publication of final 'Guideline on quality documentation for medicinal products when used with a medical device'. New version of the initial MAA and variation AFs and related eAFs to reflect the new MDR and IVDR. Publication of draft procedural guidance on Companion diagnostics consultation procedure by Notified body for public consultation and start running the procedure.

Pillar 3 – Programmes and projects

Project title	Long-term objective	Achievements/results in 2021
ECTD4: Implementation and adoption of eCTD v4.0 standard	The project aims at implementing the next generation standard, defining the message for exchanging regulatory submission information electronically between applicants and Regulatory Authorities.	The project has been reported and will start in January 2022.
IRIS: Platform to support regulatory business processes of the Agency	The IRIS platform will provide a single space for applicants and EMA to submit requests, communicate, share information, and deliver documents concerning regulatory and scientific procedures.	- Processes supporting Marketing status and Inspections has been delivered.

Data Analytics and Methods (TDA)

Pillar 2 – Public health activities

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Number of MLM ICSRs created	13,275	9,676	9,950	10,000	9,193
Number of healthcare data sets to which EMA access and therefore its committees can integrate analyses into assessments	3	3	3	6	3

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Number of individual reaction-monitoring reports supplied to the Member States according to the agreed timelines and data quality indicators	95%	99%	97%	94%	91%

Achievements

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
Progress the development, construction and delivery of the Data Analytics and Real World Interrogation Network (DARWIN EU).	2.1	To initiate a project to deliver DARWIN EU, including the sourcing of an external technical coordinator. A pilot with the European Health Data Space initiated.	**On track**	The DARWIN EU project was established in Q4 2020. As part of the DARWIN EU project governance, the DARWIN EU Advisory Board has been established and held its first meeting in June 2021. The Advisory Board will provide strategic guidance to the DARWIN EU project. In June 2021, a tender for a service provider to act as the DARWIN EU Coordinating Centre was published, and the dedicated DARWIN EU webpage was launched. The evaluation procedure for the appointment of the

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				DARWIN EU coordinating Centre has concluded. The contract signature is expected in February 2022. The EC has postponed European Health Data Space (EHDS) pilots to 2022.
Deliver a sustainable platform to access and analyse healthcare data from across the EU (Data Analysis Real World Interrogation Network -DARWIN). Build the business case with stakeholders and secure funding to establish and maintain a secure EU data platform that supports better decision-making on medicines, by informing those decisions with robust evidence from healthcare.	2.1	To initiate a project to deliver DARWIN EU, including the sourcing of an external technical coordinator. A pilot with the European Health Data Space initiated.	**On track**	As above
Launch and carry out CHMP pilot for individual patient-level data from clinical trials.	2.1	Pre-pilot of at least one marketing authorisation application in 2021	**On track**	Interim lessons learned from the MAA application pre-pilot for analysis of raw data were presented at the CHMP strategic review and learning meeting in May 2021. An ad-hoc advisory group on raw data was successfully established in July 2021, to assist with the pilot design and examine the practical aspects of raw data

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				analysis. The development of a draft pilot protocol for a full pilot of Individual Patient Data from Clinical Trials was postponed to Q1 2022, due to workload challenges. A business consultancy contract to support design of a pilot was signed in Q4 2021.
Work with international partners to develop roadmap and guidance.	2.1	Agreement of roadmap for international regulatory collaboration on real world evidence.	**On track**	Good progress is being made with the US FDA and Health Canada on developing a Real-World Evidence Collaboration Roadmap. Four planning meetings were held during the reporting period.
Collaborate with international initiatives on Big Data. Support the development of guidelines at international multilateral fora, a data standardisation strategy delivered through standards bodies, and bilateral collaboration and sharing of best practice with international partners.	2.1	Develop a set of documents to describe and establish a data standards development strategy, followed by a roadmap. Develop international guidelines to improve innovative drug development.	**On track**	The Data Standardisation Strategy stakeholder workshop was held on 18 May 2021. Based on the feedback received from stakeholders, the Data Standardisation strategy was further developed and consulted through the EU Regulatory Network. The final joint HMA-EMA Data Standardisation Strategy (DSS) was endorsed by the Heads of Medicines Agencies in November and EMA Management Board in December 2021, and published on 17 December 2021. Thereafter it was published on EMA and HMA websites.

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				ICH E20 members reviewed the impact of adaptive designs on the ICH M11 standard clinical trial protocol in April 2021. ICH M15 on General Considerations for Model-Informed Drug Development (MIDD) was established on 25 November 2021.
Work to develop and implement an EU framework.	2.1	Consult stakeholders on data elements to be used as real-world meta-data for regulatory purposes.	**Completed**	The technical workshop on real-world metadata for regulatory purposes was held on 12 April 2021, to gather stakeholder's feedback on: the list of metadata; options for metadata collection and maintenance processes; a proof-of-concept catalogue of data sources and metadata. Industry consultation on the new metadata list is planned in Q1 2022
Establish an EU framework for data quality and representativeness. Develop guidelines, a strengthened process for data qualification through Scientific Advice, and promote across Member States the uptake of electronic health records, registries, genomics data, and secure data availability.	2.1	The final guidance on studies from registries published.	**Completed**	The procurement process to select a consortium to deliver a data quality framework for medicines regulation was finalised in Q3 2021 and the specific contract was signed in Q4 2021. The registry-based studies guideline was published on 26 October 2021. Experience gained from CHMP qualification opinions for two networks of registries, and input collected during five workshops on specific patient registries organised by the

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				Agency, fed into the final guidance. This guidance contributes to transforming of the data-driven medicines regulation foreseen in the Big Data Steering Group Workplan, which implements the Network Strategy to 2025.
Enable data discoverability. Identify key meta-data for regulatory decision-making on the choice of data source, strengthen the current ENCePP resources database to signpost the most appropriate data, and promote the use of the FAIR principles (Findable, Accessible, Interoperable and Reusable).	2.1	Initiate a project to enhance the EU database of real-world data resources (ENCePP database).	**On track**	The Real-World Metadata project (MINERVA) was initiated in 2020 and was completed in December 2021, with the good practice guide on metadata for data discoverability and study replicability approved by the Agency. A survey of ENCePP community regarding metadata for enhanced ENCePP resources database and observational study catalogue performed in Q3 2021 with survey results were presented at the ENCePP Plenary meeting on 18 December 2021. The enhancement and delivery of a catalogue of real-world data and upgrade of the register of observational studies are within the project scope and are planned for 2022.
Develop EU Network skills in Big Data. Develop a Big Data training curriculum and strategy based on a skills analysis	2.2	Training curricula finalised on pharmacoepidemiology, biostatistics and data science.	**Completed**	The survey on Big Data skills in the EU Regulatory Network was completed in Q2 2021, with clear training priorities identified for

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
across the Network; collaborate with external experts including academia, and target recruitment of data scientists, omics specialists, biostatisticians, epidemiologists, and experts in advanced analytics and AI.		Integrate curriculum on modelling and simulation.		each training curriculum. The pharmacoepidemiology and biostatistics training curricula were finalised in 2020. The Data Science curriculum was adopted by the Big Data Steering Group on 16 September 2021. Market research was launched in September, to judge capacity for a potential procurement for training content development. Based on the market research results, a procurement process to select a training content provider will be initiated in 2022. The drafting of the Modelling and Simulation curriculum was delayed due to COVID-19 activities.
Create and maintain a Health Data Science and AI forum to engage with a diverse set of stakeholders in novel digital technologies and artificial intelligence. This will include the technical, ethical, legal, regulatory, and scientific perspectives of the use of digital technologies, and AI-powered applications.	2.2	Stakeholder workshop on AI held.	**Completed**	The joint HMA/EMA workshop on artificial intelligence (AI) in medicines regulation was held on 19-20 April 2021. The workshop report was published in June 2021, summarising the workshop outputs and the list of prioritised recommendations on AI. Recommendations from the workshop are being implemented in the Big Data Steering Group workplan to 2023.
Develop Big Data learning initiative	2.2	Review of real-world data in marketing	**On track**	The retrospective analysis of centralised

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
with a view to developing guidelines and processes that learn from applications.		authorisation applications from 2018 and 2019 completed and learnings presented to CHMP and Big Data Steering Group. Hold a workshop with stakeholders to learn from Big Data in regulatory submissions.		marketing authorisation applications (MAA) and extensions of indications (EoI) submissions, for inclusion of RWD/RWE in 2018-2019 was completed. Preliminary results were presented to Big Data Steering Group and EMA committees in April 2021. An article summarising the retrospective analysis results was published in Clinical Pharmacology & Therapeutics journal in October 2021. The 'Learnings initiative' webinar for optimal use of Big Data for regulatory purpose was held on 30 November 2021.
Strengthen EU Network processes for Big Data submissions. Launch a 'Big Data learnings initiative' where submissions that include Big Data are tracked and outcomes reviewed, with learnings fed into reflection papers and guidelines. Enhance the existing EU PAS register to increase transparency on study methods.	2.2	Initiate project to upgrade the EU Post-Authorisation Studies Register with agreed meta-data and functionalities to enable posting of protocols and results and complex searches.	**On track**	'The Real-World Metadata project was initiated in December 2020. The enhancement and delivery of a catalogue of real-world data and upgrade of the register of observational studies are within the project scope and are planned for 2022. The stakeholder consultation on changes to EUPAS register was initiated in Q4 2021 and is planned to continue through 2022. The technical implementation of the catalogues started in Q3 2021, with successful deployment of the internal database for

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				catalogues in EMA systems.
Create an EU Big Data 'stakeholder implementation forum'. Dialogue actively with key EU stakeholders, including patients, healthcare professionals, industry, HTA bodies, payers, device regulators and technology companies. Establish key communication points in each agency and build a resource of key messages and communication materials on regulation and Big Data.	2.4	Multi-stakeholder forum on Big Data held.	**Completed**	The second Big Data multi-stakeholder forum was held on 7 December 2021. The event aimed at informing stakeholders about the delivery of the data pillar of the Network Strategy 2025 via the HMA-EMA joint Big Data Steering Group 2021-2023, listening to stakeholder views and discussing areas for collaboration. The workshop report was published on 20 December 2021.
The actions in this Regulatory Science Strategy relating to RWD are included within the 10 actions listed under Big Data. In addition, specific pilots of RWD analytics will be conducted and the work on pharmacovigilance methods will continue: - Conduct a pilot of using rapid analytics of real-world data (including electronic health records) to support decision-	2.4	Final report of PRAC rapid analytics pilot Initiate pilot with one other committee	**On track**	The PRAC pilot of rapid analytics of real-world data was completed in January 2021. The survey to collect PRAC feedback on the pilot results was launched in May 2021. The executive summary and recommendations from the final report were published on the EU PAS register on 22 July 2021. The RWE use cases for PRAC, PDCO, COMP and CAT have been developed and the pilots with these committees have started. The first studies based on in-

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
making at the PRAC and CHMP; - Review of the utility of using electronic health records for detecting drug safety issues (including drug interactions).				house analyses have been delivered to COMP, PDCO, SAWP and CAT in Q3-Q4 2021. The technical specifications for an EMA-funded study on spinal muscular atrophy have been finalised and will be launched in January 2022.
Develop a regulatory framework for emerging clinical data generation.	3.2	Over a three-year period, compile a review of current experience of novel trial design concepts or statistical methods related to estimands, master protocols, Bayesian, single arm trials, indirect comparison Include considerations for special populations Plan guidance drafting or revision, where necessary Implement recommendations, including via training	**On track**	The ICH E20 sections on need for adaptation, principles, examples, and Bayesian aspects were partly or fully drafted by December 2021. The drafting on operational issues and documentation has commenced. The ICH E11A sections on Modelling and Simulation have been extensively drafted, re-drafted and commented upon. Sections on the extrapolation of safety and the inclusion of adolescents in adult trials were fully drafted. The ICH E11A document for Step 1 was finalised in December 2021 and is expected to be published for consultation in Q2 2022. The questions and answers document on complex clinical trials by a cross-Agency drafting group, in collaboration with the European Commission and the Clinical Trials Facilitation Group, was drafted in December 2021.

Pillar 3 – Programmes and projects

Project title	Long-term objective	Achievements/results in 2021
- Lifecycle Regulatory Submission Raw Data	- Report on review of experience with IPD at EMA and other international regulatory agencies and develop protocol for IPD	- Contract signature for business tender to support design of future proof-of-concept pilot
- Lifecycle Regulatory Submission Metadata	- Identify relevant data sources; by defining and standardising the structure of the information (i.e. defining the 'metadata' and supported through relevant standards), the scientific information will become more accessible	- Data Standardization Strategy published on EMA website Q4/2021
- Real-world Metadata, Quality Framework and Catalogues	- Conduct external studies to identify data sources of real-world data; define and collect metadata, and deliver a data quality framework.	*Real-world Metadata and Rapid Analytics merged with DARWIN into one project in November 2021* – Procurement launched for a service provider to establish and operate the Coordination Centre and DARWIN EU Network of Data Holders Q2/2021. - Signature of framework contract EMA/2020/13/TDA 'Strengthening the use of real-world data in drug development – Metadata and Data Quality Framework' in Q4/2021.
- Observational Studies Rapid Analytics	- Increase the amount of real-world evidence and real-time evidence analysis in committee decision making	
- Observational Studies DARWIN EU	- Establish a network of data, expertise, and services to support better decision-making by EMA and NCA scientific committees on the benefits and risks of products via rapid access and analysis and increased reliability; validity and representativeness of EU health data	
- Signal and Safety Analytics	- Increase saleability and efficiency in processing of signals & safety data	- Project kick-off in Q4/2021

Regulatory Science and Innovation (TRS)

Pillar 2 – Public health activities

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2020 result
Innovation Task Force briefing meetings	22	29	27	35	36
Innovation Task Force Art 57 CHMP opinion requests	5	4	0	3	0
Business Pipeline briefing meetings[1]	-	-	-	18	15
Regulatory assistance, including SME briefing meetings[2]	-	-	-	223	180
Requests for SME qualification	487	536	518	532	504
SME status renewal requests	1,334	1,235	1,205	1,362	1,293

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Satisfaction level of SMEs	95%	n/a[1]	89%	80%	98%

Achievements

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
Identification of new technologies via HS and scientific advice activities and their integration into the EU-NTC	3.1	New technologies identified and integrated within EU-NTC	On track	Horizon scanning reports produced (e.g., ICMRA Artificial Intelligence Report, EU-IN Genome Editing Report, Covid-19 scientific reports).
Leverage collaboration between academia and network scientists to address the rapidly emerging regulatory science research questions.	3.3	Emerging regulatory science research questions addressed in support of committee decision-making	On track	The Regulatory Science Research Needs was published in December. Engagement with SAWP and TDA on use of RWE in advice procedures.
Identify, in consultation with research institutions, academia and other relevant stakeholders, fundamental research and associated training/education topics in	3.3	Regulatory training modules developed	On track	Contribution to the Strengthening Training of Academia in Regulatory Science (STARS) project. four modules were developed: Quality, Non-

[1] New indicator introduced in Work Programme 2021
[2] New indicator introduced in Work Programme 2021

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
strategic areas of regulatory science relevant to patients.				Clinical, Clinical and Post-marketing surveillance
Disseminate and exchange knowledge, expertise, and innovation across the network and to its stakeholders.	3.4	Establishment of platform for systematic dissemination and exchange of knowledge and expertise on emerging innovation	**On track**	Identification of new data sources and semi-automatic collection of information as we plan towards an automatic dissemination system. Business case prepared for TRIP platform development and budget secured for 2022.
Integrate EMA's Regulatory Science Strategy into the EMRN strategy, conduct horizon-scanning to ensure understanding of and preparedness for emerging technologies in medicines, identify gaps in expertise and provide continuous training through the EU Network Training Centre.	6.1	RSS integrated within EMAN Strategy Implementation tracked systematically to ensure delivery	**Delayed**	RSS integrated within EMAN Strategy and reflected into EMA's SPD to 2024. Work is currently performed to establish a systematic tracking system.

Clinical Studies and Manufacturing (TCS)

Pillar 2 – Public health activities

Achievements

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
Develop data-sharing principles with stakeholders and provide regulatory guidance.	2.4	Questions and Answers (Q&As) on the GDPR and the Secondary Use of Data for Medicines and Public Health Purposes. Prepare a high-level paper, guiding the Agency and the stakeholders with respect to the use of clinical trial and other health data for the purpose of the	**Delayed**	Finalisation of Q&As put on hold as instructed by EC, to await EDPB guidance on scientific research and secondary use of health data, which is now expected by the end of Q2 2022.

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
		development, authorisation, and safety monitoring of medicines.		
Modernise the GCP regulatory oversight to enable decentralised models of clinical trials coupled with direct digital data accrual.	3.2	Finalisation of ICH E6 (R3) GCP (principles and Annexes 1 and 2).	**On track**	Work on redrafting ICH E6 continues. It is anticipated that the draft Principles and Annex 1 which together will replace the existing E6 will reach step 2 and enter public consultation in Q3 of 2022. The revision of ICH E8 (general considerations on clinical studies was finalised in October 2021. This revision is a key deliverable of the GCP renovation process.
Drive development and adoption of novel practices that facilitate clinical trial authorisation, GCP and HTA acceptance at EU and international level.	3.2	Finalisation of ICH E6 (R3) GCP (principles and Annexes 1 and 2).	**On track**	See also the action above. The ACT EU (accelerating Clinical Trials in the EU) was adopted by the European Medicines Regulatory Network (HMA/EMA/EC) in December 2021.
Establish a multi-stakeholder, neutral platform, to enable new approaches to clinical studies and to position the EU as a preferred location for innovative clinical research.	3.2	Establish a framework, mandate, and objectives for a multi-stakeholder platform for discussion of new approaches for Clinical Studies.	**On track**	The ACT EU (accelerating Clinical Trials in the EU) was adopted by the European Medicines Regulatory Network (HMA/EMA/EC) in December 2021. The establishment of a key multi-stakeholder platform is a key objective of ACT EU.
Work with stakeholders, the EU Medicines Regulatory Network, and the European Commission to promote and facilitate the conduct of	3.2	Using the multi-stakeholder framework from 3.2.1.11, develop action plan and	**On track**	Public workshops on complex clinical trials have taken place and EMA continues to contribute to the

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
complex clinical trials and other innovative clinical trial designs.		workstreams on complex clinical trials.		drafting of Q&As on these topics.
Promote the inclusion of neglected populations, such as pregnant and lactating women, the elderly, and those of diverse ethnicities in clinical trials.	3.2	Use the revision of ICH E8 and E6 to remove barriers and to encourage the inclusion of neglected populations in clinical trials.	**On track**	The revision of ICH E8 - general considerations on clinical studies, was finalised in October 2021. This revised guideline (ICH E8 R1) contains revised wording, supporting the inclusion of these populations in clinical trials.
Define approaches for review of data with international regulators.	4.6	Build on the experience acquired with COVID-19 to establish the approach for future emergencies.	**On track**	A reflection paper on variants has been issued and a discussion with stakeholders and other developers is progressing. In addition, discussions with regulators and ICMRA have taken place with regard to booster doses and vaccines.
Communicate proactively with key stakeholders on benefit-risk, using evidence-based tools to tackle vaccine hesitancy.	4 (additional RSS recommendation)	Interaction with the ECDC and public health authorities and ICMRA	**On track**	Extensive proactive public communication, webinars, and information on EMA website on COVID-19 vaccines. Support to European Vaccine Information Platform (EVIP) and EC. Public stakeholder meetings on COVID-19 vaccines. Product-related communications and safety updates issued. Lancet publication on COVID-19 vaccines. User-testing of COVID-19 information materials. Visual risk contextualisation for Vaxzevria Art 5.3. Additional work in terms of risk-benefit in

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				paediatric population, pregnant women, and about the use of booster doses is taking place continuously. Further webinars, updating of information on EMA websites and press briefings have continued throughout the year.
Engage with public health authorities and NITAGs to better inform vaccine decisions.	4 (additional RSS recommendation)	Attend meetings of the NITAG and contribute.	**On track**	Regular interactions with NITAG, including bi-weekly teleconferences in the context of the pandemic.
Establish a platform for EU benefit-risk monitoring of vaccines post-approval.	4 (additional RSS recommendation)	Set up the platform and conduct first studies.	**On track**	Pilot with the Vaccine Platform has commenced and studies are progressing.

Pillar 3 – Programmes and projects

Project title	Long term objective	Achievements/results in 2021
CTIS – Clinical Trials Information System (formerly EU portal and clinical trials database; renamed including a merger with SUSAR)	The project aims to deliver Clinical Trials Information System (CTIS) to support the harmonisation of the assessment and supervision processes for clinical trials throughout the EU.	- The CTIS was delivered and tested for the go-live at end of January 2022. - Due to the go-live in January 2022, a hyper care contract had to be put in place in 2021, and the need for infrastructure for the CTIS also increased the budget. - The scope was increased to support the Safety assessment regulation on the Clinical Trials for the go-live in January 2022.

Deputy Executive Director Division

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Energy consumption (change in % per workstation)	-3%[4]	n/a[1]	n/a[1]	n/a[1]	n/a[1]
Water consumption (change in % per workstation)	-7%[4]	n/a[1]	n/a[1]	n/a[1]	n/a[1]
Paper consumption (change in % per workstation)	-8%[4]	n/a[1]	n/a[1]	n/a[1]	n/a[1]
Non-recyclable waste produced in restaurant and kitchenette (change in % per workstation)	-5%[4]	n/a[1]	n/a[1]	n/a[1]	n/a[1]
Recyclable waste produced (change in % per workstation)	-22%[4]	n/a[1]	n/a[1]	n/a[1]	n/a[1]
Recycling rate (change in % per workstation)	3%[4]	n/a[1]	n/a[1]	n/a[1]	n/a[1]
Change in carbon emissions from work-related travel (including delegates, missions, trainings and candidates)	-6%[4]	n/a[1]	n/a[1]	n/a[1]	n/a[1]
Overall net CO2 emissions (per workstation)	-14%[4]	n/a[1]	n/a[1]	n/a[1]	n/a[1]

Achievements

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
Develop a common framework/methodology for forecasting demand data for medicines in the EU/EEA	1.1	Common Framework methodology for forecasting demand data for medicines in the EU/EEA developed and adopted by the network	Completed	Reflection Paper on forecasting demand data in the EU/EEA published in early June 2021.

Advisory functions (International affairs, Internal audit, Legal department)

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Interactions with FDA	584	454	644	700	696

[1] Due to EMA's two-stage relocation to Amsterdam the environmental performance indicators cannot be estimated. During 2019-2021 EMA will occupy 3 buildings; 30 Churchill Place in London (Jan-Feb 2019), Spark building in Amsterdam (Mar-Dec 2019) and EMA building in Amsterdam (Jan 2020 to 2021 and beyond). To provide meaningful environmental targets, at least one base year of gathering data with regular building occupancy is required and therefore it is envisaged that the new environmental indicators will be set up only for 2022.

