HMA
Heads of Medicines Agencies

EMA
EUROPEAN MEDICINES AGENCY

European medicines agencies network strategy to 2025

Mid-point report to Q2 2023

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Foreword by Emer Cooke, EMA Executive Director and Karl Broich, Chair of HMA Management Group

In December 2020, when the European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA) published the European Medicines Agencies Network Strategy (EMANS) to 2025, we set up an ambitious - yet realistic - plan to make available safe and effective medicines to EU citizens, while adapting to emerging scientific developments and digital technologies. At that time, hardly could we have imagined that the COVID-19 public health emergency would extend for over three years, posing unprecedented challenges and absorbing large amounts of resources from the medicines regulatory network. Yet despite the difficulties, looking back at the work done halfway through the period to 2025, much progress has been made in the six priority focus areas originally planned for:

- Availability and accessibility of medicines
- Data analytics, digital tools and digital transformation
- Innovation
- Antimicrobial resistance and other emerging health threats
- Supply-chain challenges
- Sustainability of the network and operational excellence

This mid-term report provides a summary of the key achievements and concrete deliverables of EU medicines regulators as they implement the strategy planned until 2025. While a lot remains to be done, undoubtedly many important milestones have been met, with EU regulators awarded new roles in recognition of their work during the COVID-19 emergency. The structures, processes and new technologies built throughout this period will serve as cornerstones for implementing the upcoming revision of the pharmaceutical legislation. The end of the public health emergency and the lifting of the business continuity planning means we will once again be in a position to focus more fully on delivering patient-relevant medicines across the board and restarting some of the activities that were temporarily placed on hold, while continuing to deal with health threats and supply issues.

We will continue to work together on delivering the strategy 2025 with confidence, knowing that we are on the right track and collaborating closely with our stakeholders and partners. From the network's point of view, the experience of the last few years has strengthened the desire to continue building together a better regulatory system and focus on all the priorities envisioned as part of the EMANS.

Introduction

As the main strategy guiding the delivery of the operational, regulatory and scientific output of the EU medicines regulatory system, the EMANS identified shared challenges, goals and priorities for a five-year period to give strategic direction to the work of the European medicines regulatory network.

The EMANS was developed following an extensive period of outreach, analysis and consultation with EMA's scientific committees, stakeholders and EU regulatory partners before its final publication in December 2020. It sets out how the network continues to enable the supply of safe and effective medicines, adapting to new developments in science, medicine, digital technologies, globalisation and emerging health threats, such as antimicrobial resistance (AMR) and the COVID-19 pandemic.

The strategy outlined six priority focus areas in line with the European Commission's roadmap for a pharmaceutical strategy for Europe. Initial work on the pandemic was fed into the strategy's development and the numerous lessons learned from COVID-19 will continue to inform future reviews of the strategy and subsequent work plans. The EMANS identifies strategic goals and objectives for each focus areas, which were subsequently translated by EMA and the HMA into concrete actions in their respective detailed work plans and programmes. Implementation of the EMANS also took place through the Regulatory Science Strategy (RSS) to 2025. Mid-point reporting of the RSS includes key achievements to March 2023 (which are also reflected here) and we have elaborated on further achievements since.

This report provides an overview of main achievements from January 2021 to date with the links to more detailed information. The structure follows the strategic goals and objectives described originally in the EMANS. This report does not attempt to be exhaustive but rather to provide a snapshot halfway through the implementation to confirm that the network is heading in the right direction and to monitor progress, which will be complemented and delivered through the upcoming work in 2024-2025.

Highlights of the main achievements for each strategic focus areas

Availability and accessibility of medicines

"Recent years have brought many challenges in the area of medicines availability, but the work of the SPOC Working Party and the EMA's enhanced remit have made a huge difference. The agreement to change our approach to shortages and move towards prevention has been materialised through numerous activities, such as the publication of the first Union list of critical medicines and the good practices for industry for the prevention of human medicinal product shortages. These initiatives anticipate the implementation of the revised legislation and set the scene for future work."

Lorraine Nolan, Chair EMA Management Board, Chief Executive of Irish Health Products Regulatory Authority (HPRA), HMA

"The connector of various decisions towards patient access is the clinical evidence generated for a particular healthcare solution. It is therefore great to see how multiple stakeholders get together progressing such critical technical topics. Particularly the collaboration at the HTA/regulatory interface has been trailblazing and sets the scene for the future, on the basis of new legislation."

Michael Berntgen, Head of Scientific Evidence Generation Department, EMA

Goal 1

Strengthen the availability of medicines to protect the health of European citizens and animals.

Objectives

- Identify the specific root causes of shortages of medicines for human and veterinary use and develop strategies to improve prevention and management of shortages. (A better understanding of the specific causes for shortages of generics/off-patent products vis-à-vis products still under patent protection is essential.) Based on the outcome of a study of the causes, the aim is to identify and suggest areas where changes to EU or national legislation could improve supply.
- Foster the awareness among the public and healthcare professionals of the approval standards, safety, effectiveness and immunogenicity of similar biological products to facilitate the uptake of biosimilars in healthcare systems.
- Improve coordination of information and actions, including implementation of best practices, of EU regulatory authorities, stakeholders and international partners.
- Empower EMA with sufficient capacity to monitor and coordinate medicines' availability and supply. EMA should also coordinate the activities of the EMRN in order to ensure availability of critical medicines in the EU and the European Economic Area (EEA) by supporting increase of production capacity to meet demand.
- Increase transparency on availability/launch of medicines to facilitate targeted regulatory actions and communication with patients, Healthcare (HC) professionals and Health Technology Assessment (HTA) bodies.

Achievements

- The HMA/EMA multi-stakeholder workshop on shortages of human and veterinary medicines was held on 1-2 March 2023.During the workshop, stakeholders were updated on the activities and deliverables of the HMA/EMA Task Force on Availability of Authorised Medicines (TF AAM). Stakeholders also shared their perspectives on issues relating to medicines availability and discussed methods to contribute to future deliverables of the Task Force.
- A Good practice guide for industry on prevention of shortages was published in Q2 2023. The document recommends good practices to marketing authorisation holders, wholesalers, distributors and manufacturers on shortage prevention and mitigation for human medicines.
- An analysis of responses to a survey on multilingual packaging was undertaken, with subsequent preparation of action points.
- Expanded collaboration between the EMA-HMA TF AAM and the Joint Action on Coordination and Harmonisation of the Existing Systems against Shortages of Medicines – European Network (JA CHESSMEN) was supported to avoid potential duplication of work.
- Regulators and industry participants reported positive experience with the International Coalition of Medicines Regulatory Authorities' (ICMRA) Pharmaceutical Quality Knowledge Management System (PQ KMS) pilot programmes. A joint ICMRA-industry virtual workshop was held on 20 July 2023, during which participants discussed their experience of involvement in the pilots, as well as the future direction of the project.
- Development of an electronic product information (ePI) Common Standard for human medicines was completed. The EU ePI Common Standard will support the provision of harmonised electronic information on medicines within the EU and is a step towards

improved delivery of information for patients, consumers, and healthcare professionals to aid their informed decision-making.

- A joint statement on the scientific rationale supporting interchangeability of biosimilar medicines in the EU was published by the HMA and EMA, with an accompanying Questions & Answers document.
- Actions to monitor and coordinate medicines' availability and supply:
    - Implementation of EMA's extended mandate commenced, including the establishment of the Executive Steering Group on Shortages and Safety of Medicinal Products (also known as the Medicines Shortages Steering Group, MSSG), and a network of Single Points of Contacts in companies (iSPOC) to monitor shortages and availability issues.
    - Joint recommendations was issued by the European Commission (EC), HMA and the EMA for actions to avoid shortages of key antibiotics used to treat respiratory infections for European patients in the 2023/2024 winter season. The recommendations are based on data collected by EMA and the EC's Health Emergency Preparedness and Response Authority (HERA) on estimated demand and supply of a number of key antibiotics used to treat respiratory infections.
    - The EC, the HMA and EMA published the first version of the Union list of critical medicines. The list contains more than 200 active substances of medicines for human use considered critical for healthcare systems across the EU/EEA, for which continuity of supply is a priority and shortages should be avoided.

In progress

- The report on the root causes of shortages is under preparation.
- Development of Member States' Toolkit on biosimilars is under preparation.
- A pilot to test use of ePI started in Q3 2023.
- As a follow-up activity of the good practice guide for industry on prevention of shortages, HMA/EMA TF-AAM will develop a shortage prevention and mitigation plan (SPMP)[1] template.
- EMA-HERA (Health Emergency Preparedness and Response) exercise on antibiotics.
- Work is ongoing at multi-stakeholder level to quantify scale of impact of shortages of veterinary medicines.
- EU Veterinary Big Data Workplan has been developed for implementation of prioritised use cases. Use case on the availability of veterinary medicines includes real-time monitoring of shortages and identification of treatment alternatives.

[1] Corr.1 - on page 7 'software project management plan' corrected to 'shortage prevention and mitigation plan' (SPMP)

Goal 2

Optimise the path from development, evaluation through to access for beneficial medicines (innovative and follow-on) through collaboration between medicines regulators and other decision-makers.

Objectives

- Develop better scientific evidence which serves different decision makers along the decision chain (regulators, Health Technology Assessment (HTA) bodies and payers), including evidence to support post-licensing follow-up of medicinal products, thereby using a life-cycle approach to evidence generation and the possibility to adjust decisions based on new evidence.
- Develop clear and enhanced communication for patients, healthcare professionals, veterinarians and animal owners as well as downstream decision makers about the regulatory assessment including information gap inherent for medicinal products approved on the basis of limited scientific data and secondary endpoints (e.g. orphans, limited market veterinary medicinal products).
- Develop new metrics for accessibility of medicines that better represents real patient access to newly authorised medicinal products in different markets.
- Foster alignment of national implementation of compassionate use programmes to promote equity in access for patients during late-stage development and improved utilisation of data from such programmes to support later decision making.

Achievements

- Fostering mutual understanding of perspectives on evidence for decision making through EMA/EUnetHTA 21 bilateral discussions, including a dedicated meeting with focus on ATMP assessment which was held in Q1 2023.
- Progressing parallel joint scientific consultation involving the Scientific Advice Working Party (SAWP) and EUnetHTA under EUnetHTA21 service contract and the later launch of transitional arrangements for parallel scientific advice in the interim period until operations under the new HTA Regulation.
- Ensuring multi-topic technical engagement between regulators and HTA bodies at European level with a view to support the implementation of the new HTA Regulation and joint reporting about the achievements under the work plan.
- Conducting a multi-stakeholder workshop on patient experience data with a view to discuss ways to improve the collection and use of patient experience data to achieve patient-centred medicine development and regulation.

- Holding a PCWP/HCPWP Annual Meeting session exploring the intersection between regulatory and HTA assessments and its role in access. The follow-up survey has been completed and the analysis is underway.