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Interactions with PMDA/MHLW	122	96	132	150	117
Interactions with Health Canada	175	125	224	200	138
Interactions with any other stakeholders	734	506	866	700	920
Number of information and/or document exchanges	920	461	988	900	976
Number of teleconferences organised	172	142	235	150	230
ICMRA executive committee and full membership TC	n/a	n/a	52	10	30
International stakeholders' visits (fellowships, experts, observers)	n/a	n/a	1	25	3
Organisation of International awareness sessions	n/a	n/a	0	2	0

Pillar 2 – Public health activities and Business Services

Achievements

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
COVID-19 and ICMRA secretariat	1.1	Continue demonstrating leadership of ICMRA: regulatory convergence and in particular, vaccine safety monitoring collaboration Regulatory communication	**On track**	- Significant effort devoted to COVID-19 response, including wide range of collaborative projects. In addition to the 7 ongoing collaborative workstreams and 2 support workstreams for governance & membership and communications, 2 new workstreams were initiated: COVID-19 Clinical Trials Working Group and Pregnancy and Lactation Working Group Six key public statements on COVID-19 vaccine confidence, transparency and data integrity, product quality knowledge management system, Emergency Use Approval deep dive report, statement on need for continued focus on COVID-19 therapeutics, and reflections on the regulatory experience of remote approaches to GCP and GMP regulatory oversight during the COVID-19 pandemic; COVID-19 technical workshops (vaccine safety, pregnancy & lactation, 2 x vaccine development) - Start of the EMRN (European Medicines Regulatory Network)

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				lessons-learnt exercise - regulatory agilities and flexibilities
Nitrosamines	1.1 5.5	Participation in Nitrosamines International Steering Group (NISG)	**On track**	- Continuous collaboration with international regulators on identifying new medicines containing Nitrosamine impurities, new Nitrosamines acceptable intakes, corrective action and preventive actions and supporting safety information, and sharing of Safety Working Party report through participation in the Nitrosamines International Steering Group (NISG). - Information was exchanged on 32 different products containing nitrosamine impurities
Extension of US MRA	1.1 5.5	Extension to vaccines and vet medicines	**On track**	'SUPPORT TO THE EXTENSION OF THE MRA FOR VETERINARY PRODUCTS: - Agreement reached for extension of the scope of the MRA to veterinary medicines once 14 MS (9 dual and 5 vet only authorities) would be assessed by FDA and FDA Center for Veterinary Medicines (CVM) has been recognised by EU. - Progress with capability assessments for single (veterinary only) Competent Authorities (some audits of Vet authorities were delayed or not completed; however, not expected to impact on MRA potential implementation date). - FDA (CVM) not yet recognised by EU but very good progress has been made and only few clarifications pending regarding FDA implementation of corrective and preventive actions (CAPAs) from EU audit. - Input to EC on establishment of timeline for implementation of MRA for veterinary products. SUPPORT TO THE EXTENSION OF MRA TO VACCINES AND PLASMA DERIVED PRODUCTS: - No practical progress on this (COVID-19 prevented joint inspections). Joint Sectoral Committee in October agreed to restart this work

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				(exchange of inspection plans and set up technical working group). Initial discussions took place with FDA on that regard. SUPPORT TO MRA HUMAN RELATED ACTIVITIES: - Internal discussions with GMDP IWG and with FDA on (proposals for) improvement of functioning of MRA Human regarding exchange of GMP documents (in the absence of GMP certificates from FDA); further to JSC meeting in October, discussions have been formalised with FDA and work is ongoing to explore possibility of a 'cover letter' template which would compile all information needed by EU in a single document. - Agreement to set up a technical group to discuss redactions in Inspection Reports (both EU and FDA IRs). - Discussions with GMDP IWG and informal discussions with FDA on recognition of third country inspections. - Discussion on pre-authorisation inspections put on hold at EMA request. Meeting of Joint Sectoral Committee (EC, EMA, FDA) took place in October where above topics were discussed and actions/next steps agreed.
Article 58 – EU-M4all	1.2	Support to developers and promotion of parallel art 58 and centralised submissions	**On track**	- Review the SA for EUM4all with stakeholders (WHO, SA, international affairs department) in relation to WHO involvement, nomination of experts, training material needed and optimisation of the process, and templates and support to ongoing procedures. Revision of the pre-submission meeting form to prompt applicants to consider the possibility of a parallel application for EUM4all and CAP.

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				- Revision and simplification of the eligibility process and CHMP templates to confirm/deny eligibility to EUM4all. - Support to WHO in their decision to recommend Mosquirix for broad deployment in sub-Saharan Africa. - Meetings with 2 Scientific Opinion Holders to understand any bottleneck in the process. - Input to Product team tier2 champions meeting. - Up-to-date tracking of National Marketing authorisations.
Develop international collaboration and reliance, including through Confidentiality Arrangements.	6.5	Update existing and putting in place new confidentiality arrangements	**On track**	- Finalisation of confidentiality arrangement with Brazil and 13 ad-hoc Confidentiality Arrangements for exchange of information on COVID-19 signed, as well as three ad hoc CAs on nitrosamines and one on the dengue vaccine. Strategy for future CAs agreed with Commission. - As of the end of 2021, seven formal requests for Confidentiality Arrangements have been received by EMA
Capacity building Provide assistance to candidate countries (IPA), to align their standards and practices with those established in the European Union, and to further foster their integration process.	6.1	- Increased visibility of EMA - Training on acquis Communautaire of candidate and accessing countries	**On track**	- 10 webinars delivered in three virtual training sessions attracting 300+ participants with 2/3 from IPA countries - Unable to deliver face to face training due to COVID-19 travel restrictions - Planning of future activities for IPA in 2022 - five contact points teleconferences on exchange of information
Supply chain	5.2	Work with project on shortages, on API with priority countries China project on API	**On track**	- Regular participation and input to Global Shortages and API TCs/discussions - Streamlining of the process for exchanges on shortages with FDA - Support to EC for China API project
Support to priority countries	5.2	India and Russia joining PIC/S and ICH, GMP and GCP	**On track**	- Engagement limited to COVID-19 related activities - Russia application to PIC/S ongoing; EU-India Joint Expert Group on

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
		improved compliance		Ayurveda established (ToR and group members agreed) and ready to start its activities beginning of 2022 - Enhanced cooperation activities with Ukraine discussed and agreed
OPEN project	6.5	Active collaboration of selected regulatory authorities in CHMP and European Task Force for COVID-19 MEDICINES	**On track**	- five authorities involved (TGA, HC, MHLW/PMDA, Swissmedic, WHO) - 36 experts and 23 observers participating - nine vaccines (including 5 authorised) and 10 therapeutics (including 6 authorised) reviewed/assessed under the OPEN Initiative - Analysis of the first year of the pilot, including a survey to non-EU regulators, CHMP/ETF, applicants and EMA, and presentations of the preliminary findings to CHMP and MB - Participation of WHO in the OPEN pilot facilitated the EUL of all five EU approved vaccines, with EMA as regulatory authority of reference
Active participation in WHO activities, international fora, and communication to stakeholders, including but not limited to ICDRA, DIA, ICH, IPRP.	1.1	Promote convergence of global standards and contribution to international fora	**On track**	- Participation in IPRP, ICH meetings - nine ICH meetings: 2 Feb, 25 Feb, 15-16 March, 29-30 March, 26 April, 11 May, ICH MC on 9, 15 and 16 November, Virtual ICH assembly on 17-18 November, 3 IPRP meetings on 20 April, 5 October, 22 November - Chairing and presenting at DIA Europe, DIA US and DIA Japan meetings (9 sessions) - Presentation at the ad-hoc ICDRA week 20-24 September - Participation in the WHO Workshop on PQ and CRP for Accelerated Registration of Prequalified Medical Products - Promoting reliance - participation in the WHO facilitated meeting for registration of Janssen Ebola vaccine - TOPRA annual symposium presentation on reliance, work-sharing, and recognition as 21st

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				century regulatory tools on 22 September - Presentation at the 10th Conference of the Pan American Network for Drug Regulatory Harmonization - Presentation of EMA International for IFPIA International Regulatory Expert Group on 8 November
Enhance mechanisms to facilitate local observers' participation in inspections carried out in non-EU countries	5.3	Improve application of equivalent standards of good manufacturing and clinical practices throughout the world	**On track**	- Joint WHO/EMA inspection in Russia - Sharing inspection reports with several authorities and discussion with Brazil - Joint SAHPRA/Health Canada/EMA in the US - WHO inspections in China at request of EMA
Promote increased international cooperation in the area of supply chain security, in particular through efforts to coordinate and integrate initiatives at the level of ICMRA.	5.1	Assure product supply chain and data integrity	**On track**	- Pharmaceutical Quality Knowledge Management System (PQKMS) developed and hosted the ICMRA-Industry Manufacturing Capacity Workshop for COVID-19 and beyond (workshop took place on 6-7 July). Two pilots were created after this workshop to enable manufacturing capacity and streamline regulatory assessments: Collaborative distant/remote and local inspections, and Collaborative assessment of COVID-19 related post approval CMC changes, including PACMPs. - EMA led finalisation and publication of the interoperability recommendations of ICMRA supply chain group.
Increase the number of opportunities for non-EU regulators, in particular those of candidate and potential candidate countries, to participate in scientific and regulatory training activities[1].	6.1	Support training and capacity building of non-EU regulators	**On track**	- Contribution to the project on Expansion of the EU NTC learning ecosystem (internal discussions and input to consultants regarding extension to International Regulators). - Agreed to have International Regulators as the pilot project for the extension of EU NTC to other stakeholders. Discussion with EU NTC

[1] Including contributing to the IPA activities of the European Commission (Instrument for Pre-accession Assistance) and a virtual meeting/training related to IPA will be organised in Q1 2021.

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				colleagues regarding development of the International Regulators Curriculum Framework.
Explore and foster opportunities for the EU Network to contribute to scientific and regulatory training events organised outside the EU.	6.1	Support training and capacity building of non-EU regulators	**Suspended**	The action is currently suspended due to resource constraints linked to the COVID-19 pandemic.
Re-start of the International awareness sessions for regulators	6.1	Increase the awareness of the EU system through dedicated sessions	**Suspended**	The action is currently suspended due to resource constraints linked to the COVID-19 pandemic.
Collaborating with EC/EMA to develop a joint long-term strategy for targeted and effective training programs on pharmaceutical GMP/GCP in China and India.	6.1	Capacity building through training	**Suspended**	The project has been suspended.
ICMRA secretariat management, including operational and financial contribution to bi-annual ICMRA meetings.	1.1	Communication	**On track**	- The frequency of COVID-19 Policy TC changed from bi-monthly to monthly - Active engagement with membership maintained through written procedures for approval of documents, e.g. joint ICMRA-WHO statement on transparency, PQKMS, vaccine confidence, etc.; - Weekly updates on ICMRA activities and information of general interest, including updated spreadsheet on vaccines and therapeutics - six new Associate Members joined ICMRA in 2021 - six Expressions of Interest to join ICMRA have been received Meetings organised: - 10 Executive Committee meetings (2 were cancelled) - 15 COVID-19 Policy Teleconferences

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				- two ICMRA Plenary meetings on 28 April and 2 December 2021 - one ICMRA Summit on 1 December 2021 (first one since 2019) - two ICMRA Covid-19 Vaccine workshops
Communication of information, answer to queries, internal coordination. Monitoring of the matrix of the tracking of interactions. Organisation of cluster meetings, teleconferences and preparations of visits, missions' preparation, support to FDA, Health Canada, PMDA and other international partners, fellowships and expert visits. Selected redaction of documents.	1.1	Support to the International Affairs Division and its specific activities	**On track**	- Update of four guidance documents, including the International guidance for sharing documents and on Parallel Scientific Advice - Relaunch and publication of the 'International affairs highlights' newsletter, after one year following the BCP period related to the COVID-19 crisis - Organisation of the 2nd IPA training with full support to the organisation of 10 virtual webinars - Work programme report on the overall 2020 activities - Organisation of 112 cluster meetings, teleconferences - 52 documents redacted - 696 interactions with FDA - 138 interactions with Health Canada - 117 interactions with PMDA/MHLW - 920 interactions with other stakeholders - full tracking of international affairs interactions in 2021
Support EU and EU/MRA team meetings	5.2	Reliance and supply chain integrity	**On track**	Participation and support to all MRA meetings
Collaboration in the establishment of the African Medicines Agency (AMA)	6.1	Capacity building through providing adequate guidance	**Delayed**	In May, the EC announced the intention to back with 1 billion euro the Team Europe initiative on manufacturing and access to vaccines, medicine and health technologies in Africa. The Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) contacted EMA in the context of their BACKUP programme, commissioned by the German Federal Ministry for Economic Cooperation and Development (BMZ), to support local vaccine manufacturing in Africa and the future AMA. EMA asked to consider

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				providing support to this initiative by conducting joint assessments of vaccines (involving CHMP Rapporteurs), training, and providing experience with the EU collaborative model. The AMA treaty entered into force in November 2021. Discussions were held with the African Union (AU), the European Commission (EC) and the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA).
Initial implementation of the EU-DPR	6.2	Assistance and guidance to Internal Controllers regarding data protection obligations (update existing and develop new records, privacy statements, DPIA reports, joint controllership agreements; adopt instruments for international data transfers; conclude appropriate contracts with data processors)	**On track**	- Draft Joint Controllership Arrangement and related privacy statement for CTIS prepared and finalised internally. Consultation process with EC, MSs and sponsor representatives on track. - Draft Joint Controllership Arrangement and related privacy statement for CTIS prepared; internal consultation ongoing. - Administrative Arrangement for personal data sharing with Health Canada prepared and negotiated; submitted for EDPS authorisation, which resulted in authorisation with conditions. - Advice regarding the tender procedure for DARWIN EU Network provided, participation in evaluation committee. Preparation of preliminary DPIA regarding the project. - Advice regarding handling of personal data breach caused by the cyberattack; participation and support provided to Steering Committee and Risk Assessment Subcommittee. - Ongoing consultation and advice on A-Division Data Protection Impact Assessment for the EMA Talent Hub and BI@Admin project. Review of CCTV policy update.
Full implementation of the EU-DPR and monitoring of compliance	6.2	As necessary, update and adopt further annexes to	**On track**	- Advice and preparation of records and privacy statements (e.g., https://www.ema.europa.eu/en/about-

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
		0055-2020 Internal Guidance of Personal Data Protection. Update, develop and deliver data protection trainings on request or upon own initiative.		us/legal/privacy-statement/central-register-data-processing-records) - Tailor-made training presentations given by the Data Protection Officer and Data Protection Coordinators - Co-drafting and finalisation of two Joint Controllership Agreements (CTIS, UPD) - Co-drafting and finalisation of a Data Protection Impact Assessment (CTIS); review of on-going Data Protection Impact Assessment (DPIA, Microsoft Office 365); providing initial reflections on new DPIAs (EudraVigilance; use of raw data for regulatory purposes) - Major contribution to strategic activities such as drafting the revised Cloud strategy and the tender for DARWIN EU platform - Providing reflections on the use of artificial intelligence and RWE data in regulatory decisions - Analysis of the conditions for compliance with EUDPR in respect of COVID-19 checks for visitors accessing the EMA building, also in respect of prevailing practices amongst EU institutions and bodies - Negotiation of an Administrative Arrangement with Health Canada and filing with the EDPS: authorised with conditions, but no implementation due to Health Canada's refusal to accept some of the requirements imposed by the EDPS - Monitoring of Case 2021-0165 regarding EDPS audit on Executive Director's decision on the Article 25 restrictions (published in the Official Journal): audit closed with the outcome that EMA is compliant

Significant efforts by the International Affairs were also devoted to the development of international collaboration and reliance (including Collaborative Registration Procedure (CRP)), to the collaboration with WHO and EAU on tuberculosis and to the development and implementation of pregnancy strategy with FDA and MHRA.

Stakeholders and Communication Division

Pillar 2 – Public health activities

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Number of cases of patient/consumer engagement[1] in EMA (medicines-related) activities	493	769	594	600	485
Number of cases of healthcare professionals engagement[1] in EMA activities	212	212	176[2]	200	202
Number of professional membership organisation events attended by participating Agency staff[3]	-	-	-	30	27
Number of sessions with Agency representatives[4]	-	-	-	136	138
Number of messages circulated via 'Early Notification System'	440	411	612	1,100	1,206
Number of EMA communications pro-actively sent to stakeholders	175	128	178	200	182
Number of EPAR summaries and EPAR summaries updates published	343	286	297	250	239
Number of summaries of orphan designation published	169	117	154	120	167
Access to documents, requests received	822	783	597	650	710
Access to documents, documents released	2,422	1,429	1,024[5]	1,300	1,136
Requests for information	7,554	7,200	7,055	9,000	12,500
Number of documents published on the EMA corporate website	4,840	9,012	5,963	7,500	6,712
Number of pages published and updated on the EMA corporate website	6,307	3,383	2,511	3,500	3,064
Number of press releases and news items published	183	143	217	170	220
Completed requests for interviews and comments by media representatives	1,517	1,476	1,770	7000	5,000
Number of reports, brochures, leaflets laid out or printed, social media visuals	85	206	357	500	989

1 These include any interactions that a patient, consumer, carer, or healthcare professional may have with the Agency, such as acting as a committee/working party member, reviewing a package leaflet, being invited to a SAG meeting, or any other activity which entails engagement from both sides.
2 Revised 2020 final figure.
3 New indicator introduced in 2021 Work Programme.
4 New indicator introduced in 2021 Work Programme.
5 2020 figure updated from dataset completed in February 2021.

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Satisfaction level of patient and consumer organisations	n/a[11]	n/a[1]	90%	90%	93%
Satisfaction level of healthcare professional organisations	n/a[1]	n/a[1]	92%	90%	94%
Triage of incoming requests received via AskEMA within set timelines[2]	-	-	-	100%	100%
Responses to ATD requests provided within set timelines	96%	89%	90%	90%	92%
Responses to RFI requests provided within set timelines	97%	96%	82%	95%	85%
Satisfaction level from patients and healthcare professionals who received a response from the Agency to their RFI	85%	84%	83%	80%	81%
Satisfaction level of partners/stakeholders with EMA communications as per "EMA perception survey for communication"	n/a	n/a	78%	n/a	n/a
Average rating of pages on corporate website during the year	3.1	3.4	3.4	3.4	3.6

Achievements

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
Develop content strategy in key public health areas and hot topics: - Design communication materials and campaigns in collaboration with relevant stakeholders to proactively approach to key public-health areas (e.g., COVID-19 vaccines) - Improve communications for patients, healthcare professionals and other stakeholders, including HTAs and payers - Enhance professional outreach through scientific publications and conferences - Embed best practices in key areas, such as audience	1 (additional RSS recommendation)	Effective delivery of communication materials and campaigns on key topics, with focus on COVID-19	**On track**	*COVID-19* Production, publication and evaluation of content on a daily basis, including regular reporting: - continued refinement of COVID-19 webpage, further development and regular updates in view of queries and lines to take (LTT) - communication by developing Agency's COVID-19 general LTTs (14 updates) distributed to the Network - a record number of external queries responded

[1] Due to BCP next survey expected in 2020
[2] New indicator introduced in 2021 Work Programme

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
research, user-experience design, user and usability testing, social-media strategy, and evaluation of communication activities				- user testing finalised, information material updated accordingly and related scientific publications under preparation - updated information materials from public meetings published (videos and slides) -70 communications on COVID-19 developed and disseminated to key stakeholders in 2021 - weekly / bi-weekly regular coordination calls with communication counterparts in EC, ECDC, Council and national competent authorities *Media relations* - a record number of media queries were received, processed, and responded to - 56 interviews of EMA spokespeople - six ad hoc and 13 regular press briefings organised, focusing on COVID-19 Social media: - over 80% increase in Twitter followers (110,000) due to relevant daily updates, use of visual elements for over 90% of tweets and use of live-tweets, e.g., during press briefings - over 40% increase in LinkedIn followers (215,000) - use of new social media formats, e.g. use

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				of LinkedIn live and participation in Twitter chats - establishment of Emer Cooke's personal LinkedIn account as an influencer *Non-COVID-19* - consolidated approach to scientific publication strategy approved *Corporate website* - corporate website kept up to date, also taking into account user needs, web analytics, feedback and good practices in online communication - based on increased UX expertise, website search improved - expertise in UX was used to support development of clinical trials website and veterinary medicines information website *Communications campaigns* - campaign on European Antibiotic Awareness Day - campaign around safety of vaccines in all EU member states (3 mil. views, 1.2 mil. reach)

Pillar 3 – Programmes and projects

Project title	Long-term objective	Achievements/results in 2021
e-PI set up	This e-PI set-up project for human medicines (CAPs and NAPs) will provide the initial building blocks towards creation of electronic product information (summary of	The set-up project and FHIR standard have been completed and a new project to deliver a pilot will start in 2022.

Project title	Long-term objective	Achievements/results in 2021
	product characteristics, package leaflet and labelling) for EU medicines. Product information is currently only provided in PDF format.	

Information Management Division

Workload indicators

Procedure	2018 result	2019 result	2020 result	2021 forecast	2021 result
Number of Telematics information services provided by EMA	25	25	25	26	25
Number of ongoing Telematics IT projects where EMA is the delivery organisation	3	3	5	10	5
Number of ongoing non-Telematics IT projects where EMA is the delivery organisation	5	8	8	12	8

Performance indicators

Performance indicators related to core business	2018 result	2019 result	2019 result	2021 target	2021 result
Satisfaction of EMA internal and external users	91.92%	80%	93%	80.00%	95.8%
Availability of corporate/Telematics IT systems and corporate website	98.11%	98%	98%	98%	99%

Pillar 3 – Programmes and projects

Project title	Long-term objective	Achievements/results in 2021
DREAM replacement Agency document: Management system end of lifecycle and need to be replaced.	The objective is to replace the Agency Document Management System, which is at the end of its lifecycle, with a modern, flexible, collaborative solution	Project kick-off and contract in place in Q4/2021.

Administration Division

Performance indicators/Forecast activity

Performance indicators related to core business	2018 result	2019 result	2020 result	2021 target	2021 result
Posts on the Agency establishment plan filled	98.3%	98.65%	100%	99%	98%
Total TA staff recruited against vacant posts	29	36	51	90	70
Staff turnover rate (staff leaving against total no. of staff TA & CA)	4.57%	7.25%	4.81%	6%	5.10%
Time to run selection procedures from vacancy notice to establishment of reserve list	-[1]	79% < 3 months	88% < 3 months	100% < 3 months	65%[2]
Revenue appropriations implemented	93.88%	96.29%	104.30%	97%	99.87%
Expenditure appropriations implemented	90.76%	98.56%	98.83%	97%	96.38%
Payments against appropriations carried over from year N-1	90.57%	94.94%	95.49%	97%	92.87%
The maximum rate of carryover to year N+1, of total commitments within the title:					
Title 1	1.23%	2.19 %	4.62%	1%	5.75%
Title 2	16.31%	10.79%	20.71%	15%	24.31%
Title 3	30.21%	29.16%	31.47%	25%	37.59%
Payments made within 30 days' time	97.04%	97.59%	96%	98%	96.6%
Receivable overdue for more than 30 days (including provision for bad debts)	8.10%	7%	6%	<10%	2.89%

Achievements

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
Develop and implement a framework for integrated planning and monitoring activities	6.2	Finalisation of the Human Medicines Division business processes and full implementation of the time and capacity model.	**Delayed**	The time and capacity model applied to the Paediatrics activities did not start in 2021, but only in 2022, due to an unsuccessful procurement process to find a suitable advisor. However, in the context of the planning exercise, the activities were mapped with a template developed and tested in

[1] New indicator introduced in 2019 work programme.
[2] The current average selection procedure time is 2.92 months and it has been influenced by the increase in workload linked to the COVID-19 pandemic and the extended mandate. Specifically, 50% of selection procedures were standard (single post) and their average completion time was 2.78 months; 38% of selection procedures were medium selections (a few posts for multiple requirements) and their average completion time was 2.8 months; 12% were large selection procedures (multiple requirements across the Agency) and their average completion time was 2.9 months.

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				the Administration division.
Consolidate the human resource and talent management strategy	6.2	The strategy will consolidate practices into a coherent system and will lead to continuously improving approaches in domains of staff wellbeing, leadership and management, talent management, and culture.	**Delayed**	- Plan agreed within HR and senior management - Themes/streams identified - Work on refining problems and solutions ongoing, to be finalised by Feb 2022
Implement a competency management framework	6.2	Competency framework (behavioural and technical competencies); revised role descriptions with embedded competency profiles and proficiency levels of competencies leading to higher effectiveness, contributing to job satisfaction and development opportunities.	**Completed**	- Competency framework completed and launched - Competencies have been embedded in revised role description, which will be launched on the 11 January 2022
Digitalise HR-related processes (recruitment, onboarding, appraisal, continuous performance management, internal mobility, career development, succession planning)	6.4	Key HR processes are digitalised and automated to better support the HR teams and enable them to provide a better service with more active and added value tasks to performance and development of our staff members.	**Completed**	1) Performance management processes are now in the EMA Talent Hub: Objective setting, Continuous Performance Management, Probation and Appraisal, Performance Support Plan. 2) Internal mobility processes are now in EMA Talent Hub: Employee profile, internal mobility, mentoring, career coaching concept developed. 3) Personal file is now fully digital

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				4) External training application form will be replaced by Success Factors module Training Planner (changes have been made - awaiting Sharepoint launch) 5) Recruitment module in Success Factors is now linked to the Occupational Personality Questionnaire provider. Recruitment module now also has a chatbot feature.
Digitalise procurement, contract management, risk management and some reporting processes.	6.4	Almost real-time information is available for managers for decision making across contract management, budget, human resource domains. Introducing updated procurement, contract management and risk management processes that reduce processing times and enable automating processes easier access to information.	**On track**	Tooling short-term improvements: - Prioritised and urgent JIRA improvements have been implemented in test environment Tooling long-term improvements: - Tooling for procurement and contract management has been selected after market research
Review project governance in line with Agile development approach	6.2	Put in place a more agile governance by implementing a project planning tool and the SAFE methodology across programmes and projects in the organisation in collaboration with the I Division.	**Delayed**	- New terms of reference have been drafted and finalised in Q3 - Kick-off of the first projects (DADI, PMS and ePI) under the Agile governance as a pilot
New Fee Regulation: optimisation and review of revenue and expenditure process.	6.3	Implementation of the New fee regulation with an optimised and more efficient revenue and expenditure process.	**On track**	EC consultation launched in July 2021, implementation to start in 2022, following extensive financial modelling and data

Action	MAWP Strategic Goal	Expected result	Status	Achievements/results
				gathering, comments, and proposals post-consultation.

Pillar 3 – Programmes and projects

Project title	Long-term objective	Achievements/results in 2021
Administration Digitalisation: Optimisation of the Administration supporting tools	Providing modern digital tools to support administration processes, increasing efficiency of processes and staff (as customers) satisfaction with improved services and reduced manual work.	- BI@Admin – started in 2020, ongoing - Intranet – started in 2021, ongoing - Risk Management – started in 2021, ongoing - Digital Personal File – completed and closed in 2021 - Goals and Performance – completed in 2021

2. (a) Management

EMA is headed by the Executive Director, who is appointed by the Agency's Management Board. The Executive Director is the legal representative of the Agency. She is responsible for all operational matters.

2.1. Management Board

The Management Board (MB) is the European Medicines Agency's governance body. It has a supervisory role with general responsibility for budgetary and planning matters, the appointment of the Executive Director and the monitoring of the Agency's performance.

The Board's operational tasks range from adopting legally binding implementing rules, to setting strategic directions for scientific networks, to reporting on the use of European Union (EU) contributions for the Agency's activities. The tasks and responsibilities of the Management Board are set out in the Agency's founding Regulation (EC) No 726/2004 of the European Parliament and of the Council.

The most significant issues discussed at the Management Board in 2021 included:

- **Response to COVID-19 pandemic:**
    - At each meeting, the Board was given status reports on recent scientific evaluations related to COVID-19 vaccines and therapeutics, as well as on the implementation of the Agency's Business Continuity Plan for COVID-19 procedures.
    - The Board was also informed on ongoing reflections within the EU medicines regulatory network on lessons learned from the initial response to the COVID-19 pandemic and options for further improvement.
    - Revised Rules of Procedure of the EMA Management Board and Scientific Committees were adopted in October to allow, amongst others, fully virtual meetings also in non-emergency situations and hybrid (i.e., remote and in-person) meetings during emergency situations.
- **Development of the Clinical Trials Information System (CTIS) for the implementation of the EU Clinical Trials Regulation:**
    - Throughout the year, the Board was updated on the status of the development of the CTIS by means of monthly reports. At every MB meeting, an oral update on the implementation of go-live plan for the delivery of CTIS was provided to the Board by both EMA and representatives of the Clinical Trials Regulation Coordination Group.
    - An ad-hoc informal meeting of the Board was organised on 23 February to inform Board members on the methodology, preliminary findings, and timeline for conclusion of the independent audit on the new EU Clinical Trials Portal and Database.
    - At an extraordinary meeting held on 21 April 2021, the Board endorsed the final report of the independent audit on the EU Clinical Trials Portal and Database developed by EMA. On the basis of this independent audit report, in accordance with Article 82(2) of Regulation (EU) No 536/2014, the Board officially confirmed to the European Commission that it had verified that the EU Portal and Database have achieved full functionality and met the agreed functional specifications.

- In October, the Board endorsed the CTIS Joint Controllership Arrangement, which describes the processing operations of personal data within the CTIS.

- **Preparation for implementation of the Veterinary Medicinal Products Regulation:**
  - At each meeting, the Board was given status reports on the preparation of the legal acts and IT systems required for the implementation of Regulation (EU) 2019/6.
  - In October, the Board adopted an Addendum to the Cooperation Agreement between EMA and NCAs to adapt it to the new procedures established under Regulation (EU) 2019/6.
  - In December, the Board adopted a revision of the Rules of Procedure of the Committee for Veterinary Medicinal Products to align them with the new provisions of Regulation (EU) 2019/6. At this meeting, the Board also adopted the mandate of a new Advisory Group for prioritisation of the post-go-live improvements to the IT databases required by the new veterinary regulation.
- **Review of activities of the EMA Working Parties:**
  - In March, the Board endorsed a revision of the high-level implementation plan for the review of activities of the EMA Working Parties, incorporating more details on the Operational Expert Groups, temporary Drafting Groups, and Special Interest Communities agreed with the network and the Heads of Medicines Agencies.
  - In October, the Board endorsed a set of high-level recommendations for engagement of the new EMA Domains and Working Parties with relevant European and international stakeholders.
  - The Board was provided with progress updates on the implementation of the revised WP structure by EMA's Implementation Task Force, at the October and December MB meetings.
- **European Commission's legal proposal for extending the mandate of EMA in crisis preparedness and management of medicinal products and medical devices**:
  - The Board was informed by the European Commission (EC) representative about the key elements of the EC legal proposal and regularly updated on the status of the legislative procedure between the Council and the European Parliament.
  - At the request of the Board, an informal ad hoc Management Board meeting was organised on 9 September 2021, to update MB members on EMA preparations for the implementation of the EC legal proposal, which started in parallel with the legislative procedure in light of the requirement for the Agency to start operating the new tasks soon after entry into force of the new regulation.
- **Information Management governance review**:
  - In June, the Board endorsed a revised Information Management governance system, replacing the Telematics governance and based on the Agile way of working, as well as the launch of a pilot to implement the new governance and apply the Agile methodology to a subset of the Agency's Information Management project portfolio. The governance review process had started in late 2020, in order to improve the delivery and maintenance of Information Management projects for EMA and for the EU medicines regulatory network.

- The Board was provided with progress updates on the implementation of the new Agile governance structure and on the Agile pilot at each subsequent Board meeting.

- **Activities of the joint EMA-HMA Steering Group on Big Data:**
  - The Board was regularly informed on the activities of the joint EMA-HMA Big Data Steering Group, which is implementing the ten priority recommendations of the HMA-EMA Big Data Task Force.
  - In March, the Management Board adopted the mandate of an Advisory Board to enable stakeholders to advise on the establishment of the Data Analysis and Real World Interrogation Network (DARWIN EU).
  - In December, the Board endorsed the European Medicines Regulatory Network Data Standardisation Strategy, which sets out principles to guide data standardisation efforts and the adoption of data standards by members of the European Medicines Regulatory Network in Europe and in other international fora.

- **Accelerating Clinical Trials in the EU (ACT EU) programme:**
  - In December, the Board endorsed a joint EC/HMA/EMA paper setting out proposals for the establishment of the ACT EU programme, which aims to strengthen the environment for clinical trials in Europe.

Other topics discussed by the Board in 2021 included:

- **Cyber attack:**
  - The Board was regularly informed on the response to contain and mitigate the impact of the cyber attack against EMA of 1 December 2020 and on the activities and investments to enhance the Agency's IT security operations.

- **Brexit:**
  - The Board was informed about the Agency's activities to implement the EU-UK Trade and Cooperation Agreement and its IE/NI Protocol, with a focus on changes to EMA IT databases and systems, the limitation of participation of UK authorities in EMA's scientific committees and Working Parties, preparedness of Brexit-affected medicinal products to comply with EU acquis, and the flexibilities in the application of the EU pharmaceutical acquis in markets historically dependent on medicines supply from Great Britain (Cyprus, Ireland, Malta and Northern Ireland).
  - The Board's concerns regarding the Agency's previous premises in London, continuously voiced in the past, were once again echoed in the 2020 Annual Activity Report as Emphasis of matter. The Board stressed its concern over the Agency managing a commercial property in a third country and diverting resources from its mission of public health protection, including from COVID-19 activities, and operating outside its remit.

Significant additional items adopted or decided by the Management Board in 2021 included:

- **Activities required by the EMA's founding and financial regulations:**

  The Board's operational tasks include reporting on the use of EU contributions to the Agency's activities. In 2021, these activities involved:
  - adopting the Board's assessment of the Executive Director's Annual Activity Report for 2020;

- adopting the 2022-2024 Programming document, including the 2022 budget;
- adopting the EMA's annual report for 2020; and
- delivering an opinion on the Agency's final accounts for 2020.

- **Revised Fee Implementing Rules:**
  - The Board adopted a revision of the Fee Implementing Rules coming into force on 1 April 2021 and covering changes in fees for pandemic influenza vaccines, human vaccines authorised for preparedness in the context of bioterrorism, and fees for EMA consultations on medical devices.
  - In June, a further revision of the Fee Implementing Rules was adopted to establish 'transitional fees' coming into force on 28 January 2022 for future procedures and activities envisaged in the new veterinary medicines regulation.
- **Internal audit and advisory activities at the European Medicines Agency:**
  - In June, the Management Board was provided with an annual report for 2020 on the internal audit and advisory activities at EMA.
  - In December, the Management Board adopted EMA's Audit Strategy 2022-2024 and the Annual Audit Plan for 2022.
- **2020 EMA Annual Report on Independence:** In March, the Board endorsed the EMA 2020 annual report on independence.
- **Eleventh annual report: MUMS/limited market scheme for veterinary medicines:** In March, the board endorsed the 11th annual report on the operation of the Minor Use Minor Species (MUMS)/limited market scheme for veterinary medicines.
- **Revised EMA Anti-Fraud Strategy and related Action Plan 2021-2023**: The Board adopted a revision of the EMA's Anti-Fraud Strategy and related action plan 2021-2023.
- **Composition of the Pharmacovigilance Risk Assessment Committee (PRAC):** In June, the Board endorsed EMA's assessment of the current composition of the PRAC and of the areas of expertise identified by EMA as beneficial for future PRAC activities, as required by EU legislation and by the Rules of Procedure of the PRAC.
- **EU Telematics Management Board (EU TMB):**
  - A report on the activities of EU Telematics has been provided to the Board at each Board meeting in 2021 by the EU TMB, a strategic governance body principally responsible for establishing the EU Telematics Strategy and providing strategic governance as to its implementation.
- **EMA Cloud Strategy 2022-2025:**
  - In December, the Board endorsed the EMA Cloud Strategy 2022-2025.

2.2. Major developments in 2021

COVID-19 PANDEMIC

The COVID-19 pandemic's impact on the Agency continued throughout 2021, bringing a significant level of workload, further exacerbated by the emergence of different virus variants. EMA continued to

deliver on its mandate, while keeping as one of its top priority the protection of the health and safety of staff, delegates, contractors, and community at large.

EMA focused on COVID-19 related activities while ensuring the highest level of quality in the evaluation and supervision of non-COVID-19 related medicines. The Agency and the EU medicines network joined forces to fast-track the evaluation of COVID-19 vaccines and therapeutics, urgently needed to tackle the pandemic and protect the health of EU citizens.

In 2021, the pandemic also led to the intensification of EMA's communication, media monitoring and social listening activities. The Agency carefully scrutinised public queries and closely collaborated with other EU entities and international public health bodies to identify harmful health advice and to address concerns in a timely manner. Frequent updates on EMA's corporate website for the general public, regular press briefings and media interviews with EMA key experts, as well as frequent social media posts provided the public with factual, complete and up-to-date information about COVID-19 related activities.

REVISED MANDATE FOR EMA

As part of the European Health Union package proposed by the European Commission to strengthen the EU's preparedness for crisis situations and response, the extended mandate puts structures and processes established by EMA during the COVID-19 pandemic on a permanent footing, while entrusting several new tasks to the Agency.

EMA will be tasked with the **monitoring of events, including medicine shortages**, which might lead to a crisis, as well as with the reporting of shortages of critical medicines during a crisis. The Agency will also coordinate responses of EU countries on **shortages of critical medical devices and *in vitro* diagnostics** occurring in crisis situations, after an initial transition period.

EMA will set up, maintain, and manage, by early 2025, a **European Shortages Monitoring Platform** to facilitate data collection and reporting by companies and Member States on shortages, supply, and demand of critical medicines. EMA has also been given the responsibility to coordinate twelve EU expert panels to provide advice to Member States and the European Commission on high-risk medical devices and *in vitro* diagnostic medical devices.

Under its extended mandate, EMA will also facilitate a **coordinated EU-level response to public health emergencies**.

2.3. Budgetary and financial management

Budget overview

The total 2021 budget (revenues and expenditure), as adopted by the EMA Management Board on 17 December 2020, amounted to €385,919,000, representing a 7.78% increase compared to the 2020 initial budget (€358,071,000). One amending budget was processed in 2021, in order to increase expected revenue from scientific applications, decrease revenue from the 2021 EU contributions to match revised expectations for activities related to the Agency's extended mandate, and increase miscellaneous revenue in order to enable regularisation of payments related to the subletting of 30CP. The resulting final budget amounted to €379,288,000.

The draft financial outturn, a surplus of approx. €24.98 million, representing 6.13% of total revenue, was caused partly by higher than budgeted fee-related income being collected at the end of the year, and partly by under-consumption of expenditure appropriations, across all three expenditure titles (more details can be found in Annex II).

Revenue (income from evaluation activities and EU contribution)

As stipulated in the Financial Regulation, budget revenue is based on cash received in terms of fees for applications for marketing licenses for pharmaceutical products and for post-authorisation activities, contributions from the European Union, as well as for various administrative activities.

Total C1 cash revenue entered in the accounts as of 31 December 2021 amounted to €382,156,343.70 (2020: €376,246,022.54).

Of total C1 income, 89.40% derived from the evaluation of medicines and other business-related activities, 9.85% from the European Union budget to fund various public health and harmonisation activities, and 0.75% from various sources (2020: 84.22%/15.65%/0.13%).

Assigned revenue (external, R0, and internal, CL), which is handled outside the adopted budget, totalled €25.45 million.

Expenditure (commitments and payments)

Of the adopted budget (i.e., fund source C1), commitments totalled €365,490,700.73, or 96.38% of final appropriations (2020: 98.83%). Payments totalled €274,400,002.19, or 75.08% of commitments (2020: 79.39%).

Appropriations carried forward from 2021 to 2022

Automatic carry-forward

Automatic carry-forward to financial year 2022, C1 to C8, totalled €91,090,698.54, or 24.92% of appropriations.

Implementation of appropriations carried forward from 2020 to 2021

Automatic carry-forward from financial year 2020 to 2021 (i.e., fund source C8), totalled €75,300,936.06. Payments against these appropriations equalled €69,928,804.85 (92.87%) of appropriations (2020: 95.49%) and €5,372,131.21 were cancelled.

Appropriations from external and internal assigned revenue

External assigned revenue (R0) stems mainly from inducements related to the Agency's new headquarters in Amsterdam. In 2021, €501,960.42 were received, and expenditure amounting to €476,545.27 incurred.

Internal assigned revenue (CL) stems from payments of rent, service and other charges received from the sub-tenant of the Agency's former headquarters in London. This revenue matches the payments made to the Agency's landlord in London. In 2021, €24.9 million were received, and expenditure amounting to €19.9 million incurred.

While R0 and CL appropriations do not expire, the revenue and expenditure must balance over time.

The Agency's available appropriations in 2021 included external and internal assigned revenue. In accordance with the revised Financial Regulation which came into effect on 1 July 2019, this revenue, matched by expenditure appropriations, is managed outside the adopted budget and under separate fund sources, i.e., R0 for external assigned revenue, and CL for internal assigned revenue.

The vast majority of the assigned revenue relates to the Agency's office buildings, with the remainder relating to grants received from the EU budget to fund projects within the IMI and IPA programmes.

Due to the restrictions imposed by the pandemic, these programmes saw no activities in 2021, and hence no expenditure was incurred.

Budget transfers

In line with Art. 26 of the Financial Regulation, the Executive Director may make unlimited transfers within a title and of up to 10% of appropriations from one title to another. Transfers *per se* are not an indication of deficiencies in budget management, but are a necessary tool to adjust the budget in a changing environment; e.g. resigning staff members receiving allowances related to their departure rather than their salaries, increased expenditure due to exchange rate fluctuation, etc.

During 2021, one transfer exceeded the 10% ceiling for transfer between titles, thus requiring Management Board approval. Of the eleven transfers, all involved expenditure appropriations and one also revenue appropriations.

The transferred expenditure appropriations were primarily needed to cover additional commitments for rapporteur payments and scientific studies, due to the increase in the number of scientific applications and the COVID-19 pandemic, as well as IT project development, data management and interim contractor services, as approved by the EXB.

Cancellation of appropriations

Expenditure appropriations should be understood as estimates of requirements, and not as an entitlement to create the corresponding commitments. Being reliant on fee income, as the Agency is, this means that the level of cancelled expenditure appropriations does not indicate delays in the implementation of the work programme, but should rather be considered the result of stringent monitoring of actual revenue and adjustments to the expenditure.

Of the amended budget, expenditure appropriations totalling €13,737,299.27 remained unused, corresponding to 3.62% of final appropriations (2020: €4,315,768.07, 1.17%).

The underuse of commitment appropriations is considered to be within the acceptable range, with 3.19% of appropriations cancelled in title I (staff expenditure), 11.91% in title II (infrastructure and operating expenditure) and 1.61% in title III (operational expenditure).

Payment of interest on late payments

In compliance with the Agency's standard contract, established in accordance with Art. 77 of the Financial Regulation, the terms of payment are 30 days upon receipt of a valid invoice. If these terms are not respected, from day 31 until the actual day of payment, default interest accrues at the rate applied by the European Central Bank to its principal refinancing operations, as published in the C series of the Official Journal of the European Union, increased by 8%[1]. The default interest accrued is paid automatically to the supplier/contractor if it amounts to more than €200 at the time of payment of the valid invoice.

In 2021, 886 payments out of a total of 26,076, i.e., 3.40% of all payments, were made later than 30 days after receipt of a valid invoice (2020: 4.35% of all payments). This resulted in default interest of €5,095.00 being paid to suppliers and contractors (2020: €12,638.45).

[1] Cf. Article 116 of Regulation (EU, Euratom) 2018/1046 of the European Parliament and of the Council

Procurement

The procurement team continues to operate under challenging times. Over the last few years, the Agency has experienced significant changes in its internal and external working environment – including substantial internal reorganisation and the current COVID-19 crisis, all of which have required additional procurement of goods, services and works.

In 2021, the procurement team was heavily involved in successfully supporting strategic developments, like DARWIN (data analytics) or EXPAMED (transfer of the Experts for medical devices). The procurement team is also supporting the I-Division and the significant increase of IT projects and external resources needed, particularly in context of the new mandate.

As a result, the last years have continuously seen a substantial number of procedures run in parallel.

Sixty-three procurement procedures were closed in 2021 by signing a contract (compared to 40 in 2020, + 57%) and 13 were cancelled or closed without awarding the contract.

The procurement activity overview shows a growing trend as of the end of February 2021; EMA had a total of 109 procurement procedures planned (compared to 52 at the same time of 2020, +109%).

Procurement procedures	Closed in 2021	Ongoing	Planned for				Total planned
			2022	2023	2024	beyond	
EMA-only procedures	35	12	43	24	5	29	
Interinstitutional	28	2	5	2	0	1	
EMA-led	*2*	*1*	*1*	*2*	*0*	*0*	
Non-EMA led	*26*	*1*	*4*	*0*	*0*	*1*	
Total	**63**	**14**	**48**	**26**	**5**	**30**	**109**

Regarding the type of procurement procedure used in EMA-led procedures (including interinstitutional ones), negotiated procurement procedures are used in 21% of cases, open procedures are used in 20%, and re-opening of completion has been the case for 39% of procurement procedures.

Procedure type (EMA-led procurements)	Closed in 2021		Ongoing		Planned		Total	
Negotiated 1-15k	4	11%	0	0%	5	5%	9	**6%**
Negotiated >15-60k	1	3%	1	7%	4	4%	6	**4%**
Negotiated >60-139k	2	6%	3	21%	10	9%	15	**9%**
Negotiated without contract notice	0	0%	1	7%	2	2%	3	**2%**
Negotiated subtotal	*7*	*20%*	*5*	*36%*	*21*	*19%*	*33*	***21%***
Open procedure	7	20%	5	36%	20	18%	32	**20%**
Re-opening of competition	21	60%	4	29%	37	34%	62	**39%**
Others/to be decided	0	0%	0	0%	31	28%	31	**20%**
Total	**35**		**14**		**109**		**158**	

A total of 48 procurement procedures are currently planned to be launched during 2022.

Cost and benefits of controls

In 2021, EMA allocated approximately 11 FTEs for control activities (amounting to 1.3 M euros or 0.34% of the Agency's 2021 total budget). These activities were centred on the following areas: integrated quality management, audit, anti-fraud, finance and verification processes, corporate risk

management and self-assessment activities. Considering the positive result of the ex-ante and ex-post control verifications, the absence of critical recommendations stemming from audits, the well-established framework to manage exceptions and the regularity of operations, the overall balance between effectiveness, efficiency and economy of controls is reasonably satisfactory.

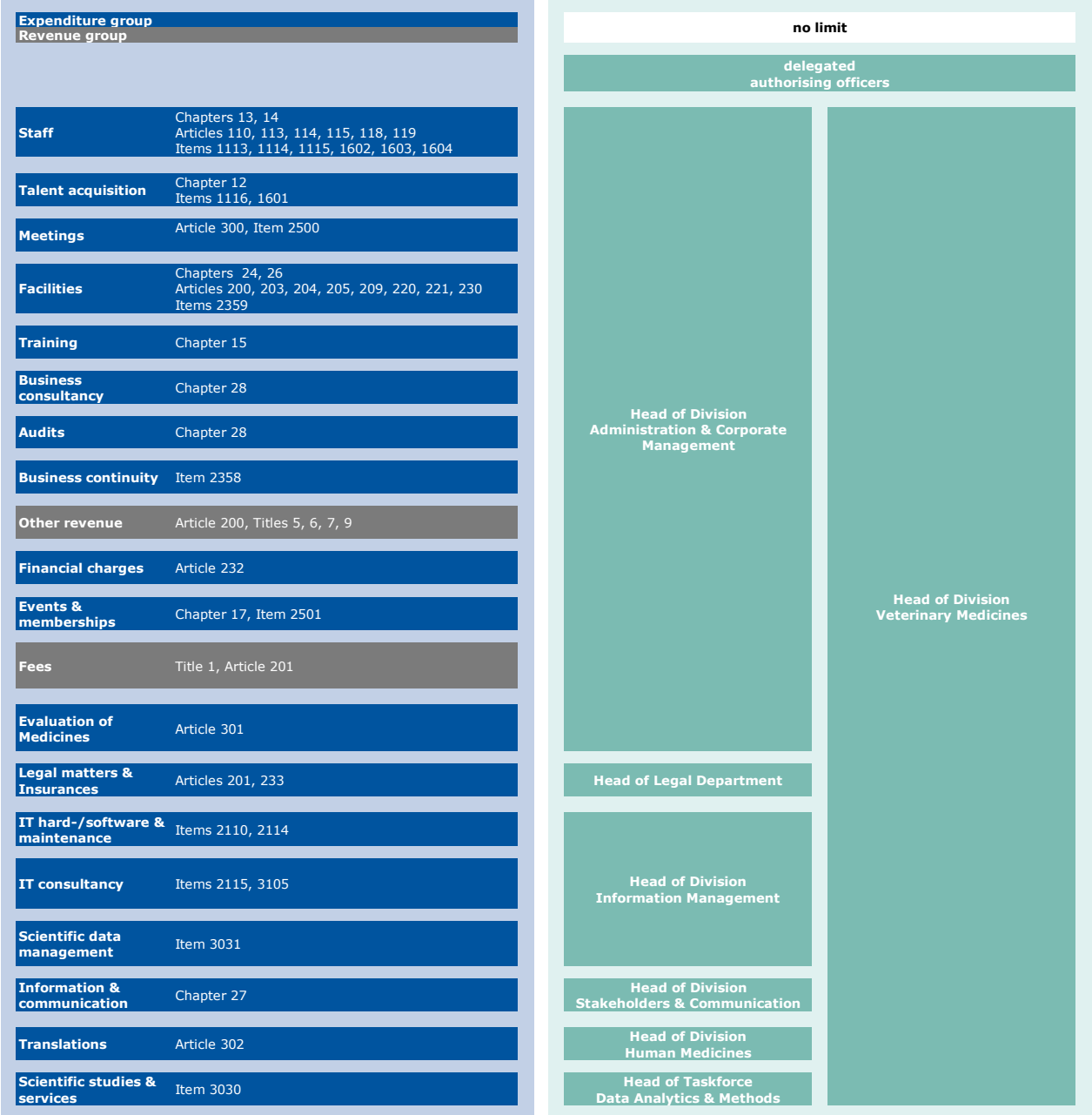
2.4. Delegation and sub-delegation of powers of budget implementation

To enact the most effective management of the Agency, responsibilities are dispersed across various management levels to ensure proportionality and effective decision-making at the lowest possible level, corresponding to the associated risks. To this effect, financial, operational, and staff-related delegations have been put in place at the Agency, without prejudice to the Executive Director's power. These delegations are updated as required, to reflect any relevant organisational or staff changes.