In progress

- Support the implementation of the HTA Regulation:
    - Establishing collaboration with the new HTA Coordination Group (HTACG) and its four subgroups (with representation from all Member States and based on the new legislation);
    - Contribute to the work by the EC, the Member States and the HTACG and its subgroups in establishing the operations under the new HTA Regulation;
    - Continue promotion of opportunities for parallel joint scientific consultations.
- Started work on Patient Experience Data (PED):
    - EMA has established an internal working group on patient experience data (PED) and agreed to introduce a dedicated section on PED in the CHMP assessment report (AR) template;
    - Call for expressions of interest for EU Network experts to join the PED expert group to work on the reflection paper (agreed as part of the actions of the 2022 PED workshop);
    - Drafting of reflection paper on best EU approach to generating and collecting PED planned, with public consultation expected by Q2 2024;
    - Develop an Action Plan on PED.
- Developing a framework to review the evidence needs for decisions leading to access for innovative medicines that address unmet medical needs and have received specific support from a regulatory perspective.
- Finalise action plan for compassionate use programmes (CUP).

Data analytics, digital tools and digital transformation

"I am impressed to see the progress towards achieving the vision to improve regulatory decision-making by strengthening the place of data analysis to enable high quality, robust and rapid assessments of medicines. Hand in hand with stakeholders and partners, we are co-designing and co-building a better future for medicines development and regulation by leveraging data science, big data and new technology. Chances and opportunities of large language models and artificial intelligence approaches will foster these developments even further."

Karl Broich, Chair of HMA Management Group, President of German Federal Institute For Drugs And Medical Devices (BfArM)

"Digitalisation of EU regulatory network operations is essential to bring efficiencies today but also prepare foundations for the future. We are investing in experimentation with emerging technologies, including Artificial Intelligence, whilst building essential capabilities that underpin the optimisation of our regulatory work. The EU NTC is another key part of the response towards ensuring sustainable capacity and capabilities in the EU regulatory system. It represents the joining of forces to build a network of trainers and learners ready to tackle the regulatory challenges of today and tomorrow."

Zaïde Frias, Head of Digital Business Transformation Taskforce, EMA

Goal 1

Enable access to and analysis of routine healthcare data, enable analysis of individual patient data from clinical trials and promote standardisation of targeted data.

Objectives

- Deliver a sustainable platform to access and analyse healthcare data from across the EU (DARWIN EU ®).
- Pilot the analysis of individual patient data from clinical trials in initial marketing authorisation assessments with a view to a targeted roll-out of such analyses.
- Establish collaborations with external stakeholders (including patients, academia, non-governmental organisation and industry) and with international regulatory authorities on big data initiatives.
- Establish an EU framework for data quality, discoverability and representativeness through agreement on meta-data for regulatory purposes, a standardisation roadmap and registers of real-world data sources and of observational studies.

Achievements of the Big Data Steering Group (BDSG)

- DARWIN EU ® coordination centre celebrated its first anniversary in early 2023, with the onboarding of the first 10 data partners, providing to date access to more than 26 million active patient data) and with the delivery of 4 studies in 2022 to support to EMA's Pharmacovigilance Risk Assessment Committee (PRAC), EMA's Committee for Orphan Medicinal Products (COMP) and EMA's Committee for Medicinal Products for Human Use (CHMP). DARWIN EU ® was selected to take part in the European Health Data Space (EHDS) pilot for the secondary use of health data. with its use case on coagulopathy and COVID-19. DARWIN EU ® operation is supported by the DARWIN EU ® advisory board; its mandate and membership were reviewed in 2023.
- The value of real-world evidence (RWE) is being established and a solid demand for RWE studies has been seen since 2022: overall more than 50 studies have been requested by EMA committees and network. In 2023, EMA published a report on its experience in using real-world evidence to support regulatory decision-making between September 2021 and February 2023 which described studies conducted on medicine safety, medicine use, disease epidemiology, design and feasibility of clinical trials and clinical management.
- CHMP clinical trial raw data pilot was launched in 2022 to help assess the benefits and practicalities of access to clinical trials raw data in the assessment of medicines. Data for the fifth product for analysis has now been received by EMA, marking the halfway point of the pilot. The pilot is supported by the Advisory Group on Raw Data and the Industry Focus Group on Raw Data. The pilot tests three models of delivering individual patient data analyses, based on EMA, rapporteur team or a contractor. The Danish Medicines Agency (DKMA) was selected as a contractor for the third model. Support for marketing authorisation holders (MAHs) has been important and in 2023 EMA published the application of EMA's transparency principles to the raw data proof-of-concept pilot.
- Collaborations with external stakeholders and partners have been established via the annual multistakeholder big data forum and specialized workshops (such as the HTA and payers' bodies workshop on DARWIN EU, the workshop on real world data (RWD) quality and real world evidence (RWE) use, workshop on data quality framework for medicines regulation, and the artificial intelligence (AI) workshop).
- International collaboration on RWD and RWE has also increased under the umbrella of ICMRA (see the ICMRA statement on international collaboration on RWE in regulatory

decision making) and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) (see the public consultation on ICH reflection paper on RWE terminologies and studies, on ICH M14 Use of RWD for safety assessment of medicines and on ICH M11 clinical electronic structured harmonised protocol (CeSHarP)).

- The first EU data quality Framework for EU medicines regulation has been developed with the methodology working party and was published in 2023 following a public consultation.
- As a step towards enabling data discoverability and following public consultation, the Big Data Steering Group adopted and published a list of meta data for real world data which is used to collect data for the HMA EMA catalogues of real-world data sources and non-interventional studies.

In progress for the Big Data Steering Group

- DARWIN EU ® will increase the delivery of studies in its second year of operation with 19 planned studies (of which 5 has already been completed) and access to more health data with the onboarding of 10 additional data partners. Pilots with EMA scientific committees, the European Centre for Disease Prevention and Control (ECDC), the Vaccines Monitoring Platform and HTA/Payers, and EHDS2 pilot will continue in 2024.
- The HMA EMA catalogues of real-world data sources and non-interventional studies will be rolled out to the public at the start of 2024 together with the final Good Practice Guide for the use of the Metadata Catalogue of Real-World Data Sources. Through these public searchable catalogues, data will be more discoverable and of known quality and representativeness.
- In the veterinary domain, a study is ongoing to map the data landscape and identify relevant data sources. This is planned to be followed by a study on metadata and subsequently the information on veterinary data sources will also be included in the catalogue of data sources.
- A chapter on RWD/RWE data quality consideration will be released for public consultation in early 2024.
- An interim report on the CHMP clinical trial raw data pilot is planned for 2024.
- BDSG will survey the EMRN computing capability to analyse big data in 2024.
- BDSG will explore analysis of additional data types, such as nonclinical raw data, mHealth data, social media, genomics and patient experience data in 2024.

Goal 2

Build sustainable capability and capacity within the network

Objectives

- Build EU network capability to analyse big data.
- Digitally transform the EU network's scientific and regulatory processes to enable use of digital tools and analytics and create supporting digital infrastructure, for example, to support the uptake and review of big data (from electronic health record (eHR), registries, devices etc.).

Achievements of the Big Data Steering Group

- After the selection of the training providers, the big data training curricula was launched in December 2023 with the rollout of the first two modules related to the pharmacoepidemiology and real-world evidence (RWE) domains. Members of the EU medicines regulatory network can now access the first modules through the EU Network Training Centre Learning Management System (EU NTC LMS). Further modules in the pharmacoepidemiology and RWE curriculum will be published over the next two years. Work is also ongoing on the development of a data science curriculum, with the first modules in this curriculum expected to be released in January 2024.
- The first EU AI reflection paper has been published for public consultation and the 1st multi-annual AI workplan to 2028 was adopted by HMA and EMA's Management Board in December 2023. The AI workplan to 2028 has been developed in collaboration with the network and stakeholders to manage the increasing complexity in the area of AI and to collaborate and coordinate activities across the EU network to maximise the value extracted from AI. It covers activities across four domains (guidance, policy and product support; tools and technology; collaboration and change management; experimentation).
- Several initiatives to experiment on advanced analytics, including AI, have been launched under BDSG umbrella.

In progress for the Big Data Steering Group

- BDSG will discuss training needs for patients, healthcare professionals and academics and will adopt the genomic training curriculum in 2024.
- As part of its experimentation initiatives on advanced analytics and AI, in 2024 BDSG will roll-out AI knowledge management tools for core regulatory processes, starting with the Scientific Advice Working Party.

Achievements to date related to experimentation, digital tools, analytics, digital infrastructure:

- Establishment of the Digital Innovation Lab (DigiLab) and expansion of the Analytics Centre of Excellence (ACE) within the Digital Business Transformation Task Force, as a set of activities to discover, experiment and develop digital solutions that have the potential to support core business and support functions across the Agency.
- Efficiencies gained through the launch of new automation tools across a number of business areas where activities are performed manually, such as the new certificate processing system which enables the generation of medicine certificates faster using a process that is fully digital.

- Controlled experimentation with OpenAI and ChatGPT technology to explore where this technology could be used at EMA to support strategic goals.
- Launch of the Agency's first virtual reality powered training to raise cybersecurity awareness using innovative and engaging approaches.
- Development of an EMA QR code generator to eliminate paper waste, including moving to digital business cards and to increase engagement and convenient access to information.
- Experimentation with new digital technologies, such as Chatbots Power Platform automation technology, to explore areas where they can be implemented for further efficiency and productivity gains.
- Further development of EMA's change management practices internally and with respect to the network and stakeholders through a Change Management Centre of Expertise. This is to ensure readiness and long-term adoption of digital and other changes.

In progress related to experimentation, digital tools, analytics, digital infrastructure:

- There is active EU collaboration on AI via the EU Agencies Network (EUAN). The community aims to use trustworthy and human-centric artificial intelligence for increased collaboration amongst EU agencies and Member States, thereby developing and promoting the AI community, whilst seeking efficiency gains and demonstrating the overall added-value and contribution of EU agencies and Members States to the EU AI Strategy.
- The DigiLab innovation framework is being leveraged for other use cases, for example, to explore the potential for health data analytics, applications for artificial intelligence and the further use of robotics.

Achievements to date related to the EU Network Training Centre

- Endorsement of a new strategy for the EU Network Training Centre, aligned to EMANS strategic goals, that foresees further strengthening of the EU Network Training Centre (NTC), greater use of innovative learning approaches and expansion to new audiences.
- Work with regulatory partners in the network and with EU NTC Training Steering Group members to identify short- and long-term capacity needs and further development of capacity and expertise across the regulatory network through curriculum development and knowledge-sharing initiatives.
- Introduction of new incentives to promote capability and capacity building by launching a process for remuneration of National Competent Authorities (NCAs) for the development and delivery of training through addendum to cooperation agreement between EMA and NCAs, which was adopted by the EMA Management Board in June 2023.
- Launch of a learning toolkit to streamline the support to course organisers and curriculum developers developing new learning interventions.
- Delivery of a digital academy at EMA to support the development of digital skills, to increase digital literacy, capability and capacity and raise awareness of digital topics at all levels. Seven modules have now been launched on topics such as digital mindset, digital wellbeing, artificial intelligence, robotic process automation, cloud computing, design thinking and LEAN.

- Improvements in the EU NTC Learning Management System (LMS) through automation of user management processes.
- Facilitation of greater public awareness of these activities through publication of an EU NTC information webpage on EMA's corporate website.