The general principles for financial delegation and sub-delegation are set out in the Executive Decision on internal rules on the implementation of the budget of the European Medicines Agency and the Executive Decision on the charter of tasks and responsibilities of the Authorising Officer by delegation. The latter defines the conditions of delegations and sub-delegations, including reporting requirements and controls. The delegations and sub-delegations are linked to an organisational function and, as such, are issued by default for unlimited time.

The authorising officer by delegation is required to send an annual management report to the Executive Director. This report is an instrument of management accountability within the Agency and constitutes the basis on which the authorising officer takes responsibility for the management of resources, by reference to the objectives set in the work plan, and the efficiency and effectiveness of internal control systems, including an overall assessment of the costs and benefits of controls.

The Authorising Officers by Delegation (see table here below), in line with the requirements of article 3.9 of the charter, provided their report as well as their Declarations of Assurance to the Executive Director, no reservations were reported.



2.5. Human resources management

In 2021, the key developments in staff and human resources management included:

- **Continued modernisation of staff management processes and tools**

As part of the administration digitalisation programme, which aims to modernise processes and tools that EMA uses in staff management, finance and planning areas, the work undertaken in relation to staff management in 2021 included:

- Rollout of Phase 1 and 2 of the Performance and Development (P&D) programme, aimed at implementing a holistic and continuous approach to performance management for all Agency staff, as well as to foster staff development and career path opportunities. A new digital tool to manage all performance and development processes and integrated with the existing LMS and onboarding systems, was launched and became a one-stop-shop for new deliverables brought about in 2021 as part of the P&D programme.

These new concepts focus on either a new way of managing and enhancing staff performance (e.g., a new methodology for setting smart performance objectives, revised probation assessment, revised appraisal assessment, continuous performance management with flexible feedback), or on providing development and professional growth opportunities for EMA staff (e.g., mentoring, internal mobility, development objectives).

In addition, all preparatory groundwork was finalised for implementation of a new competency framework and revised job architecture, applicable from January 2022, which lay a strong foundations for the revision and continuous improvement of talent management processes at EMA

- Digital Personal File: EMA implemented the digital personal file for all statutory staff, replacing the historical paper personal file and scanned working files. The digital personal file is aligned with the principles of Article 26 of the Staff Regulations, manages secure accesses in line with data protection ('need to know principle' for HR roles), as well as an improved structure and nomenclature, and reviewed retention periods following the archiving policy. Staff members are able to view their own digital personal file.

  The digital personal file was rolled out in August 2021 to all active staff members and includes the content of the historical paper personal file content before August 2021.

  The digital personal file uses OpenText, which allows EMA for future continuous efficiency and improvements for administrative decisions workflows, staff notification and filing for defined areas

- **Internal mobility**
  - In 2021, as part of a comprehensive Performance and Development programme, HR looked into the ways of fostering more internal mobility.

    As a result of cross-divisional work, on 31 May 2021, the Guidance on Internal Talent Marketplace has been signed, with the aim of providing an overview of the opportunities for mobility at EMA, and guiding staff members and line managers through the practical application of mobility options for their own career development, and when making resourcing decisions.

    In addition, the internal careers portal and employee profile have been launched within the EMA Talent Hub. To strengthen the concept, the design of training for managers on interviewing skills and giving feedback and career reflection (coaching) was initiated.
- **Recruitment and selection**
  - In 2021, the main focus in the area of recruitment and selection was to fill COVID-19 related positions granted by the EC, as well as those relating to the Extended Mandate.
- **Impact of COVID-19 pandemic on HR management activities throughout 2021**
  - The pandemic continued to affect the Agency's operations for most of 2021, which was conducted in an environment where most of the staff worked from home for most of the year.

    The Agency's COVID-19 Task Force consisted of a dedicated workstream dealing with all matters related to staff and providing advice to EMA management. This task force was subsequently re-modelled into a Steering Group in June 2021.

    Workstream 4 was dedicated to staff matters and significant time was spent to ensure the latest advice and correct measures were in place for staff. A Coronavirus intranet page was used to communicate with staff, in addition to direct messaging. Guidance on teleworking and

presence in the office had to be refined and adapted on several occasions, as the epidemiological situation moved with the spread of the virus and the emergence of new variants. For example, detailed planning was arranged for a return to the office in Q3 of 2021, which had to be suspended in early November due to the emergence of a new variant. A lot of effort was made to ensure the Agency was aligned with other EU bodies through the dedicated EUAN working group and other fora organised in the Netherlands between International Organisations. Concretely, other workload outputs included the delivery of a teleworking framework, frequent and thorough messaging to staff on the ever-evolving epidemiological situation in the Netherlands, to ensure that everyone was fully abreast of the current rules and protocols in place. Advice also included information for colleagues who wished to come to the building due to sub-optimal home-working facilities. Significant focus was put on staff wellbeing, with numerous lunchtime sessions organised, in addition to advice to managers on maintaining contact with their staff and watching out for signals of stress, isolation or burnout.

Several HR implementing rules were adopted in 2021. The list of these can be found in Annex IV.

During 2021, the Agency recruited 114 statutory members of staff (70 TA and 44 CA). 14 national experts were seconded to the Agency, 39 trainees and 117 new interim assignments provided services to the Agency. The total number of staff joining EMA therefore amounted to 284. During the same year, 64 statutory staff members (30 TA, 34 CA) and 16 SNEs left the Agency. 36 interim assignments were also terminated. The total number of leavers was 116.

The rate of resignations in 2021 fell to 48% in comparison to previous year (53%), with a turnover rate for TA and CA of 5.1%.

The occupancy rate amongst temporary agent staff was 98%.

2.6. Strategy for efficiency gains

Despite the increase of activities over the last 5 years, and the pressure in 2021 of the COVID-19 pandemic on staff involved in scientific activities, EMA kept on implementing measures to generate efficient ways of working with the objective of increasing its productivity.

The two main axes to achieve the Agency's efficiency gains strategy continued to be process improvement and digitalisation.

Process improvement: In Q1 2021, EMA finalised the review of its Information Management governance model and, as of June, adopted an agile way of working and started the implementation of the agile governance principles across all layers of technology delivery. By the end of the year, the Agency completed the revision of the portfolio management, allowing better focus on value creation for business and effective delivery process through the systematic implementation of the agile methodology. Thanks to a reduction in steering committees and project boards, the revised governance model grants a reduced administrative burden and clearer accountability.

Digitalisation: In 2021, EMA built on its Digital Transformation, harvesting on the activities carried out by the Digital Business Transformation task force. In particular:

- Provision of strategic support to the regulatory business optimisation process (RBOP);
- Accelerating innovation via the Digital Innovation Lab (DigiLab). DigiLab developed a framework to analyse the processes in view of enhancing efficiency through technology and digital innovation across the Agency. The end-to-end procurement process was one of the most significant initiatives in 2021;

- Exploring artificial intelligence, machine learning and robotics to build pragmatic solutions to existing EMA business needs, with the main objective of gaining efficiency. Successful pilots included:
    - application of artificial intelligence to speed up core business processes, such as the validation of Type I and Type II variation applications to marketing authorisations;
    - identification and redaction of personal data in documents;
    - automation of the triage of incoming requests for information;
    - a chatbot to help stakeholders find information on the EMA website faster.
- Enhancing digital skills and change management expertise to enable digital transformation and support organisational change.

Additionally, the Administration Division progressed the revamping and streamlining of HR procedures, as well as the enhancement of the financial and reporting systems.

2.7. Assessment of audit and ex-post evaluation results during the reporting year

Internal Audit Service (IAS)

According to the risk assessment carried out by IAS in 2019, the main risk factors relating to the Agency's activities were based around the quality of the work delivered and the security of information gathered, dependence on the knowledge of highly specialised staff, and the importance of having a solid IT framework to support the medicines' evaluation, supervision, and pharmacovigilance processes. Well-managed scientific committees and working groups were also key to the functioning of the Agency and its collaboration with different stakeholders.

With these risk factors in mind, the IAS has selected 'HR and ethics', 'IT governance and portfolio management' and 'the management of meetings for EMA's committees, working parties and other groups' as the three main audit topics for the coming years.

The Human resources and ethics audit, planned to take place in 2020, was postponed to 2021 at the Agency's request, due to the COVID-19 pandemic crisis management still in progress and, at the time of writing, the final report is not yet available.

Internal audit capability (IAC)

The following internal audit engagements took place in 2021:

Physical security management

Management of post-authorisation studies, and

an advisory engagement on 'Data governance and management'.

As approved by the Management Board in December 2021, the audit engagement scope planned on 'Review of the Agency operational procedures and measures taken in response to COVID-19' was extended to include the relocation from the UK and renamed to 'Organisation and impact of transitional operational measures taken in the BCP period'.

Based on the results of the 2021 audits, follow-ups, assurance, and advisory activities and analyses performed by the Audit Advisory Function and other sources of assurance, the Head of Audit believes that the internal control systems put in place by the Agency, in the period subsequent to the move of

the Agency from London to Amsterdam, and marked by the COVID-19 crisis, provide reasonable assurance regarding the achievement of the business objectives.

This opinion is issued with due consideration to BCP arrangements and having noted the exceptions described in findings, included in the audit reports issued in 2021, for which the management has prepared improvement action plans and monitors the implementation continuously.

European Court of Auditors

The European Court of Auditors (ECA) adopted its 'Annual report on EU agencies for the financial year 2020'[1] on 21 September 2021.

In the report, ECA expressed an unqualified opinion on the reliability of the accounts and an unqualified opinion on the legality and regularity of the transactions underlying the accounts.

The report includes an emphasis of matter drawing attention to the uncertainty with the lease agreement for the Agency's previous premises in London, and two observations on the legality and regularity of transactions.

The report also includes a follow-up of eight previous years' observations, of which two have been completed, two are ongoing and four are outstanding, one of which is not under the Agency's control.

None of the observations is considered critical. The Agency is putting in place corrective actions to address the procedural issues covered by the audit recommendations.

Observation on the legality and regularity of transactions[2]	
Observation number	**Description**
10	We audited recruitment procedures at EMA and found a weakness in the process for appointing selection panels. The rules applicable to EMA stipulate that its Executive Director (ED) must take the final decision on the appointment of selection panels. In the audited cases, proposed selection panels were approved by means of an e-mail sent by the Head of the Executive Director's Office on behalf of the Executive Director himself without a formal authorisation by the ED. However, the Head of Office did not have the authority to perform that task. This approach is a recurrent practice at EMA and may expose EMA to legal and reputational risks
11	In 2020, EMA amended some prices related to a catering and restaurant services framework contract. However, this contract only permits such a change to be made in 2021. The 2020 price revision was therefore irregular. Consequently, the difference of €78 913 between the tender prices and the amount paid by EMA in 2020, based on the revised prices, is also irregular. The revision was implemented without any signed amendment to the framework contract. This contravenes the provisions of the framework contract and those of the EU Financial Regulation. Furthermore, for an audited payment of €125 954 made in March 2020, EMA did not verify that the amount invoiced by the contractor was correct. EMA was unable to reconcile the charged costs with the provisions and rates set out in the framework contract. This contravenes the EU Financial Regulation.

Follow-up of previous years' observations[3]		
Year	**Court's observations**	**Status of corrective action** (Completed / Ongoing / Outstanding / N/A)
2016-2017-2018	The Agency has been tasked by Parliament and Council with the implementation of the Regulations on Pharmacovigilance (1027/2012) and Clinical Trials (536/2014), requiring the development and implementation of two major pan-European IT systems. In the absence of the necessary own internal resources, the Agency used consultants to an extent that it became critically dependent on	Ongoing

[1] https://www.eca.europa.eu/lists/ecadocuments/agencies_2020/agencies_2020_en.pdf
[2] Ibid, page 220
[3] Ibid, page 221-222

Follow-up of previous years' observations[3]		
	external expertise. There was no adequate control over project development and implementation and project delays and costs escalated. The Agency should speed up the implementation of the mitigating action not only for the completion of the ongoing IT projects but also to get ready for significant new projects.	
2016	The founding Regulation requires an external evaluation of the Agency and its operations by the Commission only every ten years.	Outstanding (Not under the Agency's control)
2017	E-procurement: by the end of 2017, the Agency had introduced e-tendering for certain procedures, but not e-invoicing and e-submission.	E-submission: Completed E-invoicing: Completed
2019	The Agency has consultants employed by providers in their Member States. In such cases, EMA is responsible for verifying contractors' declarations of compliance with EU and national social and labour law (including legislation concerning the posting of workers), as required by the Financial Regulation applicable to the general budget of the Union. The EMA did not do so. The EMA needs to be aware of its host Member State's national legislation concerning posted workers, and to comply with any obligation that this legislation imposes on the receiver of services (i.e. the EMA) provided by posted workers.	Completed
2019	When running a public procurement procedure, contracting authorities must divide contracts into lots, if appropriate, paying attention to the need to facilitate broad competition. Technical specifications must allow bidders equal access to procurement procedures, and may not have the effect of creating unjustified obstacles to open competition.	Outstanding
2019	EMA launched a procurement procedure combining two completely unrelated services in the same lot. This may have limited the number of potentially interested tenderers from submitting an offer for either set of services, thus impairing fair competition. In addition, the Agency extended the duration of contract from four to six years. Extending contracts in this way is only allowed by the Financial Regulations in exceptional and substantiated cases. In this case, there were insufficient grounds for such an extension.	Outstanding
2019	EMA signed a framework contract with three companies for the supply of temporary workers. The price element of the tender specifications had to include an all-inclusive hourly rate conversion factor applied to the gross hourly remuneration of the temporary workers in specific staff categories. However, the Agency did not provide us with any breakdown of the estimated gross staff cost for the interim workers in each requested staff category. As a result, the EMA was not in a position to evaluate whether the service provider's mark-up or gross profit was reasonable in relation to similar contracts.	Outstanding
2019	EMA granted an additional travel allowance to its staff for their move from London to Amsterdam premises. The amount was calculated based on the cost of a business-class ticket instead of the economy-class fare. We conclude that the EMA gave little consideration to the principle of economy in calculating the amount of the additional travel allowance.	Ongoing

2.8. Follow-up of recommendations and action plans for audits and evaluations

Internal Audit Service

No recommendations were open as of 31 December 2021.

Internal audit capability

The current status of implementation of audit recommendations stemming from IAC audits includes no open critical recommendations, and 22 very important recommendations for which the implementation of some improvement actions remains ongoing: one from 2019 audits, 10 from 2020 audits, and 11 from 2021 audits.

Out of these open action plans, only 9 action plans were overdue at year-end, a significant reduction from the previous year, due to a dynamic process of quarterly reviews with Heads of Divisions.

These pertain to improvements in the areas of:

- three actions overdue on 'Information security management' (2020 audit):
  - Purple and Red teaming assessments;
  - risk assessments to be conducted as a regular, enterprise-wide exercise;
  - regular reporting to the board
- six actions overdue on 'IT Outsourcing' (2021 audit):
  - establish a sourcing strategy for vendor identification;
  - review the design of SQIs;
  - provider's performance and compliance to the contract and centralised IT tool;
  - harmonising risk management at all levels.

In 2021, 14 major recommendations were issued (0 critical and 14 very important), as a result of two assurance engagements completed on 'Physical security management and 'Management of post-authorisation studies'.

The 'Physical security management' audit included 10 very important recommendations in the domains of security governance, risk management, security awareness among employees and access control.

For the engagement on 'Management of post-authorisation studies', the IAC issued 4 very important recommendations. These pertained to adopting a PASS strategy, and seeking process workflows improvements e.g., via automation.

In 2021, the IAC closed 15 very important recommendations. The implementation of these actions led to improvements in the performance of controls, including strengthening the agency's security, including periodic and regular reporting on the Agency access control system, updating job descriptions, monitoring workload of activities, ensuring outsourcing procedures are covered end-to end, and ensuring the appointment and training of EMA scientific and SAWP reviewers are strengthened.

Follow-up on recommendations issued following investigations by OLAF

No investigations were opened by OLAF in 2020 and no recommendations were issued as of 31 December 2021

2.9. Follow-up of observations from the discharge authority

As a follow-up to the discharge decision, EMA reported on the measures taken in light of the observations made by the discharge authority for 2019, in its annual report under Article 106(2) of the Framework Financial Regulation. Most of the recommendations made by the European Parliament are currently being implemented. The Agency is not experiencing any significant delay in the implementation of the observations.

The full report describing the observations made by the Discharge Authority and the Agency's responses and measures taken is publicly available on the website of the European parliament.

On 4 May 2022, the European Parliament adopted the decision granting the discharge for EMA's 2020 accounts. This marks the final approval of the budget implementation for 2020, and the decision is based on a review of the annual accounts and the Court of Auditors' annual report.

2.10. Environment management

In 2021, the Agency continued its work towards EMAS registration, in accordance with the approved Environmental Policy and Environmental Management Roadmap 2020 to 2024.

The objectives set for 2021 had the following outcome:

- the Environmental Policy, Environmental Management Roadmap 2020 to 2024 and the Green Group mandate were approved on 14 January 2021;
- the Green Group have resumed activities since 12 March 2021;
- the inter-institutional framework contract for Green Public Procurement (GPP) helpdesk services is in place since April 2021;
- the updated EMA Internal Guidance for Green Public Procurement was approved on 10 June 2021;
- the targets for reducing energy and water consumption of 15% per square meter of lettable floor space have been calculated based on the EMA premises occupied in 2012 being 1, 7 and 11 Westferry Circus in London, with 20,096 sqm, compared with the 2021 occupancy of the EMA building at Domenico Scarlattilaan 6 in Amsterdam, with 33,411 sqm. Both targets were reached with a 45% reduction of energy consumption per square meter and 62.8% reduction of water consumption per square meter.

During 2021, the Agency's Environmental Management System (EMS) was further updated with specifics of the new EMA building in Amsterdam and consumption data becoming available.

As part of the Agency registration to EMAS, an environmental statement will be prepared with reporting of the environmental performance in compliance with the (EC) EMAS regulation 1221:2009, Annex IV, as amended.

More details on EMA environment management can be found in Annex VII.

2.11. Assessment by management

Based on the information provided in the previous sub-sections of this report, EMA Executive Director is of the opinion that overall, suitable controls are in place and working as intended, risks and opportunities are being appropriately monitored and mitigated, and necessary improvements and reinforcements are being implemented, and that no significant weaknesses that may have potential impact on the declaration of assurance of the authorising officer were identified.

2. (b) External evaluations

The latest evaluation of the Agency's operation pursuant to Article 86 of the Regulation (EC) No 726/2004 was published on 31 August 2021 and is available in the form of a report from the Commission to the European Parliament and the Council, on the experience acquired with the procedures for authorising and supervising medicinal products for human use, in accordance with the requirements set out in the EU legislation on medicinal products for human use (COM/2021/497 final). The study assessed the extent to which the current marketing-authorisation system for medicines met its objectives in the period 2010-2017. This report links to the pharmaceutical strategy for Europe and will inform its implementation, with regard to possible legislative and non-legislative measures. It also complements the ongoing revisions of: (i) the EU regulations on medicines for rare diseases and on medicines for children; and (ii) the Regulation on the European Medicines Agency's fee system.

The following studies evaluate legislative frameworks and other activities implemented by EMA:

- **European Commission's evaluation of experience with the operation of the Orphan and Paediatric Regulations**. As part of the implementation of the European Commission's Pharmaceutical Strategy for Europe, which was published on 24 November 2020, in 2021 the European Commission launched the preparation of a targeted revision of the orphan and paediatric regulations. This revision addresses shortcomings identified in a recent evaluation, results of which were published by the European Commission on 11 August 2020.
- **Revision of rules on fees payable to the European Medicines Agency**. Based on the outcome of the evaluation of the EMA fee system, finalised in 2019, in 2020 the European Commission started preparations to update the legal framework on EMA fees. The impact assessment of future policy options to update the legal framework on fees is in progress, and the European Commission legal proposal for the revised EMA's fees regulation is planned for mid-2022.
- **European Commission's evaluation of experience with the operation of the Orphan Regulation.** In line with the Commission's commitment in the context of its Better Regulation agenda to keep existing laws under review, in March 2018 the European Commission started preparing an evaluation of the functioning of the orphan regulation EC No 141/2000 over the period 2006-2017. A study was commissioned to Technopolis Group and ECORYS, which was published in August 2020, in order to analyse the impact of the incentives provided in the EU orphan legislation on innovation, availability, and accessibility of orphan medicinal products. Based on this report, a roadmap for the revision of the paediatric and orphan regulation was published at the end of 2020.
- **Evaluation of experience with shortages of medicines**. In December 2021, the European Commission published a study on medicines shortage. The study reviews activities carried out by EMA and National Competent Authorities in this area between 2004 and 2020, and proposes measures to be considered in the 2022 revision of the EU basic pharmaceutical legislation.

3. Assessment of the effectiveness of internal control systems

3.1. Effectiveness of internal control systems

3.1.1. Internal control framework review

The framework is comprised of 17 internal control principles that cover five core components of the internal control framework: control environment, risk assessment, control activities, information and communication, and monitoring activities.

The framework is based on a principle-based system, whereby the managers are offered the necessary flexibility to adapt to their specific characteristics and circumstances while ensuring a robust internal control with a consistent assessment throughout the Agency.

To assess the implementation, functioning, and improvement of the 17 principles, a questionnaire was prepared. The questionnaire was then addressed to the managers and staff members in charge of specific principles or elements of the internal control framework. This year, for the first time, several individuals with topics that needed elaboration were interviewed for further clarification of the questions/principles.

Regarding the functioning of the internal control system and its principles, the overall conclusion is that the internal control system, its components, and principles are, in general, present and functioning reasonably well. It was noted that several principles could benefit from minor clarifications or additional information, and/or some adjustments and improvements that would enhance the efficiency and effectiveness of the principle and its elements.

3.1.2. Ex-ante control system and register of exceptions

Ex-ante verifications

The day-to-day ex-ante verification is the financial control based on the subjective evaluation of risks where sound judgment applies. The Agency has decentralised the verification for fee revenue and expenditure, as these are standardised transactions requiring either an operational expertise or specific controls. The aim of the financial ex-ante verification is to assure the Authorising Officer, that the budget implementation does respect the budgetary principles, focused on legality and regularity, including sound financial management and transparency.

The financial verifying agents, as a general policy, perform checks focusing on medium/high-value commitments, sensitive contracts, or complex procurement procedures where higher risks have been identified. Transactions are checked by applying appropriate checklists in line with the EMA's internal control framework, the Financial Regulation, and the Charter of the Verifying Officer. In addition, the SAP financial system is an effective tool for mitigating financial risks associated with the payment processing.

Comparison between verified and rejected transactions	2020	2021
Number of transactions verified	53,354[1]	38,447
Number of transactions rejected	437	511

[1] Corrected data for 2020 in line with reviewed reporting structure

Comparison between verified and rejected transactions	2020	2021
• of which related to manual adjustments, technical rejections or interface issues following the decentralised verification	106 (24%)	119 (23%)
• of which other issues (incorrect currency, calculation errors, wrong allocation, etc.) or procedural issue (missing document, change of requirement, wrong cost centre, etc.)	331 (76%)	392 (77%)
Overall rejection rate	0.8%	1.3%

Register of exceptions

No financial exception was registered during the reporting year 2021.

3.1.3. Ex-post control system

Ex-post controls are part of the management and internal control procedures; they are required under Article 45 of the Financial Regulation. The purpose of the ex-post controls is to ascertain that the processes and procedures are correctly implemented, and that they comply with the applicable provisions. Agency-wide ex-post controls are conducted once a year on selected financial and non-financial procedures and processes. The areas to be subjected to ex-post controls are proposed by the divisions, and a delegated group of senior managers (Head of Administration division, Head of Audit, Heads of Legal, Head of Finance departments, and Internal Control Coordinator) decides on the specific ex-post controls to be carried out, based on the risk assessment and the results of previous controls of these proposed areas.

In 2021, a new approach and new internal guidance on the methodology for financial ex-post control was approved by the Executive Board. The revised approach introduces new timelines to run the exercise in a rolling, 18-month period (from Q4 of Y until Q1 of Y+2). Accordingly, the financial ex-post controls for 2021 will be included in the report on ex-post controls for the year 2022.

The following areas were assessed in 2021:

- Staff members' declaration of interests;
- Publication of documents prior and post Committee meetings (including CMDh) and DOI evaluation recorded in agendas/minutes;
- Handling of declarations of interests of experts;
- Criteria to be fulfilled by industry associations to be eligible for involvement in the Agency's activities;
- Compliance of the Probation Period submission deadlines according to the Article 14 of the CEOS for Temporary Staff, and Article 84 of the CEOS for Contract Staff.

Overall, the ex-post controls highlighted no significant weaknesses, although two areas of controls (staff members' declaration of interests and publication of documents prior and post committee meetings) were identified for potential improvements; these are being addressed by specific improvement action plans, and a reassessment has been recommended in the next ex-post controls cycle.

3.1.4. Annual review of sensitive functions

As in any organisation, certain Agency staff members are required to carry out functions involving a considerable amount of autonomy or executive power, implying a risk that such powers or influence may be misused for personal gain (financial or otherwise). Consequently, the identification and management of such functions, defined as sensitive, form an important part of the EMA internal control system, as they aim at preventing fraud and corruption, as well as at protecting the Agency's interests.

In line with the EMA 'Guidance on sensitive functions', a risk assessment to identify the Agency's sensitive functions was carried out in 2021. This year's exercise had to take into consideration the impact and changes stemming from the future-proofing exercise, that resulted in significant changes, either at organisational level or in scope and responsibilities of a number of roles at the Agency.

Overall, all senior management roles (Executive Director, Heads of Divisions and Task Forces, and Head of Legal Department) are by default considered sensitive, due to the considerable level of decision-making power and influence attached to these roles. Similarly, middle-level management roles (Heads of Department) are also considered sensitive, with the exception of four positions that hold mainly administrative responsibilities and/or less pervasive levels of decision-making power and influence.

The lower-level management roles (Heads of Service/Office and Task Force Work-Streams) are in general considered to have less pervasive levels of decision-making power and influence, in combination with sufficient control and oversight from staff holding posts to which such lower management roles directly report, to deem these functions non-sensitive. As an exception to this general rule, 12 positions at this managerial level are deemed sensitive due to specific aspects of their roles, such as, by way of example, significant involvement with procurement, handling of sensitive data, financial or staff-related decisions.

The functions considered sensitive were recorded in the Sensitive functions register 2021. For each function, the register describes the main activities of that function, the potential risk areas, inherent risk rating, mitigating controls in place, and the residual risk rating together with its significance.

3.1.5. Advisory Committee on Procurement and Contracts (ACPC) and procurement management

The ACPC has been set up as part of the internal control system of the Agency and provides an opinion, in an advisory capacity, on the compliance with the Financial Rules regarding procurements and contracts. The ACPC review is mandatory if the contract amounts to €1,000,000 or above.

In 2021, the committee reviewed 12 cases and expressed 11 favourable opinions, and 1 favourable opinion with recommendations.

3.1.6. Reconciliation of information in financial systems

The Agency's operational systems are interfaced with the SAP system. During 2021, reconciliations for 100% of the data between the product- and procedure-tracking systems and SAP were carried out on a regular basis, including data from the newly interfaced IRIS system. Findings were detected in the Pharmacovigilance PASS area and rectified with a minimal financial impact in terms of revenue for some transactions related to the 2019 and 2020 financial year.

3.1.7. Data protection

EMA processes personal data in accordance with the rules laid down in Regulation (EU) 2018/1725 (EUDPR, in force since 11 December 2018) and is subject to the supervision of the European Data Protection Supervisor (EDPS).

In 2021, EMA continued to pursue the implementation of the EUDPR at full speed. The Acting Data Protection Officer (DPO) and the Assistant DPO, together with the Data Protection Coordinators (DPC) appointed per Divisions and Task Forces, coordinated the performance of EMA's transparency obligations on a daily basis. This included the preparation and publication of data protection notices and records of processing operations. Moreover, during the preparation of data processing operations, huge efforts were devoted to the risk assessment of all potential data processors, and to the negotiations of the relevant contracts with the successful tenderers.

Data protection impact assessments (DPIAs) were also performed or initiated, where needed. Of note, a very comprehensive DPIA on the new Clinical Trial Information System (CTIS) was finalised and formed the basis for the preparation of a Joint Controllership Arrangement (see below). In this framework, an important area requiring careful attention was the use of cloud services, especially where they may involve the international transfer of personal data processed. In addition, personal data aspects were regularly scrutinised on the occasion of the disclosure of some documents to unintended recipients. Furthermore, advice and input to various data protection topics was provided throughout 2021, for example in relation to secondary use of health data.

Following the EDPS investigation initiated in the previous year, the topic of international data transfers possibly carried out by the Agency when performing its activities continued to be of importance in 2021. EMA initiated negotiations with Health Canada, in order to enter into an administrative arrangement pursuant to Article 48(3)(b) of EUDPR and sought the EDPS' necessary prior to authorisation to enter into this arrangement. The EDPS granted an authorisation with conditions in July 2021, but unfortunately, EMA could not proceed to signature, as some of those conditions were not agreeable to Health Canada, and the negotiation process was suspended. Such administrative arrangement with Health Canada would allow a faster and more efficient exchange of documents, including personal data as needed in the interest of public health, in particular during a cross-border threat to public health, and more broadly to jointly analyse the quality and safety of medicinal products and medical devices, whether new or already on the market globally.

To ensure data protection compliance and the protection of personal data processed in CTIS, the Agency coordinated the consultations with all Member States, EU institutions and industry, regarding a Joint Controllership Agreement (JCA). As a result, the final adopted JCA was published in December 2021 (see link here). This JCA clarifies the roles and responsibilities of different actors performing personal data processing in the system as joint controllers. As an Annex to the JCA, a data protection notice has also been adopted, informing the public and all users about the details of how personal data may be captured and processed in CTIS. In addition, a Questions and Answers document has been prepared and published (see link here), in order to support navigation around the documents and promote the understanding of the Union data protection background.

The Agency also prepared and coordinated consultations regarding a JCA pertaining to the Union Product Database (UPD) on veterinary medicinal products. This JCA is also accompanied by a data protection notice, to provide information on personal data processing in the database. The final adopted JCA and data protection notice for UPD was also published on the Agency's website (see link here).

In June 2021, the Agency launched a call for tender for a service provider to set up the DARWIN EU® Coordination Centre, in support of the integration of real-world evidence into assessment of medicines

in the EU. Taking into account the importance of this new initiative, a preliminary DPIA was performed, aimed at carefully considering all the applicable laws, their interplay and their application to DARWIN EU, including Regulation (EU) 2018/1725 (EUDPR) and Regulation (EU) 2016/679 (GDPR). The aim was to assess the prospective activities and to inform a responsible and efficient selection of contractors and subcontractors, which was supported throughout the tender process. In the last quarter of the year, the Acting DPO, with the assistance of the respective DPCs, has delivered specific training courses in each Divisions/Task Forces of the Agency with tailor-made content and case studies relevant for the specific activities of the particular organisational unit. The case studies were also chosen based on the suggestions of the specific unit's staff members. Each training course lasted at least 1.5 hours and involved all staff members working for the organisational unit concerned. Questions were raised by the participants and addressed by the Acting DPO and DPCs. The rate of acceptance and appreciation for these training courses was very high. In December 2021, during his annual report to the Management Board on data protection activities, the Acting DPO announced that a new DPO would be appointed as of 15 January 2021.

3.1.8. Prevention, detection and correction of fraud

EMA is committed to ensuring that its staff, members of committees, and all external contractors pursue the highest standards of honesty, propriety and integrity in the exercise of their duties, and has a 'zero tolerance' approach to fraud.

To improve prevention, detection and the conditions for investigation of fraud, and to pursue adequate deterrence and reparation with proportionate and dissuasive sanctions, the Agency has adopted its Anti-Fraud Strategy (AFS) in December 2014. The AFS is accompanied by a 3-year action plan. Both the strategy and the action plan are reviewed and updated every three years. The last update of the AFS was adopted by the Management Board in March 2021, together with the action plan for 2021-2023.

The AFS and action plan address specific risks that have emerged at the Agency's level, as reflected in the annual fraud risk assessments.

Prevention and awareness-raising are the most important objectives of the AFS since its first adoption back in 2014. This aspect has remained unchanged in 2021. An anti-fraud training is organised as part of the induction training for new staff members, as well as via a mandatory anti-fraud e-learning training that new staff members are required to take, which was updated in 2021.

No administrative enquires were opened in 2021. A close monitoring of Declaration of Interests compliance, including reminders to managers to assign the interest level on time, took place in 2021. New initiatives concerning staff's possible interests in the medical device domain have been prepared and will be submitted to the Management Board for adoption of some integrations to the policy concerning conflicts of interests of staff members.

In addition, a first refresher training on Ethics at EMA, including information on EMA's code of conduct and conflict of interest, was delivered in 2021 by Staff Support representatives, in cooperation with the Anti-Fraud Office.

No cases of suspected fraud/irregularity have been reported by EMA to OLAF in 2021.

3.1.9. Handling of information from external reporting persons

The Agency's main responsibility is the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use. EMA is strongly committed to carrying out all of its responsibilities and to adhering to the highest standards of professional and

personal integrity. In this regard, receiving and considering information provided by external reporting persons concerning EMA activities on the authorisation, supervision, and maintenance of human and veterinary medicinal products or other EMA activities is essential in safeguarding public interest and promoting a culture of public accountability and integrity.

A policy to handle allegations of breaches submitted by external reporting persons is in place since March 2017, complementing the policy on whistleblowing applying to the Agency's staff. The goal of the policy is to create an environment where individuals from outside the Agency feel confident to raise their concerns on breaches.

This policy outlines EMA's approach to external reporting persons of information disclosing allegations of breaches relevant to EMA's competence. Breaches are defined as acts or omissions that are unlawful or defeat the object of the purpose of the authorisation, supervision, and maintenance of human and veterinary medicinal products, and which are within the competence of EMA, i.e., any conduct or omission amounting to a violation of any legal provision governing the supervision, evaluation, and maintenance of medicinal products for human and/or veterinary use, or any other EMA activities.

The policy sets out the key principles underlying the handling of the information received from external reporting persons, and helps EMA assess these reports and coordinate any further investigation in a structured way, while protecting the identity of the reporter. The key principles relate to the confidentiality of the information received (including management and processing of personal data), acknowledgement of receipt, treatment of the information, interaction with EMA Anti-Fraud Strategy, analysis of the competence, transfer of information to other authorities, and the notification to the external reporting persons. A dedicated inbox has been created for external reporting persons to report breaches to the Agency (reporting@ema.europa.eu).

The standard operating procedure (SOP) on handling external reporting person information is effective as of 1 August 2017 and establishes a procedure providing for uniform, structured and confidential handling of information from external reporting persons disclosing allegations of breaches reported to the Agency. The procedure can be divided into six main sub-processes: receipt of information, triage of the information, initial evaluation of the information, assessment of the allegations, closure of the case, information to the external reporting person, and archiving.

EMA received 29 external whistleblowing reports in 2021 and followed up on each of these cases in accordance with the Policy and SOP. Twenty-one cases have been closed; in 8 cases the assessment is ongoing. For 11 cases, EMA was not competent on the matter (e.g., manufacturing sites not involved in centrally authorised products, supervision of ongoing clinical trials, medical devices) and handed the case over to the concerned NCAs, and in 18 cases EMA coordinated the investigation with the involvement of the relevant NCAs. For the reports in EMA remit, there were seven cases of GCP non-compliance, five cases of GMP non-compliance, four cases of GVP non-compliance with GVP, one case of falsification of medicines, and one case of conflict of interest.

3.1.10. Management of competing interests

To preserve impartiality and objectivity in every aspect of the Agency's work, a number of policies and rules on management of competing interests have been put in place, covering the different groups of people involved in and contributing to the Agency's work.

3.1.10.1. Management Board

The policy on the handling of competing interests of the Management Board (policy 0058) was last revised in June 2020, with effect from 1 July 2020. EMA requires Management Board members to sign a declaration of interests (DoI) and submit a curriculum vitae (CV) when they join the Management

Board. Members must re-submit these documents at least on an annual basis, or when a change in their interests occurs.

Since 2016, an *ex-ante* control has been carried out systematically on all DoIs submitted by Management Board members to compare the details contained in each new declaration with the previous declaration, and with the CV provided. Members are required to undertake training before their declaration of interest can be submitted.

The involvement of members and alternates in Management Board activities takes into account several factors, namely, the nature of the declared interest, the timeframe of the interest, the type of Management Board activity/topic, and the likelihood of impact on the industry (the pharmaceutical industry or any other industry related to any declared personal interests), as well as the action requested from the Management Board.

Moreover, members are informed in writing and ahead of the meeting, of the perceived conflict of interest which has been identified, and the applicable restriction to their involvement at the meeting. At the start of each meeting, members are further asked to declare any specific interests which could be prejudicial to their independence with respect to the items on the agenda. The names of members having declared competing interests which could affect their impartiality, with regard to specific items on the agenda, are noted in the minutes.

Declarations of interests of all Management Board members are published on the Agency's website.

No breach of trust procedure had to be initiated for a Management Board member in 2021.

3.1.10.2. Scientific committee members and experts

The policy on the handling of competing interests of scientific committees' members and experts (policy 0044) was last revised in June 2020 and entered into force on 1 January 2021.

The new provisions concern, for CAT members and alternates, the introduction of interests to be declared in the biotechnology and medical device sectors as foreseen in art. 22 of Regulation 1394/2007, and for all experts the introduction of interests to be declared on their personal or organisation's involvement in the repurposing of a medicinal product. There are now also restrictions for inspectors declaring close family interests and grants/funding to align with current practice in the majority of EU member states and at FDA. In addition, the same provisions as introduced in the policy for Management Board members and the decision on rules for Agency staff were incorporated; i.e., the inclusion in the definition of financial interests of stock warrants, introduction of a definition of partner and inclusion of reference to the new EU GDPR legislation.

The Agency takes a proactive approach to identifying cases where the potential involvement of an expert as a member of a committee, working party, or other group, or in any other Agency activity in the context of the evaluation, supervision, and maintenance of medicinal products for human or veterinary use, needs to be restricted or excluded, due to interests in the pharmaceutical industry.

The Agency requires experts to provide an electronic declaration of interests (e-DoI) every year, or when a change in their interests occurs, to ensure that they do not have any financial or other interests in the pharmaceutical industry that could affect their impartiality. The Agency also requires the experts to submit an up-to-date electronic curriculum vitae (e-CV) when signing the e-DoI.

The Agency screens each e-DoI and assigns it an interest level, based on whether the expert has any interests, and whether these are direct or indirect.

The Agency then uses the information provided to determine if an expert's involvement should be restricted or excluded in specific activities of the Agency. It bases these decisions on:

- the nature of the declared interests;
- the timeframe during which such interest occurred;
- the type of activity that the expert will be undertaking.

The policy reflects a balanced approach and aims to effectively restrict the involvement of experts with possible competing interests in the Agency's work, while maintaining EMA's ability to access the best available expertise. It includes several measures to take into account the nature of the declared interest, before determining the length of time for which any restrictions may apply:

- non-involvement with a company or product throughout an expert's mandate will result from them having held an executive role or lead role in the development of a medicine during previous employment with a pharmaceutical company;
- for the majority of declared interests, a three-year cooling-off period is foreseen, whereby restrictions to involvement decrease over time, and distinguish between interests that remain current and those within the last three years;
- there is no cooling-off period if certain types of interest are no longer present, such as financial interests.

Requirements for members of scientific committees are stricter than for experts participating in advisory bodies and ad-hoc expert groups, and hence more restrictions apply when the expert declares an interest. Similarly, requirements for chairs and members in a lead role, e.g., rapporteurs, are stricter than for the other committee members.

In 2021, the Agency continued to maintain the minimum implementation measures following the General Court Judgment on the Aplidin case. For SAGs and AHEGs, experts that are employed by universities or university hospitals performing development or manufacturing activities in respect of any medicinal products actually or potentially competing with the (candidate) product under review, are not allowed to be involved in the procedure. The Agency intervened in support of the appellate proceedings which were launched by two Member States in January 2021, and an outcome of the appeal is expected in 2022.

The new Regulation on a reinforced role for the European Medicines Agency in crisis preparedness and management for medicinal products and medical devices includes new tasks and responsibilities for the Agency regarding medical devices and medicines. The implications of the extended mandate in respect of competing interests have been considered for:

- Medical Devices Expert panels (EXPAMED)

  The Agency will be hosting the panels and providing a secretariat function on behalf of the European Commission. The Commission has put in place a policy on the management of competing interests for EXPAMED members with a focus on the medical device industry and notified bodies. This policy is similar to EMA Policy 0044. The Agency will maintain and apply this separate policy for EXPAMED members that is specific to this function.

- Medical Devices Shortages Steering Group (MDSSG) and Medicines Shortages Steering Group (MSSG) and Emergency Task force (ETF)

  These new Steering Groups will be established as part of the Agency. It is considered that Policy 0044 should apply to these groups and their working parties. Policy 0044 applies already to the current ETF members and no change in practical operation in this respect is needed towards the new ETF.

A revision of Policy 0044 to include these new groups and to further elaborate on medical devices interests and their restrictions on involvement in these new EMA activities is envisaged.

All members proposed for the Agency's scientific committees have their e-DoI screened before their formal nomination. In cases where the nominating authority appoints a member or alternate to a scientific committee or other forum, or an expert for participation in an Agency's activity where the expert has declared interests incompatible with involvement in Agency's activities in accordance with the policy, the Agency would not allow this expert to participate and inform the nominating authority accordingly.

Pre-meeting, meeting, and post-meeting arrangements are applied to ensure application of the policy, and to provide documented evidence. The outcomes of the evaluation of e-DoIs, and restrictions applicable to meeting participation, are included in the meeting minutes. The meeting minutes of all scientific committees are published on the Agency's website.

DoIs, their interest levels, and the CVs of scientific committee members and experts, are published on the Agency's external website for transparency purposes. The European experts' list on the Agency's website includes only those experts who have a valid e-DoI and e-CV. The Agency removes from the list the experts whose e-DoI is older than a year, until they submit an updated e-DoI.

EMA has a breach-of-trust procedure, which sets out how it deals with incorrect or incomplete e-DoIs by experts and committee members, as well as with disclosure of confidential information. In 2021, no breach-of-trust procedures were initiated.

The Agency immediately restricts scientific committee members, as well as any other experts, from any further involvement in the Agency's activities, from the date they inform the Agency that they intend to take up employment in a pharmaceutical company. In 2021, 5 delegates informed the Agency of such intention, and the restriction was immediately applied. The imminent employment in a company did not constitute a conflict for any of the ongoing procedures.

In 2021, 639 e-DoIs were checked before new experts were uploaded to the EMA Experts database as an *ex-ante* control. In eight cases, it was noted that the expert failed to declare previous employment in a pharmaceutical company as mentioned in their e-CV, requiring an update of the e-DoI. The 2021 ex-post control focused on SAG/AHEG participants as a follow-up to findings from previous ex-post controls. Overall, the control showed that the system for handling declarations of interests for meeting participation works well. For the minor findings, corrective actions were proposed. No major problems with the e-DoI completion by the experts or the e-DoI evaluation by EMA staff were identified.

3.1.10.3. Agency staff

The Agency's Code of Conduct extends the requirements for impartiality and the submission of annual declarations of interests to all staff members working at the Agency, including temporary agents, contract agents, seconded national experts, interims, visiting experts, and trainees.

MB Decision on rules relating to Articles 11, 11a and 13 of the Staff Regulations concerning the handling of declared interests of staff members of EMA and candidates before recruitment was last revised and is in force from 1 October 2020. A previous revision of 2019 incorporated an additional question for staff to also declare patent applications or intellectual property rights held in the past 5 years. The latest revision served to incorporate a broader definition of 'pharmaceutical company', to be better aligned with policy 0044 for experts.

Following the completion of a declaration of interests, and depending on the nature of the declared interests, if any, an interest level (1-3) is assigned to the staff member and/or candidate by the reporting officer evaluating the declaration. Staff members and/or candidates with interest levels 2 or

3 are subject to a documented risk-based assessment, which includes mitigating actions to reduce the risk. The decision is based on:

- the nature of the declared interests;
- the timeframe during which such interest occurred;
- the staff member's specific role and responsibilities (this includes the following aspects: the nature of the staff member's duties, the nature of the staff member's input to the Agency's activities, and the degree of influence that may be exerted on the final administrative or technical proposal, opinion or decision).

Staff declarations are available internally in SAP HR and for consultation by external persons on request. CVs and DoIs of the Executive Director and all EMA managers are published on the Agency's corporate website.

With regards to selection procedures and procurement, any competing interests must be declared by selection committee members and procurement evaluation committee members, and action taken accordingly.

Staff must request prior authorisation for outside activities during active service, in line with the Commission rules on outside activities and assignments and occupation after leaving the service of 2018, applicable to the Agency by analogy. All cases requested during 2021 were authorised without restrictions.

Post-employment

Staff members are required to seek permission to engage in an occupation within a period of two years of leaving the Agency, in accordance with Article 16 of the Staff Regulations. National experts are also required to seek permission, although the period is restricted to the equivalent duration of the secondment or two years, whichever is the shorter period. In all cases, applications are reviewed to establish any potential conflict of interests to the Agency, and if so required, based on an opinion of the Agency's Joint Committee, the Executive Director will issue a decision, which may impose restrictions on the staff member to mitigate against any potential conflict of interests.

It is important to note, that in accordance with the current rules on outside activities and assignments and on occupational activities after leaving the service, taking up employment at a European Union institution does not trigger the obligation to inform the Agency, as working for another EU institution does not lead to leaving the service of the Union for the purpose of applying Article 16 of the Staff Regulations. Therefore, any staff member leaving the European Medicines Agency to take up employment with another EU institution is not required to seek prior authorisation.