In progress

- Initiation of work on the development of an EU NTC engagement portal, which will provide a single point of access to the EU NTC LMS containing the EU NTC training courses.
- Continuation of EU NTC support to the EU4Health Joint Action on Capacity Building, including engagement with the NCA coordinator and topic leads for the sustainability and development of skills work packages. The EU NTC is exploring how best to support the work of the joint action through its governance and operational structure, methodology in the establishment of curricula, and involvement in the development and delivery of training.
- Work to integrate EU NTC LMS and EMA accounts, bringing simplicity to EU NTC stakeholders by allowing users to have the same login details for the Learning management system (LMS) as for other EMA systems.
- Expansion of the Digital Academy to the European medicines regulatory network and development of new modules within the Digital Skills Framework. Consideration will be given to those topics of shared interest and that benefit both EMA and other parts of the EMRN.
- Continuing interactions to support and build on the work of the EU4Health Joint Action on capacity building within the relevant work packages, such as IncreaseNET, as well as initiation of activities to complement the Joint Action work, (e.g. through progression of areas of training not covered by the Joint Action).

Goal 3

Promote dynamic regulation and policy learning within the current regulatory framework.

Objectives

- Modernise the delivery of scientific advice at central and national level by developing network skills and processes.

Achievements for the Big Data Steering Group

- The Methodology Working Party has been established. It has issued its 3-year workplan, the 2nd version of which is now open for public consultation. The methodology European Specialist Expert Community (ESEC) has also been established with more than 180 experts, including 51 experts in AI and 79 RWE experts.

- The multi-stakeholder workshop on qualification of novel methodologies was held in April 2023 and will inform further discussion with BDSG.
- National competent authorities (the Danish Medicines Agency (DKMA); the Federal Institute for Drugs and Medical Devices Germany (BfArM), the Federal Institute for Vaccines and Biomedicines Germany (PEI), the Spanish Agency of Medicines and Medical Devices (AEMPS), Portuguese National Authority of Medicines and Health Products (Infarmed), Swedish Medical Products Agency (SMPA) and Medicines Evaluation Board (MEB)) collaborated in 2022, sharing good practice in data and analysis (in the area of data access, legal aspects, capabilities, infrastructure, methods development and Artificial Intelligence): Principles on 'Clusters of Excellence' were agreed and the Clusters of Excellence discussion paper was published in 2023.

In progress for the Big Data Steering Group

- BDSG will adopt the network change management strategy.
- BDSG will discuss recommendation on EHDS implementation and collaborate with the joint action Towards the European Health Data Space II (TEHDAS II).
- BDSG will support discussion on and piloting of the revised Pharmaceutical Strategy for Europe.

Goal 4

Ensure that data security and ethical considerations are embedded in the governance of data within the Network.

Objectives

- Ensure data are managed and analysed within a secure and ethical governance framework.

Achievements for the Big Data Steering Group

- The review of the network data governance has been completed: the Big Data Steering Group and Network data board mandates were endorsed by HMA (May 2023) and EMA Management Board (June 2023). The BDSG mandate and membership is now strengthened with representation of EHDS, Clinical Trials Coordination Group (CTCG), HTA bodies and payers and ethic bodies or networks. (The nominations process is now also completed.)
- The BDSG has updated its workplan annually (BDSG workplan 2023-2025), informed by stakeholders and partners feedback.
- The European Veterinary Big Data strategy 2022- 2027 was adopted in 2022 and this was followed by the EU Veterinary Big Data Workplan to 2022-2025 which was adopted in 2023.

- A series of training webinars on data protection in medicines and public health have been delivered to experts from Members States.
- DARWIN EU ® data protection impact assessment has been completed and lessons learned have been shared with the network of NCA data protection officers.
- The support to EHDS, TEHDAS and revised Pharma strategy for Europe continued. BDSG also discussed and considered learnings from HORIZON-HLTH-2022-TOOL projects.
- Ethics considerations have been included in the AI reflection paper launched for public consultation.

In progress for the Big Data Steering Group

- The BDSG will deliver a first network data strategy in 2024.
- The support to EHDS, TEHDAS Joint Action 2 and the revised Pharma strategy for Europe will continue in 2024. Key deliverables of the HORIZON-HLTH-2022-TOOL projects will be presented to BDSG.

Innovation

"Regulators need to be prepared to support the development and regulation of increasingly complex medicines, including combined and borderline products, that more and more deliver healthcare solutions by converging different technologies. Addressing the different innovation goals should facilitate the translation of innovative products into novel treatments, which is called "from bench to bed," with the overall key objective of promoting and safeguarding human and animal health."
María Lamas, Executive Director of Spanish Agency Of Medicines And Medical Devices (AEMPS), HMA

"Digitalisation within pharmaceutical manufacturing leads to more robust and flexible processes enhancing continuity of supply of effective and safe medicines. Regulatory facilitation of these novel manufacturing technologies unlocks the potential for increased productivity, improved compliance, enhanced systems connectivity and actionable insights into the production processes that are essential to ensure continuity of supply in a globalised operational environment."
Tony Humphreys, Regulatory Science Adviser, EMA

Goal 1

Catalyse the integration of science and technology in medicines development and ensure that the network has sufficient competences to support innovators in various phases of medicines development.

Objectives

- Support the integration of scientific and technological progress in the development of medicines (e.g., precision medicine, biomarkers, 'omics and ATMPs) and ultimately into patient treatment.

- Transform the regulatory framework for veterinary medicines to support innovation and successful implementation of the veterinary medicines regulation.
- Implement an EU-level model for efficient, timely and coordinated horizon scanning and priority setting that fulfils the needs of both regulators and HTA-bodies and payers.
- Facilitate the implementation of novel manufacturing technologies.

Achievements

Precision medicine, biomarkers, 'omics':

- Process improvement platform for qualification of opinions: an R&D platform industry stakeholders focus group has been established and a workshop took place in March 2023. The focus group discussed horizon scanning activities as well as case studies related to common or emerging qualification objects (digital endpoints, RWE, biomarkers, modelling and simulation approaches to bioequivalence). The focus group outcome was reported at the December 2023 R&D industry platform meeting.
- Support for developers via Innovation Task Force (ITF) and Business Pipeline Meetings (BPM) is in place, expanding early points of contacts for technologies and methods related to drug development. The number of support meetings increased overall, with a high proportion focused on technology.
- Publications on the development of biomarkers from discovery to regulatory qualification for drug development: https://doi.org/10.3389/fmed.2022.878942; https://doi.org/10.1002/cpt.2554.
- EMA's Senior Scientific Adviser was nominated as the European Medicines Agency's Strategic Advisor to C-Path.
- EMA membership in the Science and Innovation Panel (SIP) of the Innovative Health Initiative (IHI).
- A number of IHI calls have been launched in this field:
    - "Personalised oncology: Innovative people-centred, multi-modal therapies against cancer";
    - "An innovative decision-support system for improved care pathways for patients with neurodegenerative diseases and comorbidities";
    - "Cardiovascular diseases – improved prediction, prevention, diagnosis and monitoring";
    - "Next generation imaging and image-guided diagnosis and therapy for cancer";
    - "Screening platform and biomarkers for prediction and prevention of diseases of unmet public health need".

Support the integration of scientific and technological progress in the development of medicines (e.g. precision medicine, biomarkers, 'omics and ATMPs) and ultimately into patient treatment:

- ATMP:
    - Launch of pilot providing enhanced support to academic ATMP development.

- ATMP cluster meetings held with the Food and Drug Administration in the USA (FDA), the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) and Health Canada.
- Fostering novel manufacturing methods with the establishment of the Quality Innovation Group.
- Quality Innovation Group (QIG) survey and ITF review summarising novel technologies.
- From 1 January 2020 to 31 December 2023, 43.1% of products that received Priority Medicines Scheme (PRIME) eligibility were ATMPs (28 ATMPs out of 65 products).
- Dedicated training modules on navigating the regulatory requirements and scientific advice for ATMPs.
- Actionable objectives for the cooperation between the EMA and the European Innovation Council (EIC) were agreed in December 2022 and various initiatives delivered through 2023.

- EU IN borderline classification group (BLCG):
  - Continues to meet regularly to discuss borderline classification cases raised by NCAs;
  - Includes representatives from other networks (e.g. medical devices, Substances of Human Origins (SOHO));
  - Provided input into the revision of the pharmaceutical legislation which includes a proposed mechanism for a scientific opinion at EMA level as to whether a borderline product is or is not a medicinal product.
- Simultaneous National Scientific Advice (SNSA):
  - Offers consolidated scientific advice from more than NCA with a single entry point;
  - Phase 2 of the pilot ongoing with an optimised procedure and a focus on advice related to clinical trials;
  - Information published on EU-IN webpages on the EMA and HMA webpage including procedural guidance, common application form and templates.

Transform the regulatory framework for veterinary medicines to support innovation and implementation of veterinary medicines regulation:

- Guidance for the implementation of the Regulation produced before the implementation date, consisting of over 50 documents, many of which concern biologicals/immunologicals.
- The EMA's Committee for Veterinary Medicinal Products (CVMP) worked with the European Food Safety Authority (EFSA) on risk assessment with a view to aligning the methodology for estimating consumer exposure to residues, including dual-use substances. A draft guideline "Development of a harmonised approach to exposure assessment methodologies for residues from veterinary medicinal products, feed additives and pesticides residues in food of animal origin" has been approved by the CVMP and EFSA. It has gone through a consultation period and is currently under revision.

- The Novel Therapies & Technologies working party (NTWP) of the Veterinary Domain has been set up and is currently producing guidance on the efficacy of cell therapies (Draft Guideline on the development and data requirements of potency tests for cell-based therapy products and the relation to clinical efficacy) and bacteriophages (Draft Guideline on quality, safety and efficacy of bacteriophages as veterinary medicines), and is also working on the safety of nanomedicines. Members from the human domain within the NTWP are also involved in the drafting of the guidance.
- Quality Innovation Group has been established and will also address requests coming from veterinary companies.
- Assessment of the efficacy of the EMA policy on minor-use-minor-species via collecting data. A paper is to be published in the short term.
- Study of chronic toxicity studies performed in the dog used for the setting of maximum residue limits (MRLs) for substances used in Veterinary Medicinal Products (VMPs).
- Trainings and webinars with stakeholders at EMA and national level about the functionality of EVVET3, adverse events reporting and recording and the signal management process. Guidance/Q&A has been published.

Implement an EU-level model for efficient, timely and coordinated horizon scanning and priority setting that fulfils the needs of both regulators and HTA-bodies and payers:

- Establishment of an EMA EU-IN horizon scanning (HS) as a systematic activity and delivery of several published or internal reports on topics of high regulatory interest via engagement with external horizon scanning initiatives, including initiatives of ICMRA, International Horizon Scanning Initiative (IHSI), World Health Organization (WHO) and Joint Research Centre (JRC).
- Publication by HS of reports on Artificial Intelligence and on Genome Editing (2021), as Rapporteur and in collaboration with ICMRA, respectively (https://doi.org/ 10.1038/d41573-021-00130-7 and https://doi.org/10.1038/d41573-022-00190-3), and on implementing the recommendations in policy and practice; Genome editing – stakeholder workshop in Q1 2023.
- Publication of a report assessing international HS signals by JRC and WHO https://doi.org/10.3389/fmed.2022.1064003;
- Identification of new technologies via HS, ITF and scientific advice activities.