For the period from 1 January 2021 to 31 December 2021, staff members and Seconded National Experts (SNEs) made a total of 26 applications under Article 16 of the Staff Regulations, resulting in 19 authorisations without restrictions, 5 staff authorisations with restrictions, and 2 SNE cases with restrictions.

Restrictions (that are grade and role related) imposed include a distance clause, whereby the former staff member may not contact individual Agency staff for a certain period of time, e.g., 6 - 24 months.

Since November 2020, the Agency publishes on EMA's corporate website a specific register for senior staff leaving the Agency. For the purposes of this register, a 'senior staff member' includes the Executive Director, the Deputy Executive Director, Heads of Division, Advisers, Heads of Task Force, and the Head of the Legal Department. The register includes the name of the senior staff member concerned, date of departure, type of post held at the Agency, name of the intended future employer,

the job title (or brief description, if self-employed) and the date of the decision and restrictions applied. The data will be removed from the register two years after the departure of the staff member.

More information on restrictions applied to applications in 2021 is given in Annex 9.

3.1.10.4. External consultants and contractors

Competing interests for external consultants and contractors are covered by the standard framework contract provisions (section II.7), specifically:

- The contractor shall take all necessary measures to prevent any *conflict of interest* or *professional conflicting interest*, i.e., any situation that could compromise the impartial and objective implementation of the contract. Such conflicts of interest or professional conflicting interest could arise, in particular, as a result of family, emotional life, political or national affinity, economic interest, any other direct or indirect personal interest, or any other shared interest with the contracting authority or any third party related to the subject matter of the contract.
- In the event of any such conflict, the contractor must notify the contracting authority, in writing, as soon as possible of any situation that could constitute a conflict of interest or a professional conflicting interest during the implementation of the contract. The contractor must immediately take action to rectify the situation.
- The Agency may do any of the following: verify that the contractor's action is appropriate; require the contractor to take further action within a specified deadline; decide not to award a specific contract to the contractor.
- The contractor must pass on all the relevant obligations in writing to its *personnel*, any natural person with the power to represent it or take decisions on its behalf, third parties involved in the implementation contract, including subcontractors. The contractor must also ensure that the persons referred to above are not placed in a situation which could give rise to conflicts of interest.

Furthermore, in compliance with section II.8 of the standard framework contract (provisions regulating confidentiality), the contractor has the obligation to treat with confidentiality any information or documents, in any format, disclosed in writing or orally, relating to the implementation of the contract and identified as confidential. In particular:

- the contractor shall not use confidential information or documents for any purpose other than to perform its obligations under the contract without the prior written agreement of the other party;
- the contractor shall ensure the protection of such confidential information or documents with the same level of protection as its own confidential information or documents and in any case with due diligence;
- the contractor shall not disclose, directly or indirectly, confidential information or documents to third parties without the prior written agreement of the other party.

In addition, the Agency requests all IT consultants to sign individual declarations of interest and confidentiality undertaking at the beginning of their assignment, which are stored centrally by the Procurement and Purchase Standards Service.

Additionally, the Agency has measures in place to mitigate the risk of project-related, commercially confidential information (CCI) being disclosed to non-EMA staff, such as consultants and contractors. CCI includes rates for payment of contracted services, quotations for delivery of contracted goods or services, and services and goods quoted in tender procedures. An internal guidance document provides

information on how project-related CCI should be handled, as well as practical measures that should be taken to avoid disclosure.

3.2. Conclusions of assessment of internal control systems

Detailed assessment of the internal control system is carried out at the beginning of each calendar year, with the results included in the Annual activity report. Based on the assessment of internal controls 2021, the Agency concluded that the internal control systems in place, both in terms of the individual elements, and the system as a whole, are effective overall, with some improvements needed to further enhance the effectiveness of specific elements of the system. Nonetheless, the internal control systems in place are considered to provide reasonable assurance that the resources under the responsibility of the Executive Director were used for their intended purposes and in accordance with the principles of sound financial management.

3.3. Statement of the manager in charge of risk management and internal control

I, the undersigned, Mario Benetti, Head of Quality and Risk Management Service within the European Medicines Agency, in my capacity as manager in charge of risk management and internal control,

- declare that in accordance with the European Medicines Agency's Internal Control Framework, I have reported my advice and recommendations on the overall state of internal control in the Agency to the Executive Director.
- hereby certify that the information provided in the present Consolidated Annual Activity Report and in its annexes is, to the best of my knowledge, accurate, reliable, and complete.

Amsterdam, 1 June 2022

[signature on file]

Mario Benetti

Head of Quality and Risk Management Service

4. Management assurance

4.1. Review of the elements supporting assurance

Taking into account the review of the elements supporting assurance, the Executive Director is of the opinion that the management and control systems in place at the Agency are working as intended, risks are being appropriately monitored and mitigated, and necessary improvements and reinforcements are being implemented.

4.1.1. Assurance from the authorising officers by delegation

In accordance with the charter of tasks and responsibilities of authorising officer by delegation, and in support of the annual activity report, all authorising officers by delegation were asked to confirm their reasonable assurance for their areas of responsibility.

The authorising officers by delegation confirmed their reasonable assurance that, overall, suitable controls have been in place and have been working as intended; identified risks have been appropriately monitored and mitigated, and necessary improvements have been implemented.

4.1.2. Conclusions

Given the review of the elements supporting assurance, the Executive Director confirms that the management and control systems in place at the Agency are working as intended, risks are being appropriately monitored and mitigated, and necessary improvements and reinforcements are being implemented.

4.2. Reservations

Based on the assurance provided by the control system results, the Executive Director sees no reason that would justify or require a reservation.

4.2.1. Materiality criteria used

In line with the suggestion of the guidelines on the preparation of the annual activity report, the Agency used the qualitative and quantitative materiality criteria described below to assess if issues identified merit a reservation.

4.2.2. Qualitative criteria used

The Agency would consider as significant the weaknesses in the internal control system that fall under the following qualitative criteria:

- significant errors detected during the control or supervision exercises;
- significant weakness in one of the control systems;
- situations where the Agency does not have sufficient evidence from internal control systems or audit coverage to be confident in providing the necessary assurance;
- situations where a major issue has been outlined by the European Court of Auditors or the Internal Audit Service of the Commission (critical audit recommendations for underlying weaknesses relevant to the area covered by the declaration of assurance that are not adequately addressed by other internal controls and where the materiality threshold is exceeded);
- situations revealed through own control work or audits where significant risks remain unmitigated;
- significant reputational risk.

4.2.3. Quantitative criterion used

According to the Commission guideline on preparation of annual activity reports, the Court of Auditors uses a 2% materiality threshold. The Agency has therefore set the quantitative criterion of materiality at 2% of its total budget, as the Agency's tasks can be considered a policy area. This enables the Agency to apply the materiality criteria to the data and results of various control activities.

5. Overall conclusions on assurance

Based on all the facts presented in the report, including the management of the control system, and in light of the opinions expressed by the Court of Auditors on the reliability of the accounts and on the legality and regularity of the transactions underlying the accounts, the Agency can conclude that the systems in place provide reasonable assurance that the resources under the responsibility of the Executive Director were used for their intended purposes and in accordance with the principles of sound financial management.

EMPHASIS OF MATTER

Without calling into question the overall conclusions on assurance, I would like to draw your attention to the following important matters:

1. A set of significant new tasks such as the Clinical Trial Regulation, the implementation of the Veterinary Medicinal Products regulation, the GDPR, the Medical device regulation and the ACT EU (Accelerating Clinical Trials in the EU) initiative, has been assigned to the Agency over the last years virtually without any increase of the establishment plan. Furthermore, despite a 63% increase in fee-related workload with associated income, and significant new tasks since 2014, EMA will have fewer establishment plan staff posts in 2022 than in 2014 (596 versus 599, excluding extended mandate staffing and the short-term temporary agent posts for COVID-related workload). The critical staffing situation will be further aggravated by the increase in COVID-19 long-term effects linked to pharmacovigilance and post-authorisation activities beyond the 2023 timeline (when short-term posts will expire), the continued increase in the portfolio of authorised products (whose safety the Agency supervises), and the requirement to phase out short-term 'Brexit' contract agent positions by 2022, resulting in approximately 12.9% reduction of contract agent positions from 2019, further reducing the available workforce.

	2014	2015	2016	2017	2018	2019	2020	2021	2022
Establishment plan[1]	599	599	602	596	591	591	596	596	596
Fee workload and income evolution (€ M)	218,7	250,7	272,2	276,2	279,7	288,9	311,7	336,8	354,2[2]

This resourcing gap has been so far only partially compensated by efficiency gains realised in the period. It is important to note that the gap concerns fee-related activities and that the Agency is put in a position whereby on one hand, the fee-related work has increased significantly and on the other hand, the resources that are supposed to carry out such work for applicants are simply not present. In conclusion, the high resource constraints combined with the predicted surge in fee-related workload linked to COVID-19 pharmacovigilance and post-authorisation activities as well as to authorised product portfolio, puts EMA under significant additional pressure at a very critical time.

[1] The figures do not include the extended mandate and Covid-19 posts
[2] Draft 2022 budget.

2. The lease on EMA's former office premises in London runs until 2039 and does not contain a break clause. The Agency's premises in the United Kingdom were not included in the EU-UK political negotiations on the Withdrawal Agreement. Further to the High Court of Justice of England and Wales ruling of February 2019, stating that Brexit is not a cause for frustrating the lease agreement, the Agency sought contractual possibilities to dispose of the premises and mitigate the financial burden on the EU budget, subletting its former office premises to a subtenant from July 2019, under conditions that are consistent with the terms of the head lease. The sublease term lasts until the expiry of EMA's lease in June 2039. It must be noted that since EMA remains a party to the head lease, it is financially responsible for running its former premises in the UK. As a result of this long-term liability, the Agency has to continuously divert some of its human resources away from its public health remit to the management of a commercial property in a third country, for which neither the Agency nor the EU have business use – an activity not foreseen in the Agency's founding regulation. Furthermore, the Agency is liable for the entire remaining amount payable under the contractual obligations of the head lease if the subtenant fails to meet its obligations. As of 31 December 2021, the total estimated outstanding rent, associated service charges and landlord insurance to be paid by EMA up to the end of the lease term is €383 million (£322 million). The EMA Management Board has stressed on numerous occasions the unsustainability of this situation in the long term and requested EU institutions to resolve this matter at the highest political level. The persistent volatility of global – and UK – economies, caused by the pandemic and now exacerbated by the war in Ukraine, makes the need of a resolution of this issue at political level even more evident, to allow the Agency to fully focus its resources on the implementation of its recently expanded mandate and the Union's fight against public health emergencies.

Declaration of assurance

I, the undersigned Emer Cooke, Executive Director of the European Medicines Agency, in my capacity as authorising officer,

- Declare that the information contained in this report gives a true and fair view.
- State that I have reasonable assurance that the resources assigned to the activities described in this report have been used for their intended purpose and in accordance with the principles of sound financial management, and that the control procedures put in place give the necessary guarantees concerning the legality and regularity of the underlying transactions.
- This reasonable assurance is based on my own judgement and on the information at my disposal such as the results of the self-assessment, ex-post controls, the work of the Internal Audit Service, the work of the Internal Audit Capability and the lessons learnt from the reports of the Court of Auditors for years prior to the year of this declaration.
- Confirm that I am not aware of anything not reported here which could harm the interests of the Agency.

Amsterdam, 01 June 2022

[signature on file]

Emer Cooke

Executive Director

Annexes

Annex 1. Core business statistics

Business statistics can be found in Part I.

Annex 2. Statistics on financial management

Budget outturn and cancellation of appropriations

Budget outturn	2018	2019	2020[1)]	2021[2)]
Revenue actually received (+)	€ 317,081,125.07	€ 339,889,499.26	€ 376,246,022.54	€ 382,156,343.70
Payments made (-)	-€ 253,281,077.77	-€ 292,769,994.74	-€ 290,132,295.87	-€ 274,400,002.19
Carry-over of appropriations (-)	-€ 54,821,802.27	-€ 59,150,354.42	-€ 75,300,936.06	-€ 91,090,698.54
Cancellation of appropriations carried over (+)	€ 4,982,084.89	€ 2,744,268.82	€ 2,423,908.71	€ 5,372,131.21
Adjustment for carry over of assigned revenue appropriations from previous year (+)	€ 0.00	€ 0.00	€ 0.00	€ 0.00
Exchange rate differences (+/-)	-€ 159,476.48	€ 1,003,466.80	-€ 585,264.08	€ 2,944,406.68
Adjustment for negative balance from previous year (-)	€ 0.00	€ 0.00	-€ 8,283,114.28	€ 0.00
Total	**€ 13,800,853.44**	**-€ 8,283,114.28**	**€ 4,368,320.96**	**€ 24,982,180.86**

1) Data as per final 2020 accounts

2) Data updated in accordance with the provisional outturn

The financial outturn for 2021, a surplus of approx. €25.0 million, representing 6.13% of total revenue collected, i.e., €407.6 million, cf. the draft budget outturn for all fund sources (C1, C11, R0 and CL), was caused by higher income from fees, exchange rate gains, and unused and cancelled expenditure appropriations.

The Agency's adopted budget consists of non-differentiated appropriations only, so no distinction is made between commitment and payment appropriations.

Title I, expenditure

- Final expenditure was 3.19% lower than final appropriations, which is considered a good result.

Title II, infrastructure and operating expenditure

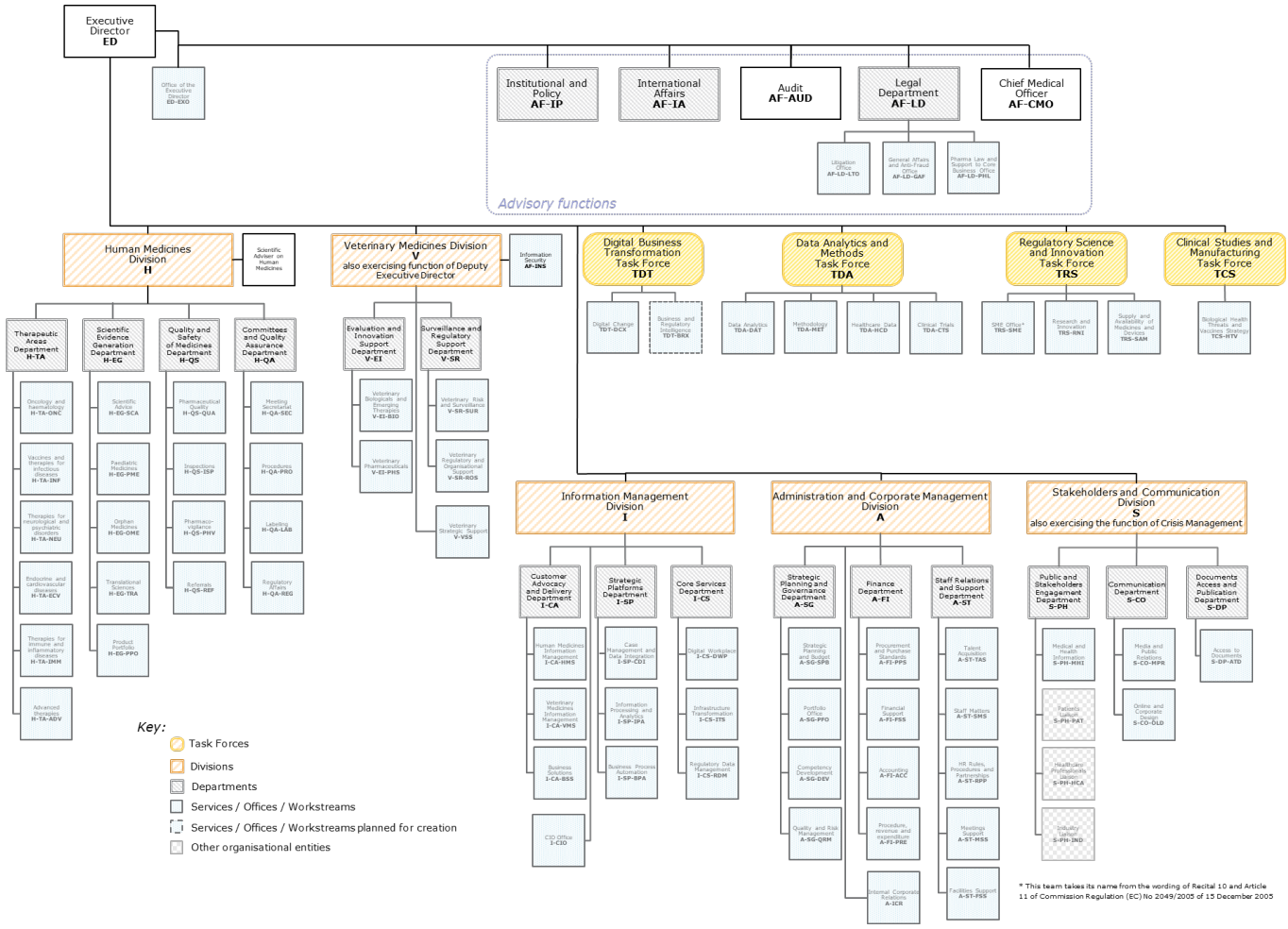
- Final expenditure was 11.91% lower than final appropriations, with surpluses resulting from changes made to project plans, legal costs not incurred and some savings from the effects of the COVID-19 pandemic.

Title III, operational expenditure

- Final expenditure was 1.61% lower than final appropriations, with main surpluses stemming from lower commitments for rapporteurs (driven by types of scientific applications submitted) and lower expenditure on scientific studies (demand driven, so difficult to predict).

The agency managed to comply broadly with the ceilings/KPIs for the amounts carried forward (C1 to C8): title I (10%), title II (20%) and title III (30%), with the following percentages achieved for the automatic carry-forward: title I: 5.75%, title II: 24.31%, title III: 37.59%. Higher amounts related to IT, scientific studies and data management contributed to higher carry-forward on titles II and III.

Annex 3. Organisation chart as on 31 December 2021



Annex 4. Establishment plan and additional information on HR management

Function group and grade	2020				2021				2022	
	Authorised budget		Actually filled as of 31/12/2020		Authorised budget		Actually filled as of 31/12/2021		Authorised budget	
	Permanent posts	Temporary posts	Permanent posts	Temporary posts	Permanent posts	Temporary posts	Permanent posts	Temporary posts	Permanent posts	Temporary posts
AD 16		0		0		0		0		0
AD 15		3		3		3		2		3
AD 14		8		8		9		9		10
AD 13		12		12		13		11		13
AD 12		44		44		45		42		50
AD 11		47		47		51		49		52
AD 10		44		44		51		47		50
AD 9		46		46		55		54		62
AD 8		66		66		71		71		77
AD 7		76		76		94		94		97
AD 6		46		46		65		65		60
AD 5		3		3		15		15		3
AD TOTAL	**0**	**395**	**0**	**395**	**0**	**472**		**459**	**0**	**477**
AST 11		2		2		2		2		2
AST 10		7		7		7		7		7
AST 9		8		8		9		9		10
AST 8		19		19		10		10		13
AST 7		15		15		19		19		19
AST 6		15		15		20		20		26
AST 5		39		39		38		38		43
AST 4		52		52		46		46		42
AST 3		44		44		32		32		23
AST 2		0		0		2		2		0
AST 1		0		0		0		0		0
AST TOTAL	**0**	**201**	**0**	**201**	**0**	**185**		**185**	**0**	**185**
AST/SC1										
AST/SC2										
AST/SC3										
AST/SC4										
AST/SC5										
AST/SC6										
AST/SC TOTAL	**0**	**0**	**0**	**0**	**0**	**0**			**0**	**0**
GRAND TOTAL	**0**	**596**	**0**	**596**	**0**	**657**		**644**	**0**	**662**

Grade filled refers to the number of staff occupying posts of a given grade, regardless of the staff member's actual grade.

Contract agents	FTE corresponding to the authorised budget 2020	Executed FTE as of 31/12/2020	Headcount as of 31/12/2020	FTE corresponding to the authorised budget 2021	Executed FTE as of 31/12/2021[2]	Headcount as of 31/12/2021	FTE corresponding to the authorised budget 2022
Function Group IV	52	78	76	110	89	90	122
Function Group III	131	62	62	81	72	94	81
Function Group II	10	28	26	10	18	0	0
Function Group I	0	0	0	0	0	0	0
Additional CA[1]	35	31	33	25	21	22	20
TOTAL	**228**	**199**	**197**	**226**	**200**	**206**	**223**

1) Additional staff to cover Brexit-related additional work (FTE)

Seconded National Experts	FTE corresponding to the authorised budget 2020	Executed FTE as of 31/12/2020	Headcount as of 31/12/2020	FTE corresponding to the authorised budget 2021	Executed FTE as of 31/12/2021	Headcount as of 31/12/2021
Total	30	28	31	30	26	28

Interims: from 1 January 2021 to 31 December 2021, 117 interims were contracted, 21 assignments started prior to 2021 and continued into that year. The average length of an interim assignment during 2021 was 10.3 months.

Information on the entry level for each type of post

Key functions	Type of contract (official, TA or CA)	Function group, grade of recruitment*	Indication whether the function is dedicated to administrative

			support or operations
Head of Division/Task Force	TA	AD12	Depending on function: operational or administrative
Head of Department	TA	AD09 (int.) AD10 (ext.)	Depending on function: operational or administrative
Head of Service/Office/Workstream	TA	AD06 (int.) AD08 (ext.)	Depending on function: operational or administrative
Adviser, Senior Expert	TA	AD13-AD14	Operational
Senior Specialist, Architect, Lead *(e.g., scientific, information technology management, communication)*	TA	AD08	Depending on function: operational or administrative
Specialist, Lead, Partner, Architect *(e.g., scientific, information technology management, communication)*	TA	AD06	Depending on function: operational or administrative
Graduate Specialist	TA	AD05	Depending on function: operational or administrative
Senior Assistant, Technical adviser	TA	AST10	Depending on function: operational or administrative
Coordinator *(e.g., scientific support, HR, communication, legal, facilities)*	TA	AST03	Administrative / Operational
Executive Assistant *(senior management support)*	TA	AST03	Administrative
Officer *(e.g., core and support functions)*	CA	FGIV	Depending on function: operational or administrative
Analyst *(information technology management)*	CA	FGIV	Operational
Assistant *(e.g., scientific support, HR, communication, department management support)*	CA	FGIII	Administrative / Operational
Special functions			
Head of Audit (Level 3)	*TA*	*AD09*	*Operational*
Data Protection Officer	*TA*	*AD06*	*Administration*

Results of the screening/benchmarking exercise as of December 2021

Job type (sub) category	2020 (%)	2021 (%)
Administrative support and Coordination	**13%**	**11%**
Administrative Support	12%	10%
Coordination	1%	1%
Operational	**79%**	**81%**
Top Level Operational Coordination	2%	0%

Job type (sub) category	2020 (%)	2021 (%)
Programme Management & Implementation	24%	27%
Evaluation & Impact Assessment	37%	36%
General Operational	16%	18%
Neutral	**8%**	**8%**
Finance / Control	8%	8%
Linguistics	0%	0%
Total	**100%**	**100%**

Article 29(3) of the Framework Financial Regulation sets the obligation for all European Union institutions and agencies to carry out a benchmarking exercise, with the aim of justifying administrative expenditure in a structured way, using a common methodology.

Jobs are grouped according to the Commission Screening methodology under three main types: Administrative support and coordination, Operational and Neutral.

The jobs screened include all establishment plan posts (TA) occupied full time, part time, or vacant, and all other types of contracts occupied by a jobholder (CA, SNE, INT, TR, long-term contractors/consultants, external service providers) fulfilling all or most of these criteria: minimum three-month contract, have a badge, occupy an office space, have a phone (personal number), have a computer (personal ID, e-mail).