Facilitate the implementation of novel manufacturing technologies:

- Establishment of the Quality Innovation Group in 2022.
- Two listen and learn focus group meetings with industry, academia and international partners participation in March and November 2023. The topics discussed reflected the priority topics identified through a stakeholders survey in 2022. These included continuous manufacturing (CM), decentralized manufacturing (DM), Pharma 4.0, AI and digitalisation. Following the meetings reports have been written (one publicly available and one soon to be published) highlighting the challenges raised by industry, possible solutions and the actions that QIG will take to help address these challenges.
- Sharing knowledge with the Network: Regular updates have been provided at the relevant Working Parties (Biologics and Quality Working Parties) and GMDP inspectors Working

Group (IWG) aiming to share experiences and learnings with the network. Guidance is being developed as regulatory understanding on the priority topics evolves, in the form of a Q&A on process models and a Q&A on decentralised manufacturing.

- Working together with our international partners: In 2023 following an FDA visit at the EMA it has been agreed that FDA and QIG will work closely to advance and align regulatory thinking in the area of advanced manufacturing. Deliverables are an action plan and agreed priority topics for joint guidance development; agreement for regular product related information exchanges and collaborative advice/ assessments.
- Product specific support:
    - Development support for applicants through one-to-one meetings with applicants and ITF contributions. Topics included decentralised manufacturing for ATMPs; alternative sterilisation methods to help ensure supply and avoid shortages, continuous manufacturing for vaccines etc.;
    - Scientific advice on use of robots for aseptic filling, AI for visual inspection of sterile products, ATMP decentralised manufacturing.;
    - Joint visit with FDA (CBER) to an EU vaccine manufacturing facility using novel facility designs and extensive automation aiming to allow flexibility in manufacturing and rapid increase in manufacturing capacity to meet demand.

In progress

- Continue to progress workplans of relevant groups (QIG, Novel Therapies & Technologies Working Party, EU-IN and ICMRA).
- Concerning the QIG:
    - Continue work on priority topics as reflected in the QIG workplans and monitor progress in other areas.
    - Close collaboration with FDA on topics of mutual interest, considering joint scientific advice, reviews of marketing authorisation applications and guidance when relevant.
    - More case studies and learnings to WPs and IWG.
    - Continue collaboration with industry interested parties and academia.

Goal 2

Foster collaborative evidence generation, improving the scientific quality of evaluations and ensuring generation of evidence useful to all actors in the lifecycle of medicines, including HTA and pricing and reimbursement authorities.

Objectives

- Foster innovation in clinical trials and develop the regulatory framework for emerging clinical data generation.
- Leverage non-clinical models and 3Rs principles and optimise capabilities in modelling, simulation and extrapolation and invest in special population initiatives.
- Develop further the collaboration of various groups involved with scientific advice and/or regulatory guidance.

Achievements

Foster innovation in clinical trials:

Clinical Trial Information System (CTIS)

- Launch of the Clinical Trial Information System (CTIS) enabling the mandatory applicability of the Clinical Trial Regulation (CTR) in January 2023.
- Online training programme dedicated to sponsors and member states user to support user journey and activity in CTIS; CTIS training materials also available.
- Onboarding of the user community on the use of CTIS with a variety of stakeholder events to enhance quality of clinical trial application (CTA) submission;
- CTIS becomes a registered data provider for the WHO International Clinical Trials Registry Platform (ICTRP) in May 2023;
- Public consultation on CTIS transparency rules in May 2023, culminating in revised CTIS transparency rules adopted in October 2023;
- Reorganised Clinical Trials Coordination Group (CTCG) and integration with SAWP, EU-IN, ACT EU etc. and facilitated by INNO governance meetings;
- Facilitation of assessors community collaboration (at an assessors round table);
- Publication of monthly Key performance indicators (KPIs) to monitor the European clinical trials environment and launch of annual sponsor surveys to identify issues with the CTR and develop tailored solutions.
- EU-IN meeting in Madrid in 2022 was successful in reinforcing collaboration between different groups (INNO collaboration). There were also increasing interactions and the delivery of an academic workshop.
- The Emergency Task Force (ETF) and European Commission hosted an event, in June 2023, to collect insights and suggestions for possible EU-level actions to improve the way clinical trials are set up and conducted in the European Union (EU) during public health emergencies.
- Launch of the CTR collaborate initiative, anchored to ACT EU, to facilitate optimised MS and NCA ethics collaboration on clinical trial authorisation under CTR.
- Launch of the COMBINE project by NCAs and European Commission to address the challenges at the interface of the the Clinical Trial Regulation and the EU Medical Device Regulation 2017/745 and In Vitro Diagnostic Regulation 2017/746 (CTR/MDR/IVDR), with

links to the multi-stakeholder platform (MSP) and EMA activity in clinical trials and medical devices.

Accelerating Clinical Trials in the EU (ACT EU)

- The ACT EU programme transitioned into an early delivery mode and issued a revised work plan 2023 to 2026 covering 11 priority actions:
- Establishment of the ACT EU Steering Group, with adoption of its mandate and membership;
- Creation of a priority action on clinical trials in public health emergencies to facilitate, together with Member State NCAs and ethics committees, the rapid approval of clinical trials when an emergency hits;
- Publication of Q&A on Complex Clinical Trials; Recommendation paper on decentralised elements in CTs in Dec 2022;
- Multi-stakeholder events embedded as part of the ACT EU activity, including workshops on ICH E6 (R3), and clinical trial methodologies in 2023;
- Public consultation on the multi-stakeholder platform (MSP) to improve clinical trials in the EU, launched in February 2023, and kick-off meeting of the MSP in June 2023;
- An open call for nominations to create the Multi-stakeholder Platform Advisory Group (MSP AG) concluded in November 2023 to provide both strategic and operational input to the programme;
- Training strategy available since 2022, setting out high-level objectives for the development of a training curriculum, with completion of the regulatory training needs assessment and gap analysis completed in 2023;
- ACT EU Steering Group prioritises support to academic sponsors in conducting multinational clinical trials and delivering a clinical trials data analytics research agenda as key areas for additional EU public funding.
- The EU-IN workplan includes the Simultaneous National Scientific Advice (SNSA) project, now in phase 2 (optimised procedure), supported by ACT-EU and CTCG, with a clear focus on clinical trials applications.

Develop the regulatory framework for emerging clinical data generation:

- ICH GCP renovation:
    - Modernised the GCP regulatory oversight to enable decentralised models of clinical trials coupled with direct digital data accrual;
    - Development and adoption of novel practices that facilitate CT authorisation, GCP and HTA acceptance at EU and international level.
- Set up of focus group on qualification of novel methodologies during 2022 focusing on horizon scanning for future methodologies, including digital endpoints and on identification of additional expertise needs and necessary improvements in the qualification process.
- Qualification of digital technologies and transfer of learnings to future guidance development. (Publication of draft CHMP Opinion for 'Stride velocity 95th centile measured by a valid and suitable wearable device' as primary endpoint in Duchenne Muscular Dystrophy clinical trials for public consultation).

- EMA expert base expanded in the areas of digital, biomechanics and devices.
- Public consultation and workshop on data quality framework launched in 2022.
- Progress on the establishment of DARWIN EU, including the pilots running at EMA committees to test the generation and use of RWE in decision making. Ten first datapartners onboarded to DARWIN EU. Studies ongoing and first analysis completed. Multi-stakeholder workshop on Real World Data (RWD) quality and Real World Evidence (RWE) use held in June 2023.

Leverage non-clinical models and 3Rs principles and optimise capabilities in modelling, simulation and extrapolation and invest in special population initiatives:

Leverage non-clinical models and 3Rs principles

- Launch of the 3Rs Working Party supporting qualification of new alternative 3R-compliant methods/models including in silico and novel in vitro assays.
- Launch of a specific ITF platform to discuss methodologies that minimise animal testing during medicines development.
- To support data driven decision-making and advanced analytics, access to state-of-the-art software packages and databases has been obtained and is available to EMA staff and the network. Lhasa software aims to aid regulatory and scientific review by providing tools for predicting safety and quality properties in medicines development, combined with in silico software packages for advanced analytics (e.g., Derek Nexus, Kaptis, Sarah Nexus).
- Implementation of the revised carcinogenicity guideline ICH S1(R1), which seeks to reduce the number of in vivo studies performed via a scientific weight-of-evidence approach:
    - Systematic review of organ-on-chip technology in medicines development: state-of-the-art and gaps to be addressed for purposes of qualifying the methods;
    - Implementation of the ICH M7(R2) guideline for the evaluation and control of mutagenic impurities.

Optimise capabilities in modelling, simulation and extrapolation

- Creation of the Methodology Working Party and associated 3-year work programme:
    - Application of new methodologies such as extrapolation and modelling & simulation through the HTA consortium (EMA/EUnetHTA21 work plan) is in progress;
    - Initiation of ICH guideline drafting work (ICH M15) – General Principles for Model-Informed Drug Development - Project initiated so action can be considered complete;
    - Q&A on PD1 / PD-L1 drafted, GCG review Q4 2022. Q&A published Q1 2023;
    - Technical advice to research funders on this topic area.

Invest in special population initiatives

- Strategic initiative in maternal-foetal health and advancing access through better understanding and communication of benefits, risks, and uncertainties of medicines use in pregnancy and breastfeeding.
    - The ICH Assembly endorsed the proposal for a new efficacy topic (E21) on "Inclusion of Pregnant and Breastfeeding Individuals in Clinical Trials".
    - Development and implementation of an algorithm to identify pregnancy-related spontaneous reports in EudraVigilance in support of enhanced signal detection for this population. The algorithm is a substantial improvement over the MedDRA SMQ used thus far and has been adopted by the WHO.
    - Initiated and leading on CONSIGN: Covid-19 infectiON and medicineS In pregnancy, an EU-led global study of the impact of COVID and its treatments on pregnant people and their babies. EMA is leading on the meta-analysis of RWE data sources, to which the US CDC, US FDA, Health Canada, Saudi FDA and academic and clinical centres from around the globe contribute with the view to expanding to other disease areas in future.
    - EMA-FDA-MHRA regulatory cluster has been set up and is meeting monthly to collaborate on strategy development and implementation on medicines in pregnancy & breastfeeding, as well as product-specific discussions between EMA & FDA.
- COMP expert group meeting and paper on orphan condition nomenclature for inherited retinal dystrophies.
- Recently launched CHMP pilot on RWE and the CHMP workplan makes reference to geriatric use cases. A number of RWE studies relevant to geriatric use will be performed in 2023 (e.g. disease epidemiology to contextualise the CT results) or RWE studies to look at safety and efficacy in very elderly and frail.
- Erythromycin project for intestinal motility using DARWIN ongoing drug utilisation study of medicines with prokinetic properties in children and adults diagnosed with gastroparesis.

Develop further the collaboration of various groups involved with scientific advice and/or regulatory guidance.

- Ongoing collaboration within the INNO framework (SAWP, EU IN, CTCG, HTA and ACT EU) through the annual meetings and regular interactions.

In progress

- Continue to progress workplans of relevant groups (CTIS, CTCG, ACT EU, 3Rs WP, EU-IN, Methodology WP, EunetHTA and INNO).

Goal 3

Enable and leverage research and innovation in regulatory science.

Objectives

- Develop network-led partnerships with academia to undertake fundamental research in strategic areas of regulatory science.