HR implementing rules adopted in 2020

Implementing rule	Adopted	Effective date
Comms decision C(2020) 4818 final of 20 July 2020 amending Commission Decision C(2011)1278 of 3 March 2011 on provisions for Articles 11 and 12 of Annex VIII to the SR on the transfer of pension rights	11/03/2021 (by analogy)	11/03/2021

Annex 5 Human and financial resources by activity

Activities	Full Time Equivalence (Temporary and Contract Agents & Seconded National Experts)	Staff expenditure	Infrastructure, IT and project exp.	Meeting exp. (incl. overhead)	Evaluation Service (NCAs)	Other operational expenditure	TOTAL
		€'000	€'000	€'000	€'000	€'000	
1 Evaluation activities for human medicines	**366**	**49,739**	**19,933**	**4,325**	**137,337**	**16,980**	**228,314**
1.1 Pre-authorisation activities	89	12,407	2,606	1,537	25,567	27	42,144
1.2 Initial evaluation activities	68	10,098	1,953	77	15,411	1,108	28,647
1.3 Post-authorisation activities	96	12,355	3,363	1,094	81,132	6,392	104,336
1.4 Referrals	10	1,186	269	167	515	44	2,182
1.5 Pharmacovigilance activities	61	7,621	1,994	821	12,136	6,007	28,579
1.6 Other specialized areas and activities	41	6,072	9,747	629	2,577	3,402	22,427
2 Evaluation activities for veterinary medicines	**60**	**8,351**	**3,668**	**1,020**	**3,827**	**525**	**17,391**
2.1 Pre-authorisation activities	2	257	59	33	260	0	610
2.2 Initial evaluation activities	8	995	247	140	632	173	2,187
2.3 Post-authorisation activities	16	1,790	522	276	869	181	3,638
2.4 Arbitrations and referrals	1	117	33	20	0	166	336
2.5 Pharmacovigilance activities	8	1,225	1,078	135	2,065	2	4,505
2.6 Other specialized areas and activities	24	3,967	1,729	416	0	1	6,114
3 Horizontal activities and other areas	**241**	**33,739**	**35,022**	**1,770**	**2,011**	**4,203**	**76,746**
3.1 Committee coordination	51	6,391	1,447	740	0	0	8,578
3.2 Inspection and Compliance	45	5,116	1,423	414	2,011	2	8,966
3.3 Partners and Stakeholders	37	6,161	1,243	364	0	904	8,672
3.3a Transparency and access to documents	31	3,817	932	0	0	0	4,749
3.3b Information	20	2,647	607	252	0	1,786	5,291
3.4 International activities	15	2,868	481	0	0	0	3,349
3.5 Information Management (incl. EU Telematics)	42	6,739	28,890	0	0	1,512	37,141
4 Corporate Governance and Support activities	**222**	**32,273**	**9,491**	**0**	**0**	**1,752**	**43,515**
4.1 Governance, Quality Management and Internal Audit	38	6,537	1,407	0	0	496	8,440
4.2 Finance	46	5,866	1,796	0	0	687	8,350
4.3 Information technology	36	6,199	1,332	0	0	0	7,530
4.4 Human resources	65	9,180	2,487	0	0	33	11,700
4.5 Infrastructure services	11	1,405	524	0	0	0	1,929
4.6 Communication (corporate)	26	3,086	1,945	0	0	535	5,566
Total	**888**	**124,102**	**68,114**	**7,116**	**143,175**	**23,459**	**365,967**

Annex 6. Contribution, grant and service level agreements. Financial Framework Partnership Agreements

Grant agreements	General information					Financial and HR impacts				
	Date of signature	Total amount	Duration	Counterpart	Short description		2020		2021	
1. STARS	17/07/2019 (EMA's accession)	€6,000	36 months as of 01/01/2019	European Commission, DG Research & Innovation, Health, Administration & Finance	Strengthening training of academia in regulatory sciences and supporting regulatory scientific advice	Amount	CA	PA	CA	PA
							1,200	0,00	1,200	0,00
						Number of CA/FTEs	0.37		0.19	
						Number of SNEs/FTEs	-		-	
2. ConcePTION	26/04/2019	€ 85,000	60 months as of 01/04/2019	Innovative Medicines Initiative 2 Joint Undertaking	Building an ecosystem for better monitoring and communicating of medication safety in pregnancy and breastfeeding: validated and regulatory	Amount	CA	PA	CA	PA
							17,000	5,520	17,000	0,00
						Number of CA/FTEs	0.30		0.08	
						Number of SNEs/FTEs	-		-	
3. PREMIER	29/06/2020	€ 47,000	72 months as of 01/09/2020	Innovative Medicines Initiative 2 Joint Undertaking	Prioritisation and Risk Evaluation of Medicines in the Environment	Amount	CA	PA	CA	PA
							2,600	0,00	5,200	8,800
						Number of CA/FTEs	0.00		0.55	
						Number of SNEs/FTEs	-		-	
4.FluCop				Innovative Medicines Initiative 1 Joint Undertaking		Amount	CA	PA	CA	PA
							6,600	78.92	0,00	0,00
						Number of CA/FTEs	0.03		0.00	
						Number of SNEs/FTEs				
5. SISAQOL	30/10/2020	€78,756.25	48 months as of 01/01/2021	Innovative Medicines Initiative 2	Establishing international standards in the analysis of	Amount	CA	PA	CA	PA
							0,00	0,00	26,250	12,930
						Number of CA/FTEs	-		0,91	

				Joint Undertaking	patient reported outcomes and health-related quality of life data in cancer clinical trials	Number of SNEs/FTEs				
Total grant agreements						Amount	CA	PA	CA	PA
							€27,400	€5,598	€49,650	€21,730
						Number of CA/FTEs	0.7		1.73	
						Number of SNEs/FTEs			0	
Contribution agreements	**Date of signature**	**Total amount**	**Duration**	**Counterpart**	**Short description**		**2020**		**2021**	
1. IPA 2020-2022	19/12/2019	€254,919	36 months as of 01/01/2019	European Union	Participation of candidate countries and potential candidates in EMA trainings and activities	Amount	CA	PA	CA	PA
						Number of CA/FTEs				
						Number of SNEs/FTEs				
Total contribution agreements						Amount	CA	PA	CA	PA
							€ 0.00	€ 0.00	€ 0.00	€ 0.00
						Number of CA/FTEs	0		0	
						Number of SNEs/FTEs	0		0	
Service-level agreements	**Date of signature**	**Total amount**	**Duration**	**Counterpart**	**Short description**		**2020**		**2021**	
EMA does not provide services for other EU entities, hence has no corresponding service level agreements						Amount	CA	PA	CA	PA
						Number of CA/FTEs				
						Number of SNEs/FTEs				
						Amount	CA	PA	CA	PA
Total service-level agreements						Amount	CA	PA	CA	PA
							€ 0.00	€ 0.00	€ 0.00	€ 0.00
						Number of CA/FTEs	0		0	
						Number of SNEs/FTEs	0		0	

TOTAL	**Amount**	**CA**	**PA**	**CA**	**PA**
		€27,400	**€5,598**	**€49,650**	**€21,730**
	Number of CA	**0.7**		**1.73**	
	Number of SNEs	**0**		**0**	

Annex 7. Environment management

In 2021, the Agency continued its work towards EMAS registration in accordance with the approved Environmental Policy and Environmental Management Roadmap 2020 to 2024.

The objectives set for 2021 had the following outcome:

- the Environmental Policy, Roadmap for Environmental Management 2020 to 2024 and the Green Group mandate were approved on 14 January 2021;
- the Green Group have resumed activities since 12 March 2021;
- the inter-institutional framework contract for Green Public Procurement (GPP) helpdesk services is in place since April 2021;
- the updated EMA Internal Guidance for Green Public Procurement was approved on 10 June 2021;
- the targets for reducing energy and water consumption of 15% per square meter of lettable floor space have been calculated based on the EMA premises occupied in 2012 being 1, 7 and 11 Westferry Circus in London, with 20,096 sqm, compared with the2021 occupancy of the EMA building at Domenico Scarlattilaan 6 in Amsterdam, with 33,411 sqm.

	2012 **Consumption at Westferry Circus, UK**	**2012** **Consumption per sqm**	**2021** **Consumption at EMA building, NL**	**2021** **Consumption per sqm**	**Reduction per sqm (target 15%)**
Energy, kWh	3,465,431	172.4	3,156,519	94.5	45%
Water, m^3	5953	0.296	3660	0.11	62.8%

During 2021, the Agency's Environmental Management System (EMS) was further updated with specifics of the new EMA building in Amsterdam and consumption data becoming available.

To support the implementation of Environmental Management activities and making sure that they are embedded into the operational business processes, the EMA EMS Manual has been updated to further identify the resources involved. New identified activities relate to integration of environmental risks in the EMA risk register, strengthening the preparation of internal and external communication material, and acknowledging the evaluation of the submitted environmental risk assessments within the applications for market authorisation of medicines for human and animal health, where the activities by EMA are recognised as having an indirect impact on the environment.

The information regarding environmental management provided to staff on the EMA intranet continues to be updated as needed, in close collaboration with Internal Corporate Relations, and external stakeholder involvement will be coordinated in contact with the EMA's Communication Department. The Green Group mainly uses a dedicated Yammer community for interactions with staff interaction and to raise awareness of EMA's environmental management activities. Information regarding the Environmental Policy and the environmentally friendly credentials of the new EMA building will be further developed as part of the induction training for all new staff.

The Agency's environmental footprint is tracked and calculated by applying the Greenhouse Gas (GHG) Protocol, scope 1, 2 and 3 with performance indicators to be monitored as of 2022, with references to the Sectoral Reference Document and the Best Environmental Management Practice for Public Administration.

As part of the Agency's registration to EMAS, an environmental statement will be prepared with reporting of the environmental performance in compliance with the (EC) EMAS regulation 1221:2009, Annex IV, as amended.

Annex 8. Draft annual accounts

Following a positive opinion by the European Court of Auditors, the Agency's annual accounts for the financial year 2020 were successfully adopted by the Management Board in June 2021 and sent to the Budget authority (European Parliament and Council) by 1 July 2021.

At the time of writing, the Court of Auditors had not yet provided the Agency with their observations on the provisional accounts 2021 and therefore, the Agency’s final accounts 2021 had not been issued yet. During the assessment of the Annual Activity Report, EMA management board has been involved in the review of 2021 provisional annual accounts. The major risk for the Agency remains the management of its former office premises at 30 Churchill Place, London. Since EMA remains a party to the headlease with its Canary Wharf landlords, should the subtenant not be able to meet its obligations, the Agency could be exposed for all the amounts remaining payable under the headlease contractual obligations.

Annex 9. 2021 report on staff engaging in an occupational activity within two years of leaving the service (Article 16 of the Staff Regulations)

Engaging in an occupational activity within two years of leaving the service - restrictions applied to applications in 2021:

No	Job title / function at EMA	Length of service	Date of application	Date of Joint Committee opinion	Restrictions	Date of Executive Director's decision
1	Scientific administrator	5 years 10 months	9/03/2021	15/03/2021	During a period of twelve months, to be counted as of the date they leave the service, they should refrain from individually liaising with any member of staff of EMA with respect to the specific products and/or areas they may have dealt with during their last three years of service. The distance clause is without prejudice to the possibility to liaise or attend meetings through the standard channels available to all members of the public, including standard procedural services and meetings offered by the Agency to the different stakeholders.	15/03/2021
2	Executive Director	9 years	16/03/2021	16/04/2021	During a period of twenty-four months to be counted as of the date they leave the service, they should refrain from individually liaising with any member of staff of EMA with regard to any professional activity they may have dealt with in the performance of their responsibilities at the Agency during their last three years of service. The 'distance clause' is without prejudice to the possibility to liaise or attend meetings through the standard channels available to all members of the public, including standard procedural services and meetings offered by the Agency to the different stakeholders.	23/04/2021
3	Scientific administrator	12 years 7 months 15 days	27/05/2021	14/06/2021	During a period of twelve months to be counted as of the date they leave the service, they should refrain from individually liaising with any member of Agency staff with respect to the specific products and/or areas they may have dealt with during their last three years of service. The distance clause is without prejudice to the possibility to liaise or attend meetings through	22/06/2021

No	Job title / function at EMA	Length of service	Date of application	Date of Joint Committee opinion	Restrictions	Date of Executive Director's decision
					the standard channels available to all members of the public, including standard procedural services and meetings offered by the Agency to the different stakeholders.	
4	Seconded National Expert	2 years	4/08/2021	27/08/2021	Holds, that during a period of 6 months, to be counted as of the date they leave the service, they should refrain from individually liaising with any member of staff of the Agency with respect to the specific products and/or areas they may have dealt with during their 3 years of Secondment. The distance clause is without prejudice to the possibility to liaise or attend meetings through the standard channels available to all members of the public, including standard procedural services and meetings offered by the Agency to the different stakeholders.	1/09/2021
5	Seconded National Expert	3 years	20/08/2021	10/09/2021	During a period of six months, to be counted as of the date they leave the service, they should refrain from individually liaising with any member of Agency staff with respect to the specific products and/or areas they may have dealt with during their last three years of service. The distance clause is without prejudice to the possibility to liaise or attend meetings through the standard channels available to all members of the public, including standard procedural services and meetings offered by the Agency to the different stakeholders.	23/09/2021
6	Junior scientific officer	1 year 10 months	6/10/2021	26/10/2021	Holds, that during a period of six months, to be counted as of the date they leave the service, they should refrain from individually liaising with any member of staff of the European Medicines Agency with regard to any professional activity they may have dealt with in the performance of their responsibilities at the Agency during their last three years of service. The distance clause is without prejudice to the possibility to liaise or attend	26/10/2021

No	Job title / function at EMA	Length of service	Date of application	Date of Joint Committee opinion	Restrictions	Date of Executive Director's decision
					meetings through the standard channels available to all members of the public, including standard procedural services and meetings offered by the Agency to the different stakeholders.	
7	SNE and scientific administrator	7 years 6 months and 15 days	27/10/2021	19/10/2021	Holds, that during a period of six months, to be counted as of the date they leave the service, they should refrain from individually liaising with any member of staff of the European Medicines Agency with regard to any professional activity they may have dealt with in the performance of their responsibilities at the Agency during their last three years of service. The distance clause is without prejudice to the possibility to liaise or attend meetings through the standard channels available to all members of the public, including standard procedural services and meetings offered by the Agency to the different stakeholders.	22/11/2021

Annex 10. Consolidated list of new public procurement contracts > €15,000 concluded by the Agency during 2021

In addition to the information provided in section 2.3 (see page 91), the list of public procurement contracts concluded by the Agency is publicly available on EMA official website:

https://www.ema.europa.eu/en/about-us/procurement

https://www.ema.europa.eu/en/about-us/procurement/procurement-archive

Annex 11. Administrative appropriations – Building policy

Financial Regulation, Article 87(3.a) Building(s) covered by the appropriation of the financial year

#	Building name and type	Location	Surface area (in m²)			Rental contract					Host country (grant or support)
			Office space	Non-office space	Total	Rent (€/year)	Duration of the contract	Type	Break-out clause Y/N	Conditions attached to breakout clause	
1	EMA premises Amsterdam	Domenico Scarlattilaan 6 Amsterdam, 1083 HS	22,574	10,837	33,411	10,721,000	20 years 1.5 months from commencement date of 15/11/2019 to 31/12/2039	Lease agreement with CGREA (NL government Agency)	Y (condition to terminate)	The Lease can be terminated - At any time by mutual consent of the parties - At any moment by the Lessee/EMA with a notice period of 6 months if a decision is made to transfer EMA headquarters to another EU location - By either party after a consecutive period of 6 months of force majeure events which make the performance of the aggrieved Party impossible.	€18 million inducement of which EUR 15 million were for enhancements to fitting out the premises and €3 million are for rent reductions over the term of the lease.
2	Former EMA premises, London	30 Churchill Place, Canary Wharf, London E14 5EU	17,946	12,394	30,340	Sub-let	25 years from 1 July 2014 to 30 June 2039	Lease agreement with Canary Wharf Mgt	N	n/a	None
Total			**40,520**	**23,231**	**63,751**	**10,721,100**					

Financial Regulation, Article 87 (3.b) Evolution of surface area and locations and building projects in planning phase

The Agency does not have any further building projects in planning phase.

Financial Regulation, Article 87 (3.c) Building projects submitted to the European Parliament and the Council

The Agency does not have building projects submitted to the European Parliament and the Council.

Annex 12. Annual report 2021

Please see the Agency's Annual report 2021, publicly available on the EMA corporate website.

Annex 13. Project implementation 2021

Project progress and delivery as of 31 December 2021 against what was planned in the work programme 2021 is reported using the following traffic-light system:

Time / budget	
	Project within +/-10% of the plan
	Project 10%~25% behind timelines or above budget
	Project more than 25% behind timelines or above budget
	No activity/result to report

Scope	
	No change to project scope
	Minor changes (expansion or reduction) to project scope (i.e. no significant effect on budget and/or timelines)
	Significant change (expansion or reduction) to project scope (i.e. impacting project budget and/or timelines)
	No activity/result to report

The traffic lights reflect the change to the overall project timeline, budget and scope that has taken place in 2021, in comparison to what was planned and approved at the end of 2020 (i.e., as noted in the work programme 2021). Notes explaining the changes are added.

In cases where the project start- or end-dates foreseen in the work programme 2021 were revised in 2021, the current dates are added in the relevant cells, with the original date from the work programme 2021 shown as crossed out.

Programme / project	Legal basis	Start date	End date	Project delivery against			Results 2021
				Time	Budget	Scope	
Clinical Trials programme							
CTIS – Clinical Trials Information System (formerly EU portal and clinical trials database, renamed including a merger with SUSAR) [continues]	Regulation (EC) 536/2014, art.80-82	Q3 2014	2023				- The CTIS was delivered and tested for the go-live at end of January 2022. - Due to the go-live in January 2022 a hyper care contract had to be put in place in 2021, as well as the need for infrastructure for the CTIS increased the budget. - The scope was increased to support the Safety assessment regulation on the Clinical Trials for the go-live in January 2022.
New Veterinary Medicine Regulation Programme - VMP-Reg							
EVVet3 - Union Pharmacovigilance Database / EudraVigilance Veterinary v3.0 [continues]	Regulation (EC) 726/2004, art.57(d) Regulation (EU) 2019/6; associated implementing acts	2017	2022				- All the deliverables to enable the go-live on 28 January 2022 were achieved
UPD - Union Product Database [continues]	Regulation (EU) 2019/6; associated implementing act	2020	2022				- All the deliverables to enable the go-live on 28 January 2022 were achieved
ASU (formerly ESVAC) - Collection of Antimicrobials Sales and Use Data [new]	Regulation (EU) 2019/6; associated implementing act and delegated act	2021	2023				- All the deliverables to enable the go-live on 28 January 2022 were achieved

Programme / project	Legal basis	Start date	End date	Project delivery against			Results 2021
				Time	Budget	Scope	
MWD (formerly EudraGMDP) - Union Manufacturers and Wholesale Distributors Database [new]	Regulation (EU) 2019/6; associated implementing act and delegated act	2021	2022				- All the deliverables to enable the go-live on 28 January 2022 were achieved
Online programme							
European Medicines web portal [restart in 2022]	Regulation (EC) 726/2004 Regulation (EC) 1235/2010, art.26	2022	2023				*- Possible restart in 2022, depending on resource and budget availability.* *There are common elements with the Union Product Database project from the VMP-Reg programme supporting some of the future developments, as well as interdependencies with SPMS and e-PI projects.*
Data Integration programme							
S&PMS *- Substances and products management services* *[moved to RBOP programme]*							
Regulatory Business Process Optimisation Programme - RBOP (new)							
IRIS Platform to support regulatory business processes of the Agency [continues]	n/a	2019	2025				- Processes supporting Marketing status and Inspections have been delivered.
Digital Application Dataset Integration (DADI) network project to replace electronic application forms (eAF) [new]	n/a	2021	2023				- A Proof of concept was delivered in 2021. - Development of the first application form, the Human Variation form, has started.

Programme / project	Legal basis	Start date	End date	Project delivery against			Results 2021
				Time	Budget	Scope	
S&PMS - Substances and products management services [continues]	Art.4 of Guideline on e-prescriptions dataset for electronic exchange under cross-border Directive 2011/24/EU Regulation 726/2004, art.57(2) Regulation (EC) 520/2012, art.25 and 26 Clinical trials regulation 536/2014, art.8193) Pharmacovigilance fees regulation 658/2014, art.7 Art.4 of Guideline on e-prescriptions dataset for electronic exchange under cross-border Directive 2011/24/EU	2017	2024				- Data migrations from Art. 57 and from SIAMED are being tested and improved, allowing the Variation form to select information from PMS.
e-PI set up [new]	n/a	2020	2021				- The set-up project and FHIR standard have been completed and a new project to deliver a pilot will start in 2022.
Data Analytics Programme (new)							

Programme / project	Legal basis	Start date	End date	Project delivery against			Results 2021
				Time	Budget	Scope	
Lifecycle Regulatory Submissions Raw Data	n/a	2021	2024				- Contract signature for business tender to support design of future proof-of-concept pilot
Lifecycle Regulatory Submissions Meta Data	n/a	2020	2022				- Data Standardization Strategy published on EMA website Q4/2021
Real-world Metadata, Quality Framework and Catalogues	n/a	2021	2025				*Real-world Metadata and Rapid Analytics merged with DARWIN into one project in November 2021*
Observational Studies Rapid Analytics	n/a	2020	2022				- Procurement launched for a service provider to establish and operate the Coordination Centre and DARWIN EU Network of Data Holders Q2/2021. - Signature of framework contract EMA/2020/13/TDA 'Strengthening the use of real-world data in drug development – Metadata and Data Quality Framework' in Q4/2021.
Observational Studies DARWIN EU	n/a	2021	2025				
Signal and Safety Analytics	n/a	2021	2023				- Project kick-off in Q4/2021
EMA Extended Mandate (new)							
Shortages – Medicines & Medical Devices [new]	Regulation (EU) 2022/123, Chapter II and Chapter IV on a reinforced role for EMA in crisis preparedness and management for medicinal products and medical devices	2021	2023				- Kick-off planning and procurement in 2021 in preparation for implementing the extended mandate adopted on 25 January 2022
Data centre refresh and cloud strategy	n/a	2020	2021				- The project has delivered all the refreshed IT infrastructure in our Data Centre - EMA Cloud strategy delivered

Programme / project	Legal basis	Start date	End date	Project delivery against			Results 2021
				Time	Budget	Scope	
							- The project is considered closed
eCTD4: Implementation and adoption of eCTD v4.0 standard [restart]	n/a	~~2021~~ 2022	2023				- The project has been reported and will start in January 2022
DREAM Replacement Agency Document Management system at end of lifecycle and needs to be replaced [new]	n/a	2021	2023				- Project kick-off and contract in place in Q4/2021.
Administration Digitalisation Optimisation of the Administration supporting tools [continues]	n/a	2019	2022				- BI@Admin (deployment of business intelligence tools) – started in 2020, ongoing - Development of new Agency's Intranet – started in 2021, ongoing - Risk Management process review and tools – started in 2021, ongoing - Digitalisation of Staff Personal File – completed and closed in 2021 - Goals and Performance process review and tools completed in 2021
SAP Finance Replacement Obsolescence of EMA SAP Finance system [new]		2021	2025				- Project kick-off in Q4/2021.
External User Journey Improvement of external user registration to access the Agency's systems [new]		2021	2022				- Project kick-off in Q4/2021.

Annex 14. Pharmacovigilance Fee Regulation: Key Performance Indicators and performance information for the calendar year 2021

Context

The Pharmacovigilance Fee regulation (Regulation (EU) No 658/2014) was adopted on 15 May 2014. The first procedural fees were charged as of 26 August 2014 and the first annual fees in July 2015.

The aim of the regulation is to enable the Agency to charge fees for the pharmacovigilance tasks introduced by the pharmacovigilance legislation, i.e., Union pharmacovigilance procedures (PSURs, PASS, pharmacovigilance referrals), literature monitoring and improved use of information technology tools.