Achievements

- Publication of EMA's Regulatory Science Research Needs (RSRN).
- Systematic engagement with research funders across Europe, including Commission Directorate General for Research and Innovation (DG RTD) and IHI.
- Ring-fenced EMA funding to address rapidly emerging regulatory science research questions.
- Coordinated involvement in regulatory science projects on RWD for regulatory decision-making, AI, obesity, mental health, biomarkers non-cancer authorised medicines, pragmatic trials.
- Best practices for collaboration with academia identified, to be implemented by NCAs.
- Completion of a study of the experience of the EMA with involvement in multi-stakeholder regulatory science research projects based on semi-structured interviews of staff members and project coordinators (submitted for publication).
- Contribution to the draft Strategic research and innovation agenda (SRIA) of the forthcoming European Partnership Animal health and welfare.
- The European Innovation Network (EU-IN) and AEMPS organized a multi-stakeholders meeting on 26 September 2023, under the Spanish EU-Presidency, to promote research and development of innovative medicines and related technologies & methodologies in the EU.
- The Strengthening Training of Academia in Regulatory Sciences, a project of the European Commission (STARS) project concluded with all deliverables achieved. Dissemination of Common Strategy of STARS with 21 recommendations. EU IN promoting the implementation of these recommendations through different channels (ACT EU priority actions, IncreaseNET).

In progress

- Continue to identify opportunities for engagement to influence the launch of funding calls.
- Continue to develop network coordination in individual regulatory science research projects through the EU Innovation Network.

Goal 4

Enhance collaboration with other stakeholders including medical device experts, notified bodies, SMEs and research/academic groups.

Objectives

- Increase collaboration with medical device authorities and notified bodies, exchange knowledge and facilitate collaboration and sharing of expertise to ensure effective and appropriate regulation of combination products.
- Promote early interaction with academia, researchers and SMEs with a view to increasing awareness of regulatory requirements and facilitating the translation of research into authorised medicinal products and ultimately into clinical practice.

Achievements

Disseminate and exchange knowledge, expertise and innovation across the network and to its stakeholders:

- Surveys for HMA and LMS users on training needs and priorities in the network.
- New domain for international regulators set up in the EU NTC LMS and access to product information modules provided to a small number of African regulators. Efforts are ongoing to offer access to certain EU NTC courses to a wider number of international regulators.
- Contract signed with an external consultant for development of a learning design and development toolkit for curriculum steering groups and course developers.
- Ongoing work with SAP to improve the reporting analytics of the LMS.
- Interactions initiated with EU-IN (training in new areas of innovation), and PIC/S (training in GMP). Discussions also initiated on future of learning topics – implementation of MAWP topics, interactions with external organisations, new areas, interactions with academia.
- Discussions initiated on a stand-alone EU NTC home page, as well as visibility on EMA corporate web page.
- Digital Academy launched, digital skills framework developed and introductory modules in a number of topic areas now available. Modules on other digital topics including artificial intelligence under development.
- Engage with academia to develop regulatory training modules, including describing innovation of new medicines and their progression from laboratory to patient:
    - Publication of video tutorial "How to apply and benefit from an Orphan Drug Designation" with European Infrastructure for Translational Research (EATRIS);
    - EMA and the European Clinical Research Infrastructure Network (ECRIN) joint training session - Implementation of the Clinical Trial Regulation (EU) No 536/2014 for academia;

- Webinar for small and medium-sized enterprises (SMEs) and academia on the Clinical Trials Regulation and the Clinical Trials Information System – CTIS.

Increase collaboration with medical device authorities and notified bodies, exchange knowledge and facilitate collaboration and sharing of expertise to ensure effective and appropriate regulation of combination products:

- Establishment and operation of the medical devices expert panels, with the creation of a list of experts and the thematic mapping of expertise.
- Establishment of a process for multi-stakeholder scientific advice to support development of medicine-device combinations, qualification methodologies and the use of companion diagnostics. Engagement with industry in the context of the R&D platform meeting resulted in following outcomes:
    - Industry (incl. MedTech industry) to provide an in-depth analysis of scope/remit as well as typical types of questions that would be subject to such scientific advice.
    - Pilot launch of scientific advice for selected medical device products.
    - Agreement that EMA will consider future engagement opportunities on the refinement of the integrated pathways concept.
- Create a process to consult medical device authorities and/or notified bodies (as applicable) for device-related aspects throughout the product lifecycle, including post-authorisation safety related events:
    - Prioritisation is still given to medical devices (MDR) and Regulation (EU) 2017/746 (IVDR) implementation, however the necessary collaborative interactions with EC MDCG and the Notified Body Coordination Group (NBCG) have been established in an effort to develop more procedural guidance in the lifecycle management.
- Adapt consultation processes to address emerging digital technologies and wearables:
    - Internal EMA Digital Therapeutics Matrix established to monitor, share and discuss cases. Existing EMA services of engagement and consultation i.e. Innovation Task Force, Scientific Advice and Qualification of Novel Methodologies (QoNM) are involved. Amendments to their scope/procedure/expertise are being discussed (e.g. Focus Group on QoNM as part of the R&D stakeholder platform and EMA workshop on QoNM in March 2023) and are being implemented.
    - Operation of the EU-IN HMA/EMA Borderline Classification Group.

Promote early interaction with academia, researchers and SMEs with a view to increasing awareness of regulatory requirements and facilitating the translation of research into authorised medicinal products and ultimately into clinical practice:

- Engaged with DG Research & Innovation, European Commission Directorate General for Health and Food Safety (DG SANTE), Directorate-General for Communications Networks, Content and Technology (DG CONNECT), the Innovative Health Initiative, the Committee on

the Environment, Public Health and Food Safety (ENVI) Agencies and Member State funding agencies to propose and issue calls to establish research collaborations:

    - Coordinated assessment of requests for EMA involvement in 30 consortia.
    - Published research and evaluation of the impact of pharmacovigilance and risk management planning;
    - Completed study of the experience of the European Medicines Agency with involvement in multi-stakeholder regulatory science research projects based on semi-structured interviews with staff members and project coordinators submitted for publication.

- EU-IN continues to promote the implementation of STARS recommendations, including encouraging early interaction with researchers / developers (facilitated by national innovation offices or the EMA's ITF) as well as highlighting the availability of other regulatory supports.
- Regular engagement between the EU-IN and stakeholders:
    - The EU-IN and AEMPS organized a multi-stakeholder meeting, under the Spanish EU-Presidency, to promote research and development of innovative medicines and related technologies and methodologies in the EU;
    - In November 2023 the HPRA hosted an EU-IN network conference aimed at strengthening life-sciences innovation across Europe with a particular emphasis on the roles of incubators, technology transfer officers and funders.

In progress

- Continue to progress workplans of relevant groups (EMA SPD and EU-IN).
- The integrated pathways project will promote interaction with stakeholders regarding the regulatory requirements of complex products.

Antimicrobial resistance and other emerging health threats

"Maintaining therapeutic options in human and veterinary medicine is the important goal in the fight against antimicrobial resistance. Measures such as collecting data on sales and use of antimicrobials in veterinary medicine is an important step forward. Improved monitoring of antimicrobial consumption will be a catalyst for identifying further potentials and for measuring the success of implemented actions against the spread of antibiotic resistance."

Thomas Heberer, Head of Division 3 of Veterinary Medicinal Products, German Federal Office of Consumer Protection and Food Safety (BVL), Germany, HMA

"The learnings coming from the COVID -19 pandemic need to be taken up to ensure we are proactively engaging to tackle the growing problem of AMR, often called the silent pandemic, but in actual fact not silent at all and already now of significant concern."

Marco Cavaleri, Head of Health Threats and Vaccines Strategy Taskforce, EMA

Goal 1

Provide high quality information on antimicrobial consumption and surveillance data on antimicrobial resistance.

Objectives

- Implement the requirements for the mandatory collection of sales and use data for antimicrobials used in animals, spread knowledge and ensure better access to data in line with the veterinary medicines regulation.
- Foster more robust surveillance systems in the EU for both antimicrobial consumption and emergence of resistance in veterinary and human medicine in order to foster analyses of the

potential relationships between antimicrobial consumption and AMR and of coselection of AMR by use of biocides and feed additives.

Achievements

- EMA provided scientific advice for the following, with the input of experts nominated by HMA:
    - Commission Delegated Regulation (EU) 2021/578 on requirements for the collection of data on the volume of sales and on the use of antimicrobial medicinal products in animals, and
    - Commission Implementing Regulation (EU) 2022/209 establishing the format of the data to be collected and reported on volume of sales and on use of antimicrobial medicinal products in animals.
- At the Agency, the IT development of the Antimicrobial Sales and Use (ASU) data system has been progressed with the input of Member States' experts from design, to building and testing, and is on track to receive Member States' data in 2024, implementing the legal requirements in line with the legal timelines and deliverables. This was supported by a change liaison programme to support Member States in their transition, while Member States progressed the implementation of their national systems for collecting antimicrobial sales and use data. EMA's IT system development is on track.
- Supporting materials like the manual for reporting data to the EMA for Member States for antimicrobial use data reporting per animal category (EMA/757638/2021) and the guideline on indicators and denominators (EMA/CVMP/882931/2022) were developed, with the latter finalised and published in October 2023.
- The European Sales and Use of Antimicrobials in veterinary medicine Working Group (ESUAvet WG) was established in 2023 to advise EMA on technical aspects, the Member States on operational aspects and CVMP on scientific aspects related to collection, analysis and reporting of antimicrobial sales and use data. This body is also the mechanism for future Member State approval of Agency reports on sales and use of antimicrobials in veterinary medicine.
- At Member State level, the HMA Working Group on the "implementation of use data collection by animal species" provides guidance to all veterinary NCAs on the transfer of data, ensuring data quality management, and on communication. The data reporting systems of some Member States were presented and discussed, most recently by Spain, Germany and France.

In progress

- At Member State level further MSs will present their national collection systems for sales and use data for antimicrobials in animals in order to allow comparisons to be made.
- Further discussion on defined daily doses for animals (DDDvet) and defined course doses for animals (DCDvet), zero reports, detection of outliers, and compliance will be addressed within the HMA work package 1 and the ESUAvet Working Group.
- Use the DARWIN EU real world data plan to monitor prescribing of antibiotics in humans, and consumption of antibiotics and performance in different patient populations.

Goal 2

Contribute to responsible use of antimicrobials and effective regulatory antimicrobial stewardship.

Objectives

- Modernise the summaries of product characteristics (SmPC) of old antibiotics for human and veterinary use.
- Define a roadmap for point-of-care (POC) diagnostics to support the development of improved diagnostic tests.

Achievements

- Restart of Article 31 referrals for old antibiotics approved for use in humans in 2023 after a pause due to the COVID pandemic.
- For human medicinal products, migration of antibiotics and antifungals susceptibility criteria from the SmPC to the EMA website, updated in real time and available to healthcare practitioners throughout the EU.
- On the veterinary side, a concept paper on the development of a reflection paper on the availability and characteristics of diagnostic tests to improve the responsible use of antibiotics in animals was adopted for publication in July 2023.
- A Reflection Paper on dose review and adjustment of established veterinary antibiotics in the context of SmPC harmonisation published in 2021.
- As part of the implementation of Regulation (EU) 2019/6, the following achievements of the Agency with the support of Member States' experts contributed to responsible use of antibacterials and effective regulatory antimicrobial stewardship:
    - Agency advice on legislation definitioning criteria for the designation of antimicrobials to be reserved for human use (Commission Delegated Regulation (EU) 2021/1760) and on recommendations for inclusion of medicines in a list of antimicrobials reserved for human use (Commission Implementing Regulation (EU) 2022/1255);
    - Agency advice on a list of antimicrobials not to be used in accordance with Articles 112, 113 and 114 of Regulation (EU) 2019/6 or only to be used according to these articles under certain conditions.