Financing the activities contributes to *"achieving an internal market as regards medicinal products, taking as a basis a high level of protection of health"* and inseparable from this is the aim *"to ensure financial resources to support the activities addressing common safety concerns, in order to maintain high standards of quality, safety and efficacy of medicinal products".*

Article 15 of the regulation, dealing with transparency and monitoring, states that the Executive Director of the Agency shall provide the Commission and the Management Board once per year with the performance information set out in part V of the annex to the regulation based on a set of performance indicators adopted by the Agency.

Section 2 of this report presents these key performance indicators for the calendar year 2020, and section 3 presents the more detailed performance information required by the regulation.

Part 1: Key Performance Indicators

KPI1: procedures started within the year for which a fee has been charged

Pharmacovigilance activities financed by PhV fees	2021 actual
Number of PSURs and PSUSAs procedures started	872
Number of imposed PASS protocol procedures started	6
Number of imposed PASS report procedures started	10
Number of pharmacovigilance referral procedures started	2
Number of pharmacovigilance annual fee chargeable units invoiced	145,641

KPI 2: percentage of marketing authorisation holders eligible for fee exemption or fee reductions within a given year for procedures carried out at Union level

Pharmacovigilance activities financed by PhV fees	2021 estimated %	2021 actual procedures	2021 actual %
MAHs invoiced for **PSURs and PSUSAs** procedures started involving **CAPs only**:		632	
· Micro-sized enterprises	2.25%	1	0.16%
· Small and medium sized enterprises	7.50%	40	6.33%
MAHs invoiced for **PSURs and PSUSAs** procedures started involving **NAPs or CAPs/NAPs**:		4,707	
· Micro-sized enterprises	2.50%	187	3.97%
· Small and medium sized enterprises	7.50%	33	0.70%
MAHs invoiced for **Imposed PASS protocol** procedures started for **CAPs only**:		6	
· Micro-sized enterprises	2.25%	0	0.00%
· Small and medium sized enterprises	0.75%	1	16.67%
MAHs invoiced for **Imposed PASS protocol** procedures started for **NAPs or CAPs/NAPs**:		71	
· Micro-sized enterprises	2.50%	0	0.00%
· Small and medium sized enterprises	7.50%	1	1.41%
MAHs invoiced for **Imposed PASS report** procedures started for **CAPs only**:		4	
· Micro-sized enterprises	2.25%	0	0.00%
· Small and medium sized enterprises	0.75%	0	0.00%
MAHs invoiced for **Imposed PASS report** procedures started for **NAPs or CAPs/NAPs**:		21	
· Micro-sized enterprises	2.5	0	0.00%
· Small and medium sized enterprises	7.50%	0	0.00%
MAHs invoiced for Pharmacovigilance **referral** procedures started for **CAPs only:**		1	

· Micro sized enterprises	2.25%	0	0.00%
· Small and medium sized enterprises	0.75%	0	0.00%
MAHs invoiced for Pharmacovigilance **referral** procedures started for **NAPs or CAPs/NAPs:**		2	
· Micro-sized enterprises	2.50%	0	0.00%
· Small and medium sized enterprises	7.50%	0	0.00%

KPI 3: percentage of chargeable units eligible for fee exemption or fee reductions within a given year for annual fees for information technology systems and literature monitoring

Pharmacovigilance activities financed by PhV fees	2021 estimated %	2021 actual	2021 percentage
Pharmacovigilance **annual fee** chargeable units invoiced		145,641	
· Micro-sized enterprises	2.50%	1,010	0.69%
· Small and medium sized enterprises	7.50%	8,613	5.91%
· Generics (non-SME)	36%	62,548	42.95%
· Authorised homeopathic, authorised herbal, and well-established use products	0%	25,056	17.20%

KPI 4: percentage of fees which has been recovered for the procedures invoiced within a given year and committed/paid to NCAs

Pharmacovigilance activities financed by PhV fees	[38] Invoiced in 2021	Cash collected in 2021	[39] Percentage	Remuneration to NCAs for assessment performed
	€ '000	€ '000		€ '000
Income recovered for PSURs and PSUSAs procedures started	17,404	15,208	87% (85% in 2020)	11,783
Income recovered for imposed PASS protocol procedures started	103	66	66% (83% in 2020)	36
Income recovered for imposed PASS report procedures started	247	247	100% (99% in 2020)	105
Income recovered for pharmacovigilance referral procedures started	318	318	100% (97% in 2020)	212
Income recovered for pharmacovigilance annual fee chargeable units invoiced	8,830	8,773	99% (99% in 2020)	n/a

[38] The figures in this table differ from the ones in tables 4,5,6 and 9 because they also include adjustments and corrections related to 2021 and processed in 2022, whereas the amounts shown in the tables below show only the value of the invoices related to the applications started between January and December 2021. In addition, some of the applications received at the end of the year were processed in the financial system in January 2022.

[39] Invoices are issued with 30 days credit, which means that the payments of the invoices issued in November and December 2020 were paid for in 2022. The final 2021 cash recovery rate as of April 2022 is 100% for PSURs and PSUSAs, 99.8% for PASS and 99.8% for Annual fee.

Part 2: Performance information criteria defined in Part V of the Annex to the Regulation

Fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use - Regulation (EU) No 658/2014: Performance Information

Reporting period: 1 January - 31 December 2021

Table	Performance Information (Part V of the Annex)
1	Number of Agency staff involved in pharmacovigilance activities pursuant to Union legal acts applicable during the reference period, specifying staff allocated to activities corresponding to each of the fees referred to in Article 4 to 7.
2	Number of hours outsourced to third parties with specification of the activities concerned and costs incurred.
3	Overall pharmacovigilance costs and a breakdown of staff and non-staff costs relating to activities corresponding to each of the fees referred to in Article 4 to 7.
4	Performance information relating to periodic update safety reports (PSURs)
5	Performance information relating to post-authorisation safety studies (PASS)
6	Performance information relating to referrals initiated as a result of the evaluation of pharmacovigilance data
7	Information on marketing authorisation holders that have claimed a small and medium-sized enterprise or micro enterprise status
8	Information on marketing authorisation holders of medicinal products referred to in Article 7(4) that have benefitted from reduced annual fees
9	Performance information relating to the annual fees
10	Attribution of Rapporteurship and co-Rapporteurship per Member State per type of procedure.
11	Number of working hours spent by the rapporteur and the co-rapporteur(s) per procedure, on the basis of information provided to the Agency by the national competent authorities concerned.

Note: The Agency has made every effort to complete the detailed reporting requirements of the following tables but, in a small number of cases, some data is not available for the full calendar year 2021, pending the development of additional IT reporting functionality, in which cases the relevant fields are left blank.

1) Number of FTEs involved in pharmacovigilance activities pursuant to Union legal acts applicable during the reference period, specifying staff allocated to activities corresponding to each of the fees	Full Time Equivalence (FTEs)
Periodic safety update reports	**11**
Post-authorisation safety studies	**2**
Referrals initiated as a result of the evaluation of pharmacovigilance data	**2**
TOTAL	**14**

2) Number of hours outsourced to third parties with specification of the activities concerned and costs incurred		2021	
		Units	Cost €'000
Identifying and managing duplicates	Number of duplicate couples assessed	144,883 (160,047 in 2020)	4,902
	Number of 'master' reports generated based on duplicated data	81,360 (85,168 in 2020)	
Coding of reported medicines and active substances	Number of reported medicinal products/active substance terms recoded	1,068,728 (54,366 in 2020)	
	Number of adverse reaction reports recoded	959,665 (76,990 in 2020)	
Providing feedback on data quality	Total number of organisations subject to ICSR data quality review	119 (120 in 2020)	
	Number of medicinal products in the xEVMPD quality reviewed and, where necessary, corrected	131,963 (145,320 in 2020)	
[50] Monitoring of substance groups and selected medical literature	Number of literature references screened and reviewed	487,635 (549,312 in 2020)	809
	Number of individual case safety reports (ICSRs) entered into Eudravigilance database and made available to National Competent Authorities and Marketing Authorisation Holders.	9,190 (9,535 in 2020)	

[50] The European Medicines Agency (EMA) is responsible for monitoring 409 substance groups (309 chemical and 100 herbal) and selected medical literature to identify suspected adverse reactions with medicines authorised in the European Union, and for entering the relevant information into the EudraVigilance database.

3) Overall pharmacovigilance costs and a breakdown of staff and non-staff costs relating to activities corresponding to each of the fees	Staff costs '000	Non-staff costs '000
Cost for assessment of periodic safety update reports	1,256	12,195
Cost for assessment of post-authorisation safety studies	157	192
Cost for assessments in the context of referrals initiated as a result of the evaluation of pharmacovigilance data	197	276
Annual cost for information technology systems and literature monitoring		8,863
Overall pharmacovigilance costs	**23,136**	

4) Performance information relating to the assessment of periodic safety update reports (PSURs)

Number of procedures started	Number of reports received	Number of MAHs expected to submit	Number of MAHs who submitted	Number of CUs[51]	Number of joint submissions[52]	Number of MAHs who submitted joint report[53]	Number of SMEs Claimed	Number of SMEs Denied	Number of Micro Claimed	Number of Micro Denied	Total Amount Invoiced (€)
872	n/a	1,538	n/a	41,977	298	4,765	142	1	27	1	17,612,834

[51] Total number of CU generated for the products falling into the scope of the procedure - total number of CU (to be) invoiced
[52] Number of received joint submissions
[53] Total number of MAHs in received joint submissions

5) Performance information relating to the assessment of draft protocols and of final reports of post-authorisation safety studies (PASS)											
Number of procedures started	Number of protocols and reports submitted[1]	Number of (parent) MAHs[54]	Total number of MAHs[25]	Number of joint submissions[55]	Number of (parent) MAHs in case of joint submission	Total number of MAHs in case of joint submission	Number of SMEs Claimed	Number of SMEs Denied	Number of Micro Claimed	Number of Micro Denied	Total Amount Invoiced (€)
6	n/a	33	77	34	29	73	2	0	0	0	102,545
10	n/a	11	25	2	2	16	0	0	0	0	274,800

6) Performance information relating to referrals initiated as a result of the evaluation of pharmacovigilance data							
Number of procedures started	Number of MAHs	Number of CUs	Number of SMEs Claimed	Number of SMEs Denied	Number of Micro Claimed	Number of Micro Denied	Total Amount Invoiced (€)
2	3	35	0	0	0	0	317,900

7 (a) Number of marketing authorisation holders that have claimed a small and medium-sized enterprise status involved in each procedure, number whose claim has been denied	Claimed	Denied
Fee for assessment of periodic safety update reports	142	1
Fee for assessment of post-authorisation safety studies	2	0
Fee for assessments in the context of referrals initiated as a result of the evaluation of pharmacovigilance data	0	0
Annual fee for information technology systems and literature monitoring	403	4

[54] Number of (parent) MAHs and total number of MAHs
[55] In case of joint submission:
• number of (parent) MAHs = number of (parent) MAHs in case of joint submission
• total number of MAHs = total number of MAHs in case of joint submission

7 (b) Number of marketing authorisation holders that have claimed micro enterprise status involved in each procedure, number whose claim has been denied	Claimed	Denied
Fee for assessment of periodic safety update reports	27	1
Fee for assessment of post-authorisation safety studies	0	0
Fee for assessments in the context of referrals initiated as a result of the evaluation of pharmacovigilance data	0	0
Annual fee for information technology systems and literature monitoring	147	2

8) Number of marketing authorisation holders of medicinal products referred to in Article 7(4) that have benefitted from reduced annual fees	2020
Generic application (Article 10(1) of Directive No 2001/83/EC)	1,830
Well-established use application (Article 10a of Directive No 2001/83/EC)	1,746
Authorised homeopathic medicinal product	82
Authorised herbal medicinal product	237

9) Performance information on annual fees

Number of marketing authorisation holders invoiced for annual fees	Number of CUs	SME status claimed	SME status denied	Micro status claimed	Micro status denied	Number of CUs: Generic Application	Number of CUs: Well-established Use Application	Number of CUs: Authorised Homeopathic	Number of CUs: Authorised herbal	Total Amount Invoiced (€)	Average Amount Invoiced (€)
3,414	145,641	403	4	147	2	67,419	24,447	2,849	1,725	8,827,608	60.61

10) Attribution of Rapporteurship and co-Rapporteurship per Member State per type of procedure started			
Member State	**PSUR**	**PASS**	**Referral**
Austria	55	0	0
Belgium	23	1	0
Bulgaria	3	0	0
Croatia	28	0	0
Czech Republic	21	0	1
Denmark	53	0	1
Estonia	8	0	0
Finland	37	0	0
France	61	2	0
Germany (BfArM)	57	1	0
Germany (PEI)	57	2	1
Greece	4	0	0
Hungary	14	0	0
Iceland	2	0	0
Ireland	46	0	0
Italy	36	0	0
Latvia	14	0	0
Lithuania	17	1	0
Malta	2	0	0
Netherlands	107	2	1
Norway	12	0	0
Poland	38	0	0
Portugal	41	2	0
Romania	4	0	0
Slovakia	6	0	0
Slovenia	3	0	0
Spain	44	1	0
Sweden	79	4	0
Total	**872**	**16**	**4**

11) Number of working hours spent by the rapporteur and the co-rapporteur(s) per procedure on the basis of information provided to the Agency by the national competent authorities (NCA) concerned							
	PSUR and PSUSA			PASS		Referrals	
NCAs	No. of procs.	Total hours	Average per proc.	No. of procs.	Total hours	No. of procs.	Total hours
Austria	14	847	61				
Belgium	25	2,407	96	1	145		
Croatia	4	244	61				
Denmark	57	5,774	101			1	427
Estonia	11	686	62				
Finland	36	2,528	70				
France	27	2,650	98				
Germany-BfArM	47	6,332	135	1	162		
Germany-PEI	59	3,020	51			1	281
Ireland	53	4,679	88				
Italy	38	3,036	80				
Latvia	13	1,210	93				
Netherlands	29	808	28				
Norway	11	718	65				
Portugal	49	1,960	40	2	54		
Romania	6	480	80				
Slovakia	3	243	81				
Slovenia	5	504	101				
Spain	24	2,062	86	1	80		
Grand Total	**574**	**44,232**	**77**	**5**	**441**	**2**	**708**

The data in the above table was provided by each NCA, in line with the reporting requirements of the relevant cooperation agreement and include only finalised procedures. Ongoing procedures will be reported in the next reporting period.

The data in the table above is based on the information received by the Agency as of 10 May2022. It was noted that not all NCAs were in a position to provide data for 2021.

Terms and abbreviations

Term/abbreviation	Definition
3Rs	'3 R' principles in testing of medicines for regulatory purposes: replacement, reduction and refinement
ACE	Analytics Centre of Excellence
ACT EU	Accelerating Clinical Trials in the EU
AD	administrator category post

Term/abbreviation	Definition
ADR	adverse drug reaction
ADVANCE	Accelerated development of vaccine benefit-risk collaboration in Europe project
ADVENT	Ad hoc expert group on veterinary novel therapies
AE	Adverse event
AEMPS	Agencia Española de Medicamentos y Productos Sanitarios (Spain)
AER	Adverse event report
Agency	European Medicines Agency
AI	Artificial intelligence
AIFA	Agenzia Italiana del Farmaco (Italy)
AMR	Antimicrobial resistance
AM & D	Application maintenance and development
ANSM	Agence nationale de sécurité du médicament et des produits de santé (France)
API	Active pharmaceutical ingredient
Art	Article
AST	Assistant category post
AST/SC	Secretarial and clerical category post
ASU	Antimicrobial sales and use
ATD	Access to documents
ATMP	Advanced-therapy medicinal product
BCP	Business continuity plan and public health threat plan
BDSG	Big data steering group
BEMA	Benchmarking of European medicines agencies
BfArM	Federal Institute for Drugs and Medical Devices, Germany (Bundesinstitut für Arzneimittel und Medizinprodukte)
Brexit	Commonly used term for the United Kingdom's planned withdrawal from the European Union
B/R	Benefit/risk
CA	Contract agent
CADVVA	CVMP ad hoc group on veterinary vaccine availability
CAMD	Competent Authorities for Medical Devices
CAP	Centrally authorised product
CAT	Committee for Advanced Therapies
CDP	Clinical Data Publication
CHMP	Committee for Medicinal Products for Human Use
CMDh	Coordination Group for Mutual Recognition and Decentralised Procedures - Human
CMDv	Coordination Group for Mutual Recognition and Decentralised Procedures - Veterinary
Commission	European Commission
committee(s)	Scientific committee(s) of the Agency
COMP	Committee for Orphan Medicinal Products
CP	Centralised procedure
Council	European Council
CT	Clinical trial
CTIS	Clinical trial information system
CTTI	Clinical trials transformation initiative
CVMP	Committee for Medicinal Products for Veterinary Use
CxMP	Scientific committees of the Agency
DARWIN EU	Data Analytics and Real World Interrogation Network
DCP	Decentralised procedure
DigiLab	EMA Digital Innovation Lab
DIMSIS II	Development, implementation and maintenance support of information systems
DoI	Declaration of interests
EC	European Commission

Term/abbreviation	Definition
ECA	European Court of Auditors
ECDC	European Centre for Disease Prevention and Control
ECHA	European Chemicals Agency
eCTD	Electronic common technical document
EDQM	European Directorate for the Quality of Medicines and Healthcare
EEA	European Economic Area
EFSA	European Food Safety Authority
EHDS	European Health Data Space
EMA	European Medicines Agency
EMANS	European Medicines Agency Network Strategy
EMAS	EU Eco-Management and Audit Scheme
EMRN	European medicines regulatory network
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
Enpr-EMA	European Network of Paediatric Research at the European Medicines Agency
EP	European Parliament
EPAR	European public assessment report
EPITT	European Pharmacovigilance Issues Tracking Tool
EPPO	European Public Prosecutors Office
ERA	Environmental risk assessment
ESEC	European Specialised Expert Community
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	European Union
EU-DPR	Data protection Regulation for EU institutions and bodies
EudraCT	European Union Drug Regulating Authorities Clinical Trials
EudraGMDP	European Union Drug Regulating Authorities good manufacturing and distribution practice
EudraPharm	European Union Drug Regulating Authorities Pharmaceutical Database
EudraVigilance	European Union Drug Regulating Authorities Pharmacovigilance
EUnetHTA	European network for health technology assessment
EU-IN	EU innovation network
EU-M4all	Medicines for use outside the EU
EU NTC	EU Network training centre
EU-SRS	EU scientific substance information system
EV	EudraVigilance, European Union Drug Regulating Authorities Pharmacovigilance
EVVet	veterinary EudraVigilance, European Union Drug Regulating Authorities Pharmacovigilance
EXB	EMA Executive Board
FDA	United States Food and Drug Administration
FG (I, II, III, IV)	Function group (for contract agent staff)
FTE	Full-time equivalent
GCP	Good clinical practice
GDPR	General Data Protection Regulation
GLP	Good laboratory practice
GMP	Good manufacturing practice
GP	General practitioner
GVP	Good pharmacovigilance practice
GxP	Good practice (e.g., laboratory, clinical, manufacturing etc)
HCP	Healthcare professional
HCWPW	Healthcare professionals' working party
HMA	Heads of Medicines Agencies
HMPC	Committee on Herbal Medicinal Products
HPRA	Health Products Regulatory Authority (Ireland)
HR	Human resources
HTA	Health technology assessment
HTAN	the HTA network

Term/abbreviation	Definition
IAS	Commission's Internal audit service
ICDRA	International Conference of Drug Regulatory Authorities
ICH	International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICMRA	International coalition of medicines regulatory authorities
ICSR	Individual case-safety report
ICT	Information and communication technologies
IHI	Innovation Health Initiative
IMI	Innovative Medicines Initiative
IMI-Advance	IMI Accelerated development of vaccine benefit-risk collaboration in Europe project
IMI-Adapt Smart	IMI Accelerated Development of Appropriate Patient Therapies a Sustainable, Multi-stakeholder Approach from Research to Treatment-outcomes project
IMI-FluCop	IMI project on seasonal flu vaccines (Standardisation and development of assays for assessment of influenza vaccine correlates of protection)
INC	International Neonatal Consortium
IPA	Instrument for Pre-accession Assistance
IPD	Individual patient data
IPRP	International Pharmaceutical Regulators Programme
IRIS	Platform facilitating the exchange of regulatory and scientific information between EMA and organisations developing medicinal research products for potential use in the European Union
ISO	International Organisation for Standardisation
IT	Information technology
ITF	Innovation Task Force
JIACRA	Joint inter-agency antimicrobial consumption and resistance analysis
KPI	Key performance indicator
MA	Marketing authorisation
MAA	Marketing authorisation application
MAH	marketing authorisation holder
MAWP	EMA multiannual work programme
Member State (MS)	Member State of the European Union
MHLW	Ministry of Health, Labour and Welfare, Japan
MLM	Medical literature monitoring
MRA	Mutual recognition agreement
MRL	Maximum residue limit
MRP	Mutual recognition procedure
MUMS	Minor use, minor species
NAP	Nationally authorised product
NCA	National competent authority
Network	European medicines regulatory network
NISG	Nitrosamines International Steering Group
NITAGs	National immunization technical advisory groups of WHO
NRG	Name review group established by CHMP
NTWP	Novel Therapies and Technologies Working Party
NUI	Non-urgent information
NVR	New veterinary regulation
OIE	World Organisation for Animal Health
OLAF	European Anti-Fraud Office
OMCL	Official Medicines Control Laboratories
PAES	Post-authorisation efficacy study
Parliament	European Parliament
PASS	Post-authorisation safety study
PB	EMA Portfolio Board
PBT	Persistent bioaccumulative and toxic substance
PDCO	Paediatric Committee
PCWP	Patient and consumer working party

Term/abbreviation	Definition
PEI	Paul-Ehrlich-Institut, agency of the German Federal Ministry of Health
PhV	Pharmacovigilance
PIC/s	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
PIP	Paediatric investigation plan
PLD	Patient level data
PMDA	Pharmaceuticals and Medical Devices Agency
POC	Point of Contact
PMF	Plasma master file
PMS	Product Management Services
PPHOVA	Pilot project on harmonisation of old veterinary antimicrobials
PQKMS	Pharmaceutical Quality Knowledge Management System
PRAC	Pharmacovigilance Risk Assessment Committee
PRIME	PRIority MEdicine, a scheme to foster the development of medicines with high public health potential
PSUR	Periodic safety-update report
PSUSA	PSUR single assessment
PUMA	Paediatric-use marketing authorisation
Q (1, 2, 3, 4)	Quarter (1, 2, 3, 4)
Q&A	Questions and answers
RA	Rapid alert
RCT	Randomised controlled trials
R&D	Research and development
RFI	Request for information
RWD	Real world data
RWE	Real-world evidence
SA	Scientific advice
SAG	Scientific Advisory Group
SAWP	Scientific Advice Working Party
SciCoBo	Scientific Coordination Board
SIAMED	Sistema de Información Automatizada sobre Medicamentos (Medicines Information System)
SME	Small and medium-sized enterprise
SmPC	Summary of product characteristics
SMS	Substances Management Services
SNE	Seconded national expert
SPM&S	Substances and product management services
SPOR	Substances, Products, Organisations, Referentials
S-REPS	Scientific and regulatory evaluation procedure support
SUSAR	Serious unexpected suspected adverse reaction
TA	Temporary agent
TATFAR	Transatlantic Taskforce on Antimicrobial Resistance
TCS	EMA Clinical Studies and Manufacturing task force
TDA	EMA Data Analytics and Methods task force
TDT	EMA Digital Business Transformation task force
TF	Task force
TF AAM	EMA/HMA joint task force on availability of authorised medicines for human and veterinary use
TGA	Therapeutic Goods Administration, Australia
TOPRA	The Organisation for Professionals in Regulatory Affairs
TRIP	Topic Relations Information Perspective
TRS	EMA Regulatory Science and Innovation Task Force
UEMO	European Union of General Practitioners
UI	User interface
UPD	Union product database
UK	United Kingdom
US	United States of America
VAR	Variation

Term/abbreviation	Definition
VICH	International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products
WGEO	HMA Working Group of Enforcement Officers
WHO	World Health Organization
WONCA	World Organization of Family Doctors
WP	Working party