In progress

- Start of internal and external discussion on potentially considering AMR-related diagnostics as high risk (category 4).
- On the veterinary side, in follow-up to the above-mentioned reflection paper on dose review, stakeholder surveys have been prepared to obtain relevant feedback.

Goal 3

Ensure regulatory tools are available that guarantee therapeutic options while minimising impact of antimicrobial resistance on public health and the environment

Objectives

- Promote guidance on antimicrobial use by adapting existing and creating new guidelines and finalise the Agency approach to antimicrobial resistance in the environment.

Achievements

- A high-level One Health AMR meeting took place on 18 and 19 October 2023 to address these issues under the Spanish Presidency of the EU.
- A joint EMA/HMA AMR workshop was held as on October 18 at the high-level meeting of the Spanish Presidency of the EU.
- Building on the updated advice on the impact on public health and animal health of the use of antibiotics in animals (categorisation of antimicrobials), EMA published a concise infographic in all official EU languages to help guide veterinarians in clinical decision making.
- Cooperation with other stringent regulators at the Transatlantic Taskforce on AMR (TATFAR) and within a quarterly dedicated cluster (involving EMA, FDA, HC, PMDA) in which a number of important aspects are discussed, including AMR relevant new drug developments (in terms of regulatory expectations).
- Other guidelines, human and veterinary, were progressed by the Agency, with concept papers developed and released for consultation and feedback taken into account during ongoing guideline development:
    - Guideline on the assessment of the risk to public health from antimicrobial resistance due to the use of an antimicrobial veterinary medicinal product in food-producing animals;
    - 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;
    - Guideline on data requirements for post-authorisation studies for antimicrobial veterinary medicinal products under Article 36(2) of Regulation (EU) 2019/6;
    - Update of the Guideline on the clinical evaluation of antifungal agents for the treatment and prophylaxis of invasive fungal disease (CHMP/EWP/1343/01 Rev. 1).
- Communication on available tools, like AMEG categorisation, to stakeholders to ensure proper implementation in cooperation with Working Group on Communication Professionals:
    - Webinar on EMA's categorisation of antibiotics used in animals (23/06/2021);

- Activities to streamline the different communication activities in the medicines agencies network (e.g. for the annual World Antimicrobial Awareness Week).

In progress

- The Agency progressed the finalisation of its approach to antimicrobial resistance in the environment. Building on the "Reflection paper on antimicrobial resistance in the environment: considerations for current and future risk assessment of veterinary medicinal products", a concept paper for a guideline is under development.

Goal 4

Define pull incentives for new and old antimicrobial agents.

Objectives

- Define value of new antimicrobial agents to inform new business models and cooperate in the establishment of new business models, including the exploration of incentives for continuous manufacturing of old antibiotics in the European medicines agencies network strategy to 2025.

Achievements

- Technical ongoing work with DG SANTE and DG HERA on the proposed pull incentives.
- In light of the proposed draft revision of the pharmaceutical legislation , many aspects of strategic goal 4.4 were incorporated into the new draft legislation.
- Discussion on pros and cons of different business models in the context of TATFAR and Member States' initiatives such as such as European Union Joint Action on AMR and Healthcare-Associated Infections (JAMRAI).

Goal 5

Foster dialogue with developers of new antimicrobial agents and alternatives to traditional antimicrobials.

Objectives

- Foster development of new antimicrobials, including new antibacterials for human use, define regulatory pathways for phages and other innovative products in human and veterinary medicine and engage with relevant stakeholders to discuss the issue effectively.

Achievements

- AMR is a focus area for the EU network, with high level meetings bringing stakeholders together and focusing on the issues including discussions on innovation and alternatives. AMR was also a main topic at the HMA II meeting in Uppsala and several other meetings.
- EMA contributed to a 2022 OECD briefing note Antimicrobial-Resistance-in-the-EU-EEA-A-One-Health-Response-March-2022
- EMA participation at the policy brief 'How can the EU support sustainable innovation and access to effective antibiotics?' produced by the European Observatory for and with the Swedish Presidency of the Council of the EU.
- For the discussion of these issues in a global context the Regulatory Agencies Global Network against AMR (RAGNA) was initiated by the Swedish Presidency (MPA) in cooperation with WHO in June 2023.
- Regulatory cluster teleconferences on bacteriophages for human use have started and progressed to the proposal for a working group within TATFAR. A workshop will be organised next year. Mapping of clinical research and support via funded research will be explored.
- Multiple guidelines and other guidance have been developed:
    - A concept paper on quality, safety and efficacy of bacteriophages as veterinary medicines was published for consultation in 2022, with the draft guideline on quality, safety and efficacy of veterinary medicinal products specifically designed for phage therapy having been released for public consultation in the first half of 2023; publication of the final guideline is anticipated for Q4 2023.
    - Guidance on vaccine platform technology master files (vPTMFs) (including guidelines and procedural advice).
    - Consultation on a draft reflection paper on application of Article 40(5) to incentivise product development and variations [for veterinary medicines] that reduce AMR.
    - Reflection paper on promoting the authorisation of alternatives to antimicrobial veterinary medicinal products.
- Promoting the use of available EMA regulatory tools to expedite antibacterial agent development and of alternative therapeutic approaches, which can be adapted if necessary. Examples include PRIME, Innovation Task Force (early dialogue with developers of medicines meeting unmet medical need), in general early dialogue with EMA.

In progress

- The future regulatory pathways have started to be discussed in connection with the new pharmaceutical legislation for medicines for human use, keeping the veterinary side involved.
- Workshop on bacteriophages with FDA in preparation for 2024

Goal 6

Improve regulatory preparedness for emerging health threats.

Objectives

- Refine regulatory activities between epidemics to increase preparedness and harmonise regulatory framework and approaches for investigation of medicinal products during emergencies.

Achievements

- With the reinforced role of the Agency (in line with Regulation (EU) 2022/123), the now permanent Emergency Task Force (ETF) was established. This task force is also governed by activities under the strategic goal 6, Sustainability of the Network and operational excellence, and the achievements are reported there.

Supply chain challenges

"Following the COVID-19 public health emergency, many challenges (e.g. geopolitical) continue to put pressure on the European supply chain due to multifactorial causes as scarcity of specific materials or demand for innovative and specific medicines. Improving security of supply chain is a European priority and the way forward is to enhance traceability of medicines in all the circuit, building inspector capacity and reinforce product quality by harmonising guidance."

Rui Santos Ivo, Executive Director of the Portuguese National Authority Of Medicines And Health Products (INFARMED), HMA

"Ensuring supply chain resilience remains a key area of focus for EMA and the regulatory Network. Traceability and oversight have been strengthened via increased use of IT systems, contribution to building inspector capacity, and strengthened good distribution practice (GDP) requirements for veterinary medicinal products via the New Veterinary Regulation. We continue to focus on promoting understanding and compliance with GMP requirements, including looking to the future to ensure innovative and advanced manufacturing is facilitated via the Quality Innovation Group."

Brendan Cuddy, Lead Scientific Officer and GMDP IWG Chair, EMA

Goal 1

Enhance traceability, oversight and security in the human/veterinary medicine supply chain from manufacturing to importation and final use of active pharmaceutical ingredients (APIs) and excipients.

Objectives

- Improve and inter-link information in current/existing databases to provide supply chain compliance overview.

- Tackle falsified medicines; prevent presence of falsified medicines in the supply chain by strengthening inspections of manufacturers' application of safety features and of the repository systems.

Achievements

- The EudraGMDP database was integrated with the Organisational Management System (OMS) so that there is only a single controlled version of the name and address of manufacturers, importers and distributors of medicines for human and veterinary use, improving the quality of supply chain compliance information available.
- The implementation of the objective to provide a supply chain compliance overview has also been linked with the work on shortages (as the latter may also require a rapid analysis of the manufacturing sites of products affected by shortages). This is intended to develop a European concept model to monitor and manage medicines shortages, taking into consideration existing tools/good practices developed at EU MS level in order to achieve an efficient merging of the available systems and information sources of MSs with an inclusive approach. (See Theme 1 in page 6 on Availability and Accessibility of medicines).
- Progress includes a report on a SWOT analysis of the current state of IT solutions in the EU and Member States.. Main findings include as weaknesses missing information on stocks and demand as well as forecasts and production plans. This would also create as a threat a tremendous workload if automated data submission cannot be established to address this issue, a high workload could be created. It is therefore essential that PMS data are in place for automated data submission. How far this approach will be supportive to enhance the visibility of the supply chains at medicinal product level has to be taken into account in the further development of the concept.
- WP 7 has also been progressing in development of identification of best practice solutions and minimum common datasets by making a survey to collect information from the Member States existing systems related to shortage situations. This survey also included technical questions for a complete overview of the multitude of different systems (e.g. service portals, platforms and networks). A report has been written from the results of the survey.
- CHESSMEN aims to support Member States to provide a harmonized response to mitigate medicines shortages and to contribute to an appropriate and timely availability of medicinal products. The project has the participation of 22 EU/EEA Member States. Successes included the kick-off meeting and several meetings of the Project Management Board.
- The strengthening of inspectorate capacities has been taken up within the Joint Action EU4H 11 included in the EU4Health Programme funded by the European Commission. The Joint Action EU4H 11 aims at strengthening capacities of EEA GMP/GDP inspectorates with respect to Good Distribution Practice. It has proceeded along 4 key action areas identified in the network strategy:
    - Strengthening the Joint Audit Programme (JAP) for EEA GMP inspectorates: The Joint Action EU4H 11 has started work on optimising training and qualification processes for auditors as well as the JAP procedure. Furthermore, the co-financing of costs related to JAP activities supports member states' participation in the Joint Audit Programme.
    - Two training sessions performed in March 2022 and October 2023 related to JAP audits for training of JAP auditors.

- Reviewing the national implementation of the European GDP legislation and guidelines and developing a proposal to add GDP to the existing Joint Audit Programme. By promoting collaboration between EEA GDP inspectorates, the Joint Action will strengthen the EEA GDP inspectorates network and work towards a harmonization of GDP inspections standards.
- Strengthening /EEA inspectors' capacities by establishing harmonised training and qualification processes for GMP inspectors, in cooperation with the PIC/S Inspectorates' Academy.

- The entry into force of Regulation (EU) 2019/6 on veterinary medicinal products has extended Good Distribution Practice to veterinary medicines and active substances used in veterinary medicine. Scientific advice providing the principles of GDP to be incorporated into these implementing acts was adopted through the GMP/GDP Inspectors Working Group (GMDP IWG) and the CVMP. The GMDP IWG has developed the template for the Wholesale Distributors Authorisation for Veterinary Medicine for use by EU authorities.
- Strengthening the supply chain also focuses on the co-operation and reliance with partner authorities on the inspection of API manufacturers that is ongoing through the API Programme and the inspection of third country manufacturers of medicinal products through the establishment of a new pilot programme evaluating and relying upon inspection reports of PIC/s authorities for GMP verification, that began in October 2022.

In progress

- Work has started on the Product Management Service (PMS) which will make available product data on all authorised medicinal products in the EU, including both CAPs and NAPs, in ISO IDMP-compatible format. Once this data intake is complete, PMS will inter-link the manufacturers of APIs and Finished Products (FP) for all products in the EU.

Goal 2

Enhance inspector capacity building at EU and international level.

Objectives

- Enhance capacity building of EU inspectors and assessors in order to harmonise approaches to regulatory inspections procedures to address requirements and challenges of APIs, medicinal products, excipients, new technologies and continuous manufacturing.
- Promote a more tailored supervision of API manufacturers through assessment and inspection of their API development and risk management practices in technology transfer; increase supervision of sites that produce medicinal products for a significant number of EEA markets or very significant numbers of products, with dedicated cooperative supervision between MSs and strategic partners for these sites.

Achievements

- Building inspector capacity:
    - A first GMDP IWG inspector training strategy was drafted and adopted by the GMDP IWG.
    - Funding was secured through EU NCT to cover trainee inspector participation at inspector training events held in the EU.
    - A pilot programme of joint inspector training visits initiated through GMDP IWG has been accepted for funding through EU4Health JA No. 11.
    - Securing inspector training on the new GMP Annex 1 through PIC/s. A series of training videos covering the main changes introduced with the new version of Annex 1 has been prepared and has been made available through PIC/s. A follow up survey confirm future topics for GMP inspectors training on Annex 1 was completed.
- A risk-based tool on pre-approval API inspections was developed and discussed at the GMDP IWG. It was agreed to pause this work until 2025 and the publication of the new pharma legislation that will provide a legal basis for risk-based inspection of API manufacturers.

Goal 3

Reinforce the responsibility for product quality by harmonising and reinforcing guidance.

Objectives

- Develop EU level data integrity guidance.
- Ensure a stable EU-GMP regulatory framework with predictable outcomes by promoting and improving the understanding of EU GMP requirements and preparedness by third country manufacturers and their supervisory authorities. Foster an environmentally friendly level playing field.

Achievements

- Providing sustainable harmonised GMP guidance:
    - Developing through GMDP IWG scientific advice for GMP implementing acts for veterinary medicines and active substances that evaluates the proposed extension of environmental measures to Good Manufacturing Practice.
    - New Annex 1 "Manufacture Of Sterile Medicinal Products" and Annex 21 "Importation of Medicinal Products" were published in 2022. Annex 1 entered into force in August 2023 and Annex 21 entered into force in August 2022.

https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-4_en.

- A concept paper to revise Annex 11 incorporating existing data integrity guidance questions and answers was published November 2022

  https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/concept-paper-revision-annex-11-guidelines-good-manufacturing-practice-medicinal-products-computerised-systems_en.pdf

Goal 4

Encourage supply chain resilience and review long-term risks resulting from dependency on limited number of manufacturers and sites.

Objectives

- Enhance the reliability of evidence available to regulators for informing the decision-making process on the supply chain and promote supply chain resilience and reliability of supply of APIs and medicinal products.

Work on this objective is pending and will be reviewed as part of the EMANS update.

Goal 5

Analyse the possible implications of new manufacturing technologies and adapt the regulatory framework to accommodate innovation in manufacturing and distribution.

Objectives

- Analyse the regulatory system with respect to new technologies and new tools used in manufacturing and in supply chain management and control; identify opportunities to improve supply chain resilience.

Achievements

- For achievements on this objective, please refer to section on Innovation, in particular achievements under the Quality Innovation Group.

Sustainability of the Network and operational excellence

"The new fee regulation will ensure the financial sustainability of the Network and EMA. This is essential to address the ongoing challenge of maintaining sufficient capacity and capabilities for the evaluation of innovative medicines, while also ensuring preparedness for health and animal emergencies."

Runa Hauksdottir Hvannberg, Executive Director of Icelandic Medicines Agency (IMA), HMA

"The shift towards the new Agile governance, the modernization, and consolidation of IT systems serve as the foundation for an integrated and streamlined IT landscape facilitating the exchange of data, processes, and technology within the European Medicines Regulatory Network. These initiatives, coupled with the new legislative framework for human medicines represent the principal catalysts for achieving operational excellence."

Hilmar Hamann, Head of Information Management Division, EMA

Goal 1

Reinforce scientific and regulatory capacity and capability of the network.

Objectives

- Ensure 'fit-for-purpose' scientific capability of the network.
- Prepare for and implement the veterinary medicines Regulation.

Achievements

- INCREASEnet Joint Action has been approved and NCAs will have significant role in delivering on this.
- Remuneration for training providers has been approved by EMA's management board.
- Additional project leader onboarded and toolkit for making online courses is being rolled out.
- Implementation of a new expertise-based governance model for working parties of CHMP to optimise the use of available expertise in the network. The new model fosters harmonised best practices in the management of the working parties and groups in order to deliver the strategic, tactical and operational goals.

Achievements to date related to the network portfolio

- EMA has implemented and continues to embed Agile delivery practices in digital transformation to bring greater flexibility, transparency and efficiency to network portfolio delivery. This approach also aims to strengthen alignment of the delivery of the network portfolio with wider strategic digital transformation initiatives. EMA established a Lean Agile Centre of Excellence (LACE) in January 2023 to further mature and evolve the Agile ways of working, to optimise delivery.
- Launch of the first version of the web-based electronic application forms (eAF) for variations to human medicines and for centrally authorised products (CAPs) in November 2022. This is an important step towards more data-driven and digitally enabled regulatory management.
- Delivery of good clinical practices (GCP) and good pharmacovigilance practices (GVP) inspections management on the IRIS regulatory procedure management platform. This brings efficiencies and a modernised and collaborative way of working.
- Implementation of iSPOC registration for the identification of focus points of contact during public health emergencies (PHE) and major events (ME) in support of medicine shortages Regulation ((Regulation (EU) 2022/123).
- Implementation of the Veterinary Union Product Database (UPD), serving as a single source of information on all authorised veterinary medicines and their availability in European Union (EU) and European Economic Area (EEA) Member States. UPD is required by the Veterinary Medicines Regulation (Regulation (EU) 2019/6), which became applicable on 28 January 2022.
- Delivery of new capabilities to support the management of experts working with EMA (Experts Management Tool).
- Delivery of a collaboration tool for expert panels for medical devices (EXPAMED), in support of the Agency's extended mandate related to medical devices.
- Development of the EU standard for electronic product information (ePI) and pilot capabilities for the authoring and publication of ePI for centralised and nationally authorised products in the EU. A pilot has started for a set of CAPs and NAPs to test the business process and develop guidance for inclusion of ePI in regulatory procedures.
- Further implemented IDMP standards in PMS, an essential foundation for high quality shared data across the EMRN.

- Delivered enhancements to the Common Repository, including improved security features, a key system in the evaluation and assessment process.

In progress

- Network portfolio workplan is being rolled out based on 5 value streams.
- Pilot for direct payment by EMA to external experts to be part of the assessment teams of rapporteurs.
- The HMA-EMA strategic resource oversight group is considering general actions to address the network capacity constraints by increased oversight of capacity andcapability of the NCAs to undertake upcoming workload and specific actions for identified shortfalls.

Goal 2

Strive for operational excellence, building on the work done in the current strategy.

Objectives

- Optimise the current regulatory framework by ensuring efficiency of the existing regulatory operations.
- Introduce governance and IT process improvements to further professionalise prioritising, budgeting, securing, provisioning and running of technology services.

Achievements

- Regulatory optimisation of mutual recognition procedure (MRP) and the decentralised procedure (DCP) for human and veterinary medicines is ongoing with CMDh/v, and IT projects are running.
- In the centralised procedure there are some ongoing activites on optimisation. Establishment of an EMA/NCA/industry focus group to streamline the management of assessment reports during the evaluation process of CAPs.
- Benchmarking of medicines agencies (BEMA) exercise of NCAs and EMA has been conducted in Q1-Q2 2023 to identify strengths, best practices and any opportunities for improvement in the agencies. The results are stored in a central database which serves as a tool to share best practices across the network.
- Regulatory Optimisation Group (ROG) activities were reactivated during 1H 2023. ROG provided strategic input to Network Portfolio Advisory Group, the HMA/EMA tactical group on resourcing and Veterinary Strategy focus group.
- Transition to Agile governance and delivery is complete.

- Network representation in Agile product teams: POs from Austria, Germany, Slovenia and Spain are very active, as well as representatives from Denmark, Germany (4), the Netherlands (3), Portugal and Sweden (3) in the role of SMEs.
- The rapporteurship bidding model has been reviewed with involvement of the HMA EMA Operational Resource Planning and Oversight Group. The new model fosters collaboration within the network in situations of resource constraints.

In progress

- A pilot project on the roll out of the new templates for asssessment reports for ther evaluation of human CAPs was launched in Q3 2023 to optimise working practices in the assessment process.
- Network portfolio workplan is being rolled out based on 5 value streams.

Goal 3

Achieve a sustainable financial and governance model for the network.

Objectives

- Contribute to the revision of the current fee regulation, and implement the final legislation.

Achievements

- On 25 September 2023, the Council and European Parliament reached a provisional agreement on the fee regulation. The text is undergoing final legal and linguistic checks prior to publication in the Official Journal. The new cost-based fee regulation will provide financial sustainability for the Agency and the network while providing administrative simplification based on a leaner fee structure.

In progress

- EMA is adapting internal processes and systems for implementation of the new fee regulation by 1 January 2025.

Goal 4

Develop a digital strategy to drive digital business transformation.

Objectives

- Establish an IT operating model and services, in support of the digital strategy and digital business transformation.

Achievements

- The Agency has continued to deliver on experimentation and automation through its Analytics Centre of Excellence (ACE) and Digital Innovation Lab (DigiLab) (see section on data analytics, digital tools and digital transformation).

In progress

- EMA expects to release the eAF for non-centralised procedures in 2024 and further develop other application forms for initial marketing applications, veterinary variations and renewals, enabling end-to-end data flows for greater accuracy, efficiency and accessibility of information and data across the product lifecycle.
- Delivery of the Product Management Service (PMS), as the central EMA source of data on all CAP and NAP products authorised in the European Union and the further integration of PMS data into product lifecycle tools and processes.
- Delivery of the Critical Medical Shortage IT System 'minimum viable product' (MVP) as an additional measure to ensure a reinforced union-level framework for monitoring and reporting shortages of critical medical devices during the crisis, related to Regulation (EU) 2022/123.
- In accordance with the Veterinary Medicinal Product Regulation (EU) 2019/6, delivery of the minimal viable product (MVP) for the Union Product Database (UPD) and the Union Pharmacovigilance Database for Veterinary Medicines.
- In accordance with the Veterinary Medicinal Product Regulation (EU) 2019/6, delivery of antimicrobials sales and use that will allow EU/EEA member states to submit data on sales and use of antimicrobials in animals, enabling data intelligence to detect patterns and help develop measures against AMR.
- Development and delivery of modern and collaborative technology for document and records management at EMA to replace technology currently used (DREAM/MMD) and technology in support of access-to-documents and request-for-information (ASK EMA) processes.

- Development of the eCTD v4.0 specification and implementation guide for the EU region and implementation of technology to enable adoption of the standard. eCTD v4.0 works towards international alignment of regulatory submissions standards and brings efficiencies.
- Launch of new regulatory procedure management capabilities in IRIS, the Agency's regulatory procedure management platform, for variations, Article 61.3 procedures and transfers of marketing authorisations – a major step in data-driven network digitalisation.
- Launch of a new product data management interface to allow industry and regulators to view product data held by EMA in Product Management Service (PMS) and work towards a simplified user journey and data management workflow, a major step towards increased data quality and enrichment and a step towards replacement of legacy systems, such as XEVMPD.
- Availability of an API to allow regulators and industry to connect to PMS to access data, a step towards increased data quality, enrichment and harmonisation.

Goal 5

Enable quick, consistent and adequate response to public and animal health challenges.

Objectives

- Build further capacity and capability within the network to support crisis management.

Achievements

- Joint meetings of the HMA Working Group on Crisis Management Affairs, Multi Annual Work Programme (MAWP), Working Group on Communication Professionals (WGCP), Working Group of Quality Managers (WGQM), Clinical Trial Coordination Group (CTCG) and World Green Economy Organization (WGEO) were held in April and July 2023.
- Establishment of the EU Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG) (also mentioned in under Availability and accessibility of medicines):
    - The MSSG has met 17 times since it was set up in March 2022.
    - The MSSG has adopted the list of main therapeutic groups, the list of critical products for two public health emergencies (COVID19 and monkeypox) and monitored their supply and demand.
    - For preparedness activities the MSSG has monitored critical shortages (thrombolytics, antibiotics, energy crisis among others).
- The MSSG has published a toolkit of recommendations that can be used in crisis (either a public health emergency or major event) or for critical shortages.

- The MSSG developed the voluntary solidarity mechanism which allows Member States to request assistance in obtaining stocks of a medicine during critical shortages from other Member States through the MSSG. This mechanism should be used only under very limited conditions and when Member States have exhausted other possibilities. The process for requesting support was published on EMA's website on 24 October 2023. For further information on the solidarity mechanism please refer to the following webpage: https://www.ema.europa.eu/en/about-us/what-we-do/crisis-preparedness-management/executive-steering-group-shortages-medicinal-products
- Establishment of the ETF in March 2022 with initial focus on emergency operations of COVID-19 and MPox and shifting into preparedness activities of public health threats following the end of the public health emergencies.
    - The ETF has regularly engaged with developers and provided scientific advice on medicines that could address a public health emergency.
    - The EMA emerging health threats plan was updated in Feb 2023.
    - EMA transparency measures for medicines addressing public health emergencies published in Jan 2023
    - The ETF's role in preparedness has been established. Scientific advice procedures have been progressed in several areas related to health threats.
    - Regulatory review of the evidence of medical countermeasure products to support HERA and MSs in stockpiling and joint procurement have started.
    - Collaboration with EU and MSs bodies related to chemical, biological, radiological and nuclear (CBRN) risk mitigation has progressed. A workshop with EU consortia such as Counteract has been held at EMA.
    - A Workshop on clinical trials during public health emergencies has been held at EMA leading to the creation of a proposal for a coordinating committee to prioritise studies and funding for CTs during emergencies and in peace time. It has also led to the addition of a priority action for clinical trials during emergencies in ACT EU.
    - A workshop on generating clinical evidence for treatment and prevention of Long-COVID was hosted by EMA with the inclusion of patients representatives, clinicians and international stakeholders.
- The COVID-19 Lessons Learned report was published on 1 December 2023.

In progress

- A Working Group of the MSSG was set up by EMA in September 2022 to advise on implementing the ESMP. The ESMP WG is responsible for developing the technical and functional specifications of the ESMP, including a data exchange mechanism with national systems and the data format for electronic submission, and to coordinate with the Joint Action on medicine shortages.
- Review of EU guidelines related to COVID-19, vaccines and other emergency health threats.

Conclusions and next steps

As outlined in the introduction, this report was prepared to provide an overview of the main achievements from January 2021 to June 2023, structured according to the strategic goals presented in the original EMANS strategy for the period up to 2025.

Upon the establishment of the EMANS strategy for 2025, stakeholders expressed concerns about whether the Agency and the network had sufficient resources to carry it out, and this concern arose even before the COVID-19 pandemic impacted the system. What is noteworthy about this report is the reflection on the actual achievements during this exceptionally challenging period for the European medicines regulatory network and the extent to which the strategic goals and underlying objectives have progressed. Instead of hindering progress, the COVID-19 pandemic seems to have acted as a catalyst for transformative changes in the European system, enabling these parallel developments to occur.

Despite this notable progress, the work must and will continue vigorously up to 2025 to fully realise the strategic objectives. As 2023 marks the third year of the COVID-19 pandemic, the EMA and the network will gradually transition from its business continuity mode and shift its focus even more towards addressing the strategic goals outlined in the EMANS to 2025 during the remaining 2023-2025 period.

It is imperative that we achieve this objective by further enhancing the network's operational capacity, building on substantial investments in digital transformation and innovation and preparing to adapt to and benefit from anticipated legislative changes in the coming years.

Glossary

3Rs	Principles relating to the use of animals in medicines testing (Refine testing to reduce the harm to the animal, Reduce the numbers of animals required, Replace animal testing wherever and whenever it is possible)
AI	Artificial Intelligence
ACE	Analytics Centre of Excellence
ACT EU	Accelerating Clinical Trials in the EU (ACT EU)
AEMPS	The Spanish Agency for Medicines and Health Products
AMR	Antimicrobial resistance
API	Active pharmaceutical ingredient
AR	Assessment report
ATMP	Advanced therapy medicinal product
BDSG	Big Data Steering Group
BfArM	Federal Institute for Drugs and Medical Devices Germany
BPM	Business Pipeline Meetings
CAP	Centrally authorised procedures
CDC	Centres for Disease Control and Prevention (USA)
CHMP	EMA' Committee for Medicinal Products for Human Use
CMDh	EMA's Coordination Group for Mutual Recognition and Decentralised Procedures
COMP	EMA's Committee for Orphan Medicinal Products
CT	Clinical trial
CTA	Clinical Trial Application
CTIS	Clinical Trial Information System
CTCG	Clinical Trials Coordination Group
CTR	Clinical Trial Regulation
CVMP	EMA's Committee for Veterinary Medicinal Products
DARWIN EU	Data Analysis and Real World Interrogation Network, a proposed EU platform to access and analyse healthcare data from across the European Union
DDD/DCDvet	Defined daily doses for animals and defined course doses for animals
DG CONNECT	European Commission Directorate General for Communications Networks, Content and Technology
DG RTD	European Commission Directorate General for Research and Innovation

DG SANTE	European Commission Directorate General for Health and Food Safety
DIA Europe	Drug Information Association
DigiLab	EMA's Digital Innovation Lab
DKMA	Danish Medicines Agency
eAF	Electronic application form
EATRIS	European Infrastructure for Translational Research
EC	European Commission
ECDC	The European Centre for Disease Prevention and Control
ECRIN	European Clinical Research Infrastructure Network
EEA	European Economic Area
EFSA	European Food Safety Authority
EHDS	European Health Data Space
eHR	Electronic health record
EIC	European Innovation Council
EMA	European Medicines Agency
EMANs	European Medicines Agencies Network Strategies
EMRN	European Medicines Regulatory Network, the Network
ENVI	European Parliament Committee on the Environment, Public Health and Food safety
ePI	Electronic product information
ESEC	European Specialist Expert Community
ETF	Emergency Task Force
EU	European Union
EU-IN	EU-Innovation Network. A collaboration between the EU NCAs and EMA, aimed at fostering medicine innovation and early development of new medicines
EUnetHTA	European Network for Health Technology Assessment. A collaboration between HTA bodies across Europe
EURIPID	European medicine price database
FDA	Food and Drug Administration (USA)
GCP	Good Clinical Practise
GDP	Good Distribution Practise
GMDP IWG	GMP/GDP Inspectors Working Group
GMP	Good Manufacturing Practise
GVP	Good pharmacovigilance practices

Health Canada	Health Canada, under the direction of the Health Minister, is the ministry responsible for overseeing Canada's healthcare, including its public policies and implementations.
HERA	Health Emergency Preparedness and Response
HMA	Heads of Medicines Agencies
HS	Horizon scanning
HTA	Health Technology Assessment body
HTA CG	HTA Coordination Group
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICMRA	International Coalition of Medicines Regulatory Authorities
IDMP	Identification of Medicinal Products, a suite of standards developed by ISO
IHI	Innovative Health Initiative
IHSI	International Horizon Scanning Initiative
INFARMED	National Authority of Medicines and Health Products Portugal
IRIS	EMA’s online Regulatory and Scientific Information Management Platform
ISO	International Organization for Standardization
iSPOC	Industry Single Points of Contact
IT	Information Technology
ITF	Innovation Task Force
JA CHESSMEN	Joint Action on Coordination and Harmonisation of the Existing Systems against Shortages of Medicines
JAMRAI	European Union Joint Action on AMR and Healthcare-Associated Infections
JRC	Joint Research Centre
KPIs	Key performance indicators
LACE	Lean Agile Centre of Excellence
LMS	Learning management system
ME	Major Event
MDCG	Medical Devices Coordination Group
MDR	EU Medical Device Regulation (2017/745)
MEB	Medicines Evaluation Board
MLS	Reflection paper on the use of macrolides, lincosamides and streptogramins

MRLs	Maximum residue limits
MRP	Mutual Recognition Procedure
MS	Member State of the European Union
MSSG	Executive Steering Group on Shortages and Safety of Medicinal Products
MVP	Minimum Viable Product
NAP	Nationally authorised procedure
NBCG	Notified Body Coordination Group
NCA	National competent authority, one of the national medicines regulators that form part of the Network
NGOs	Non-government organisations
NTC	Network Training Centre
OECD	Organisation for Economic Co-operation and Development
PA	Priority Action
PCWP/HCPWP	EMA's Patients and Consumers Working Party and Health Care Professionals Working Party
PED	Patient Experience Data
PEI	Federal Institute for Vaccines and Biomedicines Germany
PHE	Public Health Emergencies
PIC/S	Pharmaceutical Inspection Co-operation Scheme, an informal co-operative arrangement for regulators on Good Manufacturing Practice (GMP) of human and veterinary medicines
PMDA	Pharmaceuticals and Medical Devices Agency (Japan)
POC	Point of Care
PRAC	EMA's Pharmacovigilance Risk Assessment Committee
PRIME	Priority Medicines Scheme (EMA)
PQ KMS	Pharmaceutical Quality Knowledge Management System
Q&A	Questions and answers
QIG	Quality Innovation Group
QoNM	Qualification of Novel Methodologies
QR code	Quick response code
RAGNA	Regulatory Agencies Global Network against AMR
ROG	Regulatory Optimisation Group
R&D	Research & Development
RSS	Regulatory Science Strategy
RWE	Real World Evidence

SAP	System Applications and Products
Saudi FDA	Saudi Food and Drug Authority (Saudi Arabia)
SAWP	Scientific Advisory Working Party
SE/ES presidency	Swedish/Spanish Presidency of the Council of the European Union
SIP	Science and Innovation Panel
SME	Small to medium-sized enterprise
SMPA	Swedish Medical Products Agency
SNSA	Simultaneous National Scientific Advice (pilot project of the EU Innovation Network)
SPMP	Shortage Prevention and Mitigation Plan
SIRIA	Strategic research and innovation agenda
STARS	Strengthening Training of Academia in Regulatory Sciences, a project of the European Commission
TF AAM	Task Force on the Availability of Authorised Medicines
WGQM	Working Group of Quality Managers
WGEO	World Green Economy Organization
WHO	World Health Organization
WOAH	World Organisation for Animal Health
WP	Working Party

